Indexed with IndMED
Indexed with MedIND
Indian Citation Index (ICI)

ISSN 0971-0876
RNI 50798/1990
University Grants Commission 20737/15554

IJCP
A Medical Communications Group
www.ijcpgroup.com

Indian JOURNAL of CLINICAL PRACTICE

A Multispecialty Journal

Volume 31, Number 11 April 2021, Pages 1001–1100 **Single Copy Rs. 300/-**

Peer Reviewed Journal

In this issue

Full text online: http://ebook.ijcpgroup.com/ijcp/
IJCP Publications | https://goo.gl/j2nXQQ

www.emedinexus.com

HealthPlus
Diagnostic & Imaging Centre

One Stop for All Diagnostics

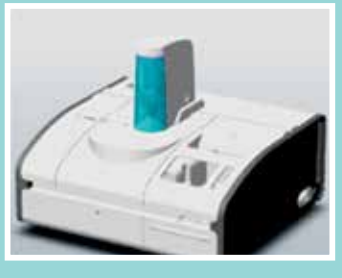
MRI
- Latest MRI by Siemens
- Ultra Short Magnet = No Claustrophobia
- 1st MRI in India on VC 15 Platform

CT Scan
- 16- Multislice Spiral CT
- Safest Scanner
- Least Radiation Dose

Health Packages
- Executive Health Check Up
- Risk Categories
- Age Based Health Packages

Fully Automated Digital Pathology Laboratory - NABL Accredited

Immunology



Biochemistry

Haematology

Special Tests

Contact Us

S-63 Greater Kailash Part 1
Opposite M Block Market, New Delhi 110048
Tel.: 011- 41234567

This journal is indexed in IndMED (http://indmed.nic.in) and full-text of articles are included in medIND databases (http://mednic.in) hosted by National Informatics Centre, New Delhi.

Indian JOURNAL of CLINICAL PRACTICE
A Multispecialty Journal
Volume 31, Number 11, April 2021

Published, Printed and Edited by
Dr KK Aggarwal, on behalf of
IJCP Publications Ltd. and
Published at
E - 219, Greater Kailash Part - 1
New Delhi - 110 048
E-mail: editorial@ijcp.com

Printed at
New Edge Communications Pvt. Ltd., New Delhi
E-mail: edgecommunication@gmail.com

Editorial Policies

The purpose of IJCP Academy of CME is to serve the medical profession and provide print continuing medical education as a part of their social commitment. The information and opinions presented in IJCP group publications reflect the views of the authors, not those of the journal, unless so stated. Advertising is accepted only if judged to be in harmony with the purpose of the journal; however, IJCP group reserves the right to reject any advertising at its sole discretion. Neither acceptance nor rejection constitutes an endorsement by IJCP group of a particular policy, product or procedure. We believe that readers need to be aware of any affiliation or financial relationship (employment, consultancies, stock ownership, honoraria, etc.) between an author and any organization or entity that has a direct financial interest in the subject matter or materials the author is writing about. We inform the reader of any pertinent relationships disclosed. A disclosure statement, where appropriate, is published at the end of the relevant article.

Note: Indian Journal of Clinical Practice does not guarantee, directly or indirectly, the quality or efficacy of any product or service described in the advertisements or other material which is commercial in nature in this issue.

IJCP's EDITORIAL & BUSINESS OFFICES

Delhi	Mumbai	Bangalore	Chennai	Hyderabad
Dr Veena Aggarwal 9811036687 E - 219, Greater Kailash, Part - I, New Delhi - 110 048 Cont.: 011-40587513 editorial@ijcp.com drveenaijcp@gmail.com **Subscription** Dinesh: 9891272006 subscribe@ijcp.com	Mr Nilesh Aggarwal 9818421222 Unit No: 210, 2nd Floor, Shreepal Complex Suren Road, Near Cine Magic Cinema Andheri (East) Mumbai - 400 093 nilesh.ijcp@gmail.com	H Chandrashekar **GM Sales & Marketing** 9845232974 11, 2nd Cross, Nanjappa Garden Doddaiah Layout Babusapalya Kalyananagar Post Bangalore - 560 043 chandra@ijcp.com	Chitra Mohan **GM Sales & Marketing** 9841213823 40A, Ganapathypuram Main Road Radhanagar, Chromepet Chennai - 600 044 Cont.: 22650144 chitra@ijcp.com	Venugopal **GM Sales & Marketing** 9849083558 H. No. 16-2-751/A/70 First Floor Karan Bagh Gaddiannaram Dil Sukh Nagar Hyderabad - 500 059 venu@ijcp.com

GM: General Manager

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Dr KK Aggarwal
President, CMAAO and HCFI
Past National President, IMA
Group Editor-in-Chief, IJCP Group

HCFI Round Table Expert Zoom Meeting on "Double Mutation in Coronavirus and Revisiting Vaccine Adverse Effects – Anecdotal Reports"

CONSENSUS STATEMENT OF HCFI EXPERT ROUND TABLE MEETING (27TH MARCH, 2021)

- The coronavirus keeps on changing in small ways as it passes from one person to another. The vast majority of these mutations are inconsequential and do not alter the virus behavior.
- Some mutations trigger changes in the spike protein and other key areas resulting in more infectiousness, severity and/or even evade vaccine.
- A double variant (E484Q and L452R) has been detected in India. It is a variant of concern. Majority have been detected in Maharashtra, while few have been detected from Delhi, Punjab and Gujarat.
- Mutations occur in the nucleotides and so the amino acid changes.
- The three major variants are the UK variant (B.1.1.7), South Africa variant (B.1.351) and Brazil variant (P.1). The N501Y mutation is common to all three.
- The UK variant has 69-70 and 144 deletions (in the NTD), N501Y substitution in the receptor-binding domain (RBD) and P681H substitution near S1 and S2 bifurcation. This variant may become the wild virus now.
- The South Africa strain has two mutations in the receptor-binding motif or RBM (E484K and K417N); the Brazil strain has K417T and E484K mutations.
- The E484Q and L452R mutation is a novel variant. It does not have NTD deletion so it may autocorrect itself and if this occurs then this mutation will not last long. It will cause a sudden rise in the number of cases, which may exceed the first wave. So, the second wave may be stronger than the first wave, but it may not become a wild virus. It may not develop as the UK strain and will remain a country-specific virus and not spread worldwide.
- The UK strain is causing S gene target failure.
- Does the new mutation cause E gene target failure? This is yet to be confirmed. If the test is based on E gene, then it may be false negative, even while other specific COVID genes may be positive. So, we must test for other markers too.
- Three phenotypes are being seen: Sudden infection with rapidly worsening pneumonia, diarrhea-predominant and the routine presentation of D614G strain. The phenotype of the double mutant virus is not yet known.

- COVID-19 infection is unexpectedly being reported after the first dose of the vaccine.
- The new mutation is double contagious but half as dangerous. It is spreading fast, but so far, no cause for panic. One must remain cautious though.
- Three cases of anaphylaxis have been reported in the media; possibly due to polysorbate 80 (also a constituent in Voveran injection) in one case.
- Non-IgE–mediated reactions within 6 hours: angioneurotic edema eye lid, rash on neck and urticaria; can be prevented by premedication.
- Type 4 reactions may be seen in 4-10 days on the site of injection and also a remote site.
- Other reactions seen include severe aphthous ulcers, local warmth/redness at the injection site on 2nd day, swelling/itching on ear and petechial rash in a patient with varicose veins, ear eczema, severe urticaria reaction on the leg, painful lymph nodes.
- Delayed local injection-site reactions to vaccine may occur, though they are uncommon (T-cell–mediated hypersensitivity) (NEJM).
- Sympathetic overactivity presenting as accelerated hypertension and transient atrial fibrillation, transient ventricular tachycardia, uncontrolled diabetes, precipitation of seizures, brain hemorrhage, exaggerated rheumatoid arthritis, worsening of Crohn's disease, superficial clots (increase in D-dimer).
- Vaccine may precipitate underlying allergy and inflammation: Ear eczema, herpes zoster, Bell's palsy, transverse myelitis.
- Vaccine can precipitate inflammation: Painful lymphadenitis, episcleritis, left eye conjunctivitis.
- Thrombotic thrombocytopenic purpura (TTP) – skin rash after 1 week.
- Post-COVID vaccine systemic inflammation with normal pulmonary function may occur manifesting as fever >101, significant rise in C-reactive protein (CRP). In antibodies after COVID infection, the first dose may act like the second dose and may precipitate systemic inflammation.
- Three cases of myocardial infarction (MI) reported; all deaths in Hong Kong, Malaysia and Sri Lanka are related to heart attacks.
- Post-vaccine COVID infection after the first dose can cause severe inflammation.
- Vaccine-induced loss of smell and taste may occur (RT-PCR negative).
- Anticipate a reaction and act accordingly. In a patient with severe thyrotoxicosis due to post-COVID severe thyroiditis, vaccine was deferred; vaccine would have precipitated a thyroid storm.
- Side effects are predictable and accordingly premedication may be taken to avoid the side effects.
- In its safety review of the AstraZeneca vaccine, the World Health Organization (WHO) has also said that the benefits are more than the risks.
- Evaluate the risks in every individual. In the high-risk and susceptible individuals, give the vaccine by doing appropriate risk reduction.
- Healthcare workers need to be sensitized about these adverse effects.
- The duration between the first and the second dose of Covishield has been increased from 4-6 weeks to 4-8 weeks. The second dose of Covaxin can also be given up to 6 weeks as per the Frequently Asked Questions on Co-WIN released by the Health Ministry (dated 22.3.21).

With input from Dr Monica Vasudev

Participants: Dr KK Aggarwal, Dr KK Kalra, Dr Ashok Gupta, Dr DR Rai, Dr Anita Chakravarti, Dr Jayakrishnan Alapet, Mr Bejon Misra, Mrs Upasana Arora, Ms Ira Gupta, Dr S Sharma

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Thyroid Disease in Pregnancy

REKHA RANI*, SHIKHA SINGH*, ASHWANI NIGAM†, ASHA*, SANGITA SAHU‡

ABSTRACT

Thyroid disease is the second most common endocrine disorder affecting women of reproductive age, and when untreated during pregnancy, is associated with an increased risk of miscarriage, placental abruption, hypertensive disorders and growth restriction. Current guidelines recommend targeted screening of women at high risk, including those with a history of thyroid disease, type 1 diabetes mellitus or other autoimmune disease; current or past use of thyroid therapy or a family history of autoimmune thyroid disease. Appropriate management results in improved outcomes, demonstrating the importance of proper diagnosis and treatment. In women with hypothyroidism, levothyroxine is titrated to achieve a goal serum thyroid-stimulating hormone level <2.5 mIU/L. The preferred treatment for hyperthyroidism is antithyroid medications, with a goal of maintaining a serum free thyroxine level in the upper one-third of the normal range. Postpartum thyroiditis is the most common form of postpartum thyroid dysfunction and may present as hyper- or hypothyroidism. Symptomatic treatment is recommended for the former; levothyroxine is indicated for the latter in women who are symptomatic, breastfeeding or who wish to become pregnant. Thyroid disease is second only to diabetes mellitus as the most common endocrinopathy that occurs in women during their reproductive years. Symptoms of thyroid disease often mimic common symptoms of pregnancy, making it challenging to identify. Poorly controlled thyroid disease is associated with adverse outcomes during pregnancy, and treatment is an essential part of prenatal care to ensure maternal and fetal well-being.

Keywords: Hyperthyroidism, hypothyroidism, postpartum thyroiditis, levothyroxine

The thyroid gland is important during pregnancy as it regulates the production of hormones triiodothyronine (T3) and thyroxine (T4), each of which plays a critical role in the development of the baby's brain and nervous system.

During the first trimester, the fetus depends on the mother's supply of thyroid hormone, which is delivered through the placenta. In order to meet this need, the mother's thyroid production will typically go into overdrive, resulting in an enlargement of the gland itself.

Diseases of thyroid hormone (hyperthyroidism and hypothyroidism) are quite commonly seen in pregnancy (2-3%) and 1 in 10 women of childbearing age group will have some indication of reduction of functional reserve of thyroid function.

*Associate Professor
Dept. of Obstetrics and Gynecology
†Professor
Dept. of Medicine
‡Assistant Professor
Dept. of Obstetrics and Gynecology
SN Medical College, Agra, Uttar Pradesh
Address for correspondence
Dr Rekha Rani
Associate Professor
Dept. of Obstetrics and Gynecology
SN Medical College, Agra, Uttar Pradesh
E-mail: drrekha.gynae@gmail.com

THYROID GLAND AND ITS ADAPTION DURING NORMAL PREGNANCY

Thyroid gland is a butterfly-shaped endocrine gland located in front of the neck and releases hormones that regulate the metabolism, heart, nervous system, weight, body temperature and many other processes in the body.

For diagnosing thyroid disease in pregnancy, we need to understand the changes in thyroid physiology and changes in the values of thyroid function tests that occur during pregnancy.

Pregnancy poses various metabolic changes in the body and to meet the increased metabolic needs, thyroid physiology and thyroid function change (Reflected as altered thyroid tests).

There is an increase in serum thyroxine-binding globulin (TBG) and stimulation of thyrotropin (TSH) receptors by hCG (human chorionic gonadotropin) in pregnancy. The serum TBG levels rise almost double because of estrogen (increased TBG production and TBG sialylation). This causes slowing and decrease in TBG clearance.

In response, the total T4 and T3 increase in first half of pregnancy up to 20 weeks, plateauing at 20 weeks of gestation.

The production of thyroid hormones T3 and T4 returns to pre-pregnancy levels at approximately 20 weeks. hCG β-subunit is similar to thyroid-stimulating hormone. Hence, hCG has a weak thyroid-stimulating activity.

1 micro U of hCG = 0.0013 micro U of TSH.

THYROID FUNCTION TESTS IN PREGNANCY

Several population studies have demonstrated that it is normal for TSH in pregnancy to be below the classic lower limit of normal. Therefore, use of non-pregnant reference ranges result in the overdiagnosis of hyperthyroid states and under-recognition of hypothyroid states. Laboratories should provide trimester-specific reference ranges but if these are not available, the trimester-specific TSH ranges indicated in Table 1 are recommended.

Because normal thyroid function is different during pregnancy, TSH values will change as the mother progresses from the first to third trimester. Under normal circumstances, the normal TSH value would range from 0.2 to 4.0 mIU/L.

The lower reference range of TSH can be reduced by approximately 0.4 mIU/L, in first trimester and upper reference range is reduced by approximately 0.5 mIU/L. This corresponds to a TSH upper reference limit of 4.0 mIU/L. This should be applied beginning with the late first trimester, Weeks 7-12, with a gradual return towards the nonpregnant range in the second and third trimesters. Reference range determinations should only include pregnant women with no known thyroid disease, optimal iodine intake and negative thyroid-peroxidase antibody (TPOAb) status.

There is an increase in total T4 concentration from 7 to 16 weeks of gestation, ultimately reaching 50% above the pre-pregnancy level. This level is then sustained through pregnancy. Upper range determination can be calculated by shifting the nonpregnant limit 50% higher.

Table 1. Recommended Trimester-specific Reference Ranges for TSH

Trimester	TSH range
First	0.1-2.5 mIU/L
Second	0.2-3.0 mIU/L
Third	0.3-3.0 mIU/L

This can only be used after 16 weeks of pregnancy. If a T4 measurement is required before that time (i.e., 7-16 weeks of pregnancy), a calculation can be made for the upper reference range based on increasing the nonpregnant upper reference limit by 5% per week, beginning with 7 weeks. Accurate estimation of the free T4 (FT4) concentrations can also be done by calculating a FT4 index. Table 2 summarizes thyroid evaluation.

TSH and FT4 are useful for diagnosis of and monitoring thyroid dysfunction in pregnancy. T3 levels are only ordered if a suspicion of T3 predominant thyrotoxicosis is there.

THYROID DISEASES

- Hypothyroidism (Overt and Subclinical)
- Hyperthyroidism (Overt and Subclinical)
- Postpartum thyroiditis
- Thyroid nodule/Goiter

Hashimoto's disease, also known as Hashimoto's thyroiditis, is an autoimmune disease which attacks and gradually destroys the thyroid gland. Hypothyroidism is a common outcome of the disorder and is treated in the same manner using hormone replacement therapy. Typically speaking, a woman with Hashimoto's should maintain her TSH under 3.0 mIU/L.

The provisions for treatment during pregnancy are the same as for other forms of hypothyroidism, although additional attention should be made to keeping the TSH under 2.5 mIU/L as higher levels are associated with a two-fold increase in the risk of miscarriage.

Hypothyroidism

Hypothyroidism in pregnancy is usually due to Hashimoto's disease (3 to 5 out of 1,000 pregnancy). Hashimoto's disease is chronic inflammation of thyroid

Table 2. Basic Thyroid Evaluation

	TSH		
	Low	**Normal**	**High**
FT4			
High	Primary hyperthyroid	Nonthyroid illness-(NTI) or Patients on levothyroxine	Secondary hyperthyroid
Normal	Subclinical hyperthyroid	Euthyroid	Subclinical hypothyroid
Low	Secondary hyperthyroid	NTI	Primary hypothyroid

gland (Hashimoto's thyroiditis is an autoimmune disorder). Euthyroid patients who are antithyroid Ab positive, post-hemithyroidectomy or treated with radioactive iodine have an increased propensity for the development of hypothyroidism in gestation and should be monitored regularly.

Overt hypothyroidism is when there is an elevated TSH and low FT4. This is clearly associated with adverse pregnancy outcomes (Lower IQ) and miscarriages, prematurity, low birth weight and stillbirths. Frequently, elevated maternal TSH is detected when FT4 concentrations are normal. Conversely, low FT4 concentrations can be detected despite normal TSH concentrations, called as isolated hypothyroxinemia.

Symptoms

- Extreme tiredness
- Weight gain
- Constipation
- Difficulty in concentration
- Memory problems
- Sensitivity to cold temperature
- Muscle cramps

Adverse outcomes with overt maternal hypothyroidism include increased risks of premature birth, risk of gestational hypertension, low birth weight, pregnancy loss and lower offspring IQ.

Overt hypothyroidism should be urgently treated by L-thyroxine (LT4) replacement. In severe cases, a loading dose for 3-4 days of 150-200 μg should be given, followed by titration with TSH levels.

In patients with pre-existing hypothyroidism already on replacement therapy, the dose needs to be increased by about 30% (Increase 2 additional doses per week or 7-9 doses per week) on suspicion or confirmation of pregnancy.

T4 and TSH should be checked every 4 weeks in first half of pregnancy and at least once in between 26 and 32 weeks. The aim is to keep TSH within trimester-specific ranges (Table 1).

After delivery, the dose can be reduced to pre-pregnant levels and should be monitored with a serum TSH measurement approximately every 4 weeks until mid-gestation and at least once near 30 weeks of gestation. Adjustment of LT4 dosage when affected women become pregnant and also for the timing of follow-up interval for TSH in treated patients is suggested. Increased requirement for thyroxine (or exogenous LT4) occurs as early as 4-6 weeks of pregnancy. Requirements gradually increase up till 16-20 weeks of pregnancy and plateau thereafter until the time of delivery. Following delivery, maternal LT4 dosing should be reduced to pre-pregnancy levels, and a serum TSH assessed 6 weeks thereafter. However, a study demonstrated that more than 50% of women with Hashimoto's thyroiditis required an increase in the pregestational thyroid hormone dose in the postpartum period, presumably due to an exacerbation of autoimmune thyroid dysfunction postpartum. In women started on LT4 during pregnancy for thyroid autoimmunity in the absence of TSH elevation, the LT4 can be stopped at delivery, with serum TSH assessment at 6 weeks postpartum. A maternal serum TSH concentration <2.5 mIU/L is a reasonable goal. Even lower preconception TSH values (<1.5 mIU/L) could reduce the risk of TSH elevation during the first trimester, but a lower treatment target may not improve outcomes because the LT4 dose can be immediately increased upon a positive pregnancy test. Achieving a TSH concentration at the lower end of the reference range could induce subnormal TSH concentrations in some patients.

Though generally safe for any developing fetus, potential effects upon conception and/or successful implantation are unknown.

If TSH is well-controlled in pregnancy and treatment is adequate, neonatal thyroid function screening is not necessary.

Subclinical hypothyroidism (SCH) is also associated with some adverse outcomes like miscarriage but not proven to cause fetal impaired cognitive functions.

Any pregnant woman with an elevated TSH concentration must also be evaluated for TPOAb status. A dose of only 50 μg/day is typically required for effective treatment of subclinically hypothyroid women.

- LT4 therapy is recommended for:
  - TPOAb-positive women with a TSH greater than the pregnancy-specific reference range
  - TPOAb-negative women with a TSH >10.0 mU/L.
- LT4 therapy may be considered for:
  - TPOAb-positive women with TSH concentrations >2.5 mU/L and below the upper limit of the pregnancy-specific reference range
  - TPOAb-negative women and TPOAb-negative women with TSH concentrations greater than the pregnancy-specific reference range and below 10.0 mU/L.

- LT4 therapy is not recommended for:
  - TPOAb-negative women with a normal TSH <4.0 mU/L.

A clear association has been demonstrated between thyroid antibodies and spontaneous pregnancy loss; however, it does not prove causality and the underlying mechanisms are not known. All women with overt and subclinical hypothyroidism should be treated irrespective of TPOAb positivity with LT4 during pregnancy to maintain serum TSH in the trimester-specific goal range. It has been recommended to check serum TSH every 4 weeks during pregnancy so that appropriate dose adjustments can be made, but our routine practice is to check every 6 weeks. The recommended therapy is with oral LT4, which should be taken on an empty stomach (45 minutes before consumption of food, beverages or other medications). In addition, calcium, iron and prenatal vitamin supplements should be avoided within 4 hours of ingestion of LT4, as these can decrease the absorption of thyroxine.

Immediately after delivery, the requirement of thyroxine drops and women who were taking thyroxine prior to pregnancy will shift to their pre-pregnancy dose, and those who started their thyroxine in pregnancy will require half the dose they were taking just before delivery. In women who had started their thyroxine in pregnancy for subclinical hypothyroidism, the medication can be stopped after delivery and thyroid balance re-assessed again after 6 weeks and decision taken regarding continuation of treatment.

Monitoring of euthyroid women who are thyroid antibody (Ab)-positive during pregnancy

TPOAb are able to cross the placenta. At the time of delivery, cord blood TPOAb levels strongly correlate with third-trimester maternal TPOAb concentrations.

However, maternal passage of either TPOAb or thyroglobulin (Tg)Ab is not associated with fetal thyroid dysfunction.

Euthyroid pregnant women who are TPOAb or TgAb positive should have measurement of serum TSH concentration performed at time of pregnancy confirmation and every 4 weeks through mid-pregnancy. LT4 administration in low dosage (25-50 μg/d) is safe. Therefore, its use among patients with recurrent pregnancy loss may be reasonably considered in the setting of early gestation, especially when no other known cause of prior pregnancy loss has been identified.

Two randomized clinical trials are currently ongoing. One of them is the Thyroid Antibodies and LevoThyroxine study (TABLET) trial in the United Kingdom. There is a greater risk for adverse events in women who are TPOAb-positive versus TPOAb-negative, even when thyroid function is identical.

The recommended treatment of maternal hypothyroidism is oral LT4. Other thyroid preparations, such as T3 or desiccated thyroid, should not be used in pregnancy.

Hyperthyroidism

Pregnancy hyperthyroidism is often due to Grave's disease (GD). It has an incidence of about 1 in 500 pregnancies (0.4%). Hyperthyroidism in pregnancy is also termed gestational thyrotoxicosis.

Pregnant women with GD should be monitored monthly. No prior history of thyroid disease, no stigmata of GD (goiter, orbitopathy), a self-limited mild disorder and symptoms of emesis favor the diagnosis of gestational transient thyrotoxicosis.

Rarely severe vomiting (Hyperemesis gravidarum) can cause dehydration and weight loss; this may be triggered by high levels of hCG and causes temporary hypothyroidism that settles in second trimester.

Symptoms

- Irregular heart beat
- Nervousness
- Severe nausea or vomiting
- Slight tremor
- Trouble sleeping
- Weight loss or low weight gain
- Eye problems (irritation, bulging and puffiness)

Uncontrolled hyperthyroidism in pregnancy can lead to:

- Congestive heart failure
- Pre-eclampsia
- Thyroid storm
- Miscarriage
- Premature birth
- Low birth weight.

Hyperthyroid in newborns can cause:

- Rapid heart rate
- Heart failure
- Early closure of soft spot of skull

- Poor weight gain
- Irritability
- Enlarged gland, causing problem in breathing.

Diagnosis is made on testing for thyroid if there is a suspicion on account of the symptoms. Tests include:

- TSH/Ultra TSH
- T3 and T4
- Thyroid-stimulating immunoglobulin (TSI).

TSH receptor antibody (TRAb) and maternal TT3 may prove helpful in clarifying the etiology of thyrotoxicosis. Radionuclide scintigraphy or radioiodine uptake determination should not be performed in pregnancy.

Mild hyperthyroidism in which TSH is low but T4 is normal does not need any treatment. Treatment of choice is PTU (propylthiouracil). If patient is on carbimazole (CM), then it is advisable to change to PTU (CM can cause rare embryopathy). If liver function is compromised, then PTU should be stopped and carbimazole should be started. Titration of treatment should be guided by TSH and free T4 levels.

Moderate doses of antithyroid drugs (ATDs) (carbimazole 25-30 mg or PTU <300 mg/day) are recommended during breastfeeding.

Thyroid function should be monitored in mothers on high doses during the postpartum period. Gestational or hCG triggered thyrotoxicosis usually does not require antithyroid treatments; this is self-limiting. Sometimes symptomatic treatment may be needed in these cases.

If the patient opts for radioactive iodine ablative therapy prior to pregnancy, the following recommendations should be provided:

First, TRAb levels tend to increase following ^{131}I therapy and may remain elevated formany months following ^{131}I therapy. Therefore, patients with high TRAb levels or severe hyperthyroidism may favor consideration of other therapeutic options, such as surgery.

Second, a subset of young patients with severe GD may not become stably euthyroid within the first year after ^{131}I therapy.

Third, if ^{131}I therapy is planned, a pregnancy test should be performed 48 hours before ^{131}I ablation to confirm absence of unexpected pregnancy.

Fourth, conception should be delayed for 6 months and until a stable euthyroid state is reached after ablation and initiation of LT4 replacement therapy.

If the patient chooses ATD therapy, the following recommendations should be given:

First, the increased risk of birth defects associated with both PTU and methimazole (MMI) use during early pregnancy should be reviewed. ATDs should be avoided in the first trimester of pregnancy, but when necessary, PTU is generally favored. PTU after the first trimester should be switched to MMI to decrease the risk of liver failure in the mother.

In thyrotoxic patients, the possibility of future pregnancy should be discussed. Women with GD seeking future pregnancy should be counseled regarding the complexity of disease management during future gestation and birth defects with ATD use. In preconception counseling, the risks and benefits of all treatment options and the patient's desired timeline to conception should be discussed.

Thyrotoxic women should be rendered stably euthyroid before attempting pregnancy. Treatment options are associated with risks and benefits. These include ^{131}I ablation, surgical thyroidectomy or ATD therapy.

Management of patients with Graves' hyperthyroidism during pregnancy

In some cases, a woman may experience an overactive rather than underactive thyroid. This is known as hyperthyroidism, commonly referred to as GD.

Obstetric and medical complications are directly related to control of maternal hyperthyroidism, and the duration of the euthyroid state throughout pregnancy.

Poor control of thyrotoxicosis is associated with pregnancy loss, pregnancy-induced hypertension, prematurity, low birth weight, intrauterine growth restriction, stillbirth, thyroid storm and maternal congestive heart failure. Moreover, some studies suggest fetal exposure to excessive levels of maternal thyroid hormone may program the offspring to develop diseases such as seizure disorders and neurobehavioral disorders in later life.

During pregnancy, GD is typically treated with an antithyroid medication such as PTU during the first trimester and another called MMI for the remainder.

Thionamide ATDs (MMI, CM and PTU) are the mainstays of treatment for hyperthyroidism during pregnancy. They reduce iodine organification and coupling of monoiodotyrosine and diiodotyrosine, therefore inhibiting thyroid hormone synthesis. The thyroid function tests return to normal gradually over weeks.

Initial doses of ATDs during pregnancy are: MMI, 5-30 mg/day (typical dose in average patient 10-20 mg); CM, 0-40 mg/day and PTU, 100-600 mg/day (typical PTU dose in average patient 200-400 mg/d). The equivalent potency of MMI to PTU is 1:20. PTU dosing should be split into 2-3 daily doses. MMI can be given in one daily dose.

Postpartum Thyroiditis

About 1 in 20 women may get postpartum thyroiditis (PPT).

- 48% are hypothyroidism.
- 22% biphasic where there is hyperthyroidism followed by hypothyroid.
- 30% have isolated hyperthyroidism.

During the thyrotoxic phase of PPT, symptomatic women may be treated with β-blockers. These are safe for lactating women, such as propranolol or metoprolol, at the lowest possible dose to alleviate symptoms; it is the treatment of choice. Therapy is typically required for a few weeks.

ATDs are not recommended for the treatment of the thyrotoxic phase of PPT.

Following the resolution of the thyrotoxic phase of PPT, serum TSH should be measured in approximately 4-8 weeks (or if new symptoms develop) to screen for the hypothyroid phase.

Treatment is on the basis of the presenting disease and long-term follow-up with annual thyroid function tests is recommended. All patients with depression, including postpartum depression, should be screened for thyroid dysfunction.

Thyroid Nodule and Cancer

If thyroid nodules are seen is prepregnant period, it is advisable to delay pregnancy by 1 year after ablation.

If detected in pregnancy after 20 weeks, then a biopsy (FNAC) can be done. For malignancy, surgery is delayed till second trimester. Special care is needed during labor and delivery due to anesthesia complications.

In postnatal period, radioactive iodine is contraindicated if patient is breastfeeding.

UNIVERSAL SCREENING

It is still controversial whether to do universal screening of all pregnant women or apply case finding approach.

Table 3. High Risk Attributes for Thyroid Dysfunction

- A history of thyroid dysfunction or surgery
- Family history of thyroid disease
- Goiter
- Antithyroid antibodies present
- Symptoms or signs of hypothyroidism
- Women with type 1 diabetes
- History of miscarriage or preterm delivery
- Autoimmune disorder
- Infertility
- Prior head or neck irradiation
- Morbid obesity
- Age 30 years or older
- Treatment with amiodarone
- Treatment with lithium
- Recent exposure to iodinated contrast

American Thyroid Association guidelines do not support universal screening but recommend ordering a TSH test at first antenatal visit for women with high risk attributes (Table 3).

KEY POINTS

- Pregnancy-specific reference ranges should be used to guide diagnosis and monitoring of thyroid conditions in pregnancy.
- The World Health Organization (WHO) recommends a daily intake of iodine 250 μg during pregnancy and lactation.
- Hypothyroid states should be treated with thyroxine aiming for TSH <2.5 prior to conception and in the first trimester and TSH <3.0 for the second and third trimesters.
- Thyroxine should be increased by two additional doses per week (or 30%) on suspicion or confirmation of pregnancy in women already taking thyroxine.
- It is important to separate thyroxine intake from preparations that may reduce absorption.
- Women with high risk attributes for thyroid dysfunction are appropriate for antenatal screening with TSH.
- Gestational thyrotoxicosis needs to be differentiated from Graves' disease and rarely requires thioamide treatment.
- It is important to maintain a high index of suspicion for postpartum thyroiditis, especially in those with known thyroid antibodies or autoimmune conditions.

Pearls of Practice – Thyroid Dysfunction

Hypothyroidism

- T4 essential for early fetal development
- Little T4 crosses placenta after first trimester
- Adequate treatment - good outcome

Postpartum Thyroiditis

- Occurs 3-4 months postpartum
- Autoimmune disorder
- Phases of hyper- and hyporecovery
- Annual thyroid function tests

Hyperthyroidism

- Careful D/D at early weeks
- Untreated poor pregnancy outcome
- Drug cross placenta: lowest optimal dosage
- Cord blood - thyroid function

Thyroid Nodule and Cancer

- Defer pregnancy for 1 year after treatment with radioactive iodine
- Nodule identified beyond 20 weeks - biopsy after delivery
- Large goiter - anesthetic complications

FIGO RECOMMENDS THE FOLLOWING

- Screening for thyroid function is recommended in the first trimester particularly in countries with a deficient iodine diet and in symptomatic patients.
  - TSH is the superior method for screening. FT4 and TPOAb testing are not recommended for screening. The best reliable tests for TSH are by chemiluminescence immunoassay (CIA) or third-generation radioimmunoassay (RIA). Notably, normal thyroid test values change in pregnancy.
- Treatment for hypothyroidism is recommended when TSH levels are >2.5 and >3.0 mIU/L during the first and second/third trimesters, respectively. The only replacement therapy is LT4. Treating subclinical hypothyroidism, in the presence of negative thyroid autoantibodies, is still debatable. Importantly, women on LT4 before pregnancy should increase their dosage by 30-50% when they first recognize the pregnant state.
- Treatment of hyperthyroidism due to GD is by ATDs (PTU/CM/MMI). It is not recommended to change drugs during pregnancy. Symptomatic treatment with β-blockers for short-term may be needed.
- Primary prevention of hypothyroidism is by a healthy diet and iodized fortified salt (especially in iodine deficient areas).
- If the patient has a thyroid nodule, she should be evaluated and treated during pregnancy. The first steps are performance of a thyroid ultrasonogram and a fine needle aspiration (FNA), as needed. Surgery should be preferably deferred to the postpartum period.
- Follow-up and postpartum TSH evaluation and reduction of LT4 dose to pre-pregnant levels in patients with hypothyroidism.

SUGGESTED READING

1. Negro R, Mestman JH. Thyroid disease in pregnancy. Best Pract Res Clin Endocrinol Metab. 2011;25(6):927-43.
2. Glinoer D. The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology. Endocr Rev. 1997;18(3):404-33.
3. Ain KB, Mori Y, Refetoff S. Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. J Clin Endocrinol Metab. 1987;65(4):689-96.
4. Ballabio M, Poshychinda M, Ekins RP. Pregnancy-induced changes in thyroid function: role of human chorionic gonadotropin as putative regulator of maternal thyroid. J Clin Endocrinol Metab. 1991;73(4): 824-31.
5. Yamazaki K, Sato K, Shizume K, Kanaji Y, Ito Y, Obara T, et al. Potent thyrotropic activity of human chorionic gonadotropin variants in terms of ^{125}I incorporation and de novo synthesized thyroid hormone release in human thyroid follicles. J Clin Endocrinol Metab. 1995;80(2):473-9.
6. Gilbert RM, Hadlow NC, Walsh JP, Fletcher SJ, Brown SJ, Stuckey BG, et al. Assessment of thyroid function during pregnancy: first-trimester (weeks 9-13) reference intervals derived from Western Australian women. Med J Aust. 2008;189(5):250-3.
7. Stricker R, Echenard M, Eberhart R, Chevailler MC, Perez V, Quinn FA, et al. Evaluation of maternal thyroid function during pregnancy: the importance of using gestational age-specific reference intervals. Eur J Endocrinol. 2007;157(4):509-14.
8. Lambert-Messerlian G, McClain M, Haddow JE, Palomaki GE, Canick JA, Cleary-Goldman J, et al; FaSTER Research Consortium. First- and second-trimester thyroid hormone reference data in pregnant women: a FaSTER (First- and Second-Trimester Evaluation of Risk for aneuploidy) Research Consortium study. Am J Obstet Gynecol. 2008;199(1):62.e1-6.
9. Dashe JS, Casey BM, Wells CE, McIntire DD, Byrd EW, Leveno KJ, et al. Thyroid-stimulating hormone in singleton

and twin pregnancy: importance of gestational age-specific reference ranges. Obstet Gynecol. 2005;106(4):753-7.

10. Fitzpatrick DL, Russell MA. Diagnosis and management of thyroid disease in pregnancy. Obstet Gynecol Clin North Am. 2010;37(2):173-93.
11. Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med. 1999;341(8):549-55.
12. Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocr Rev. 2010;31(5):702-55.
13. Abalovich M, Gutierrez S, Alcaraz G, Maccallini G, Garcia A, Levalle O. Overt and subclinical hypothyroidism complicating pregnancy. Thyroid. 2002;12(1):63-8.
14. Yassa L, Marqusee E, Fawcett R, Alexander EK. Thyroid hormone early adjustment in pregnancy (the THERAPY) trial. J Clin Endocrinol Metab. 2010;95(7):3234-41.
15. Alexander EK, Marqusee E, Lawrence J, Jarolim P, Fischer GA, Larsen PR. Timing and magnitude of increases in levothyroxine requirements during pregnancy in women with hypothyroidism. N Engl J Med. 2004;351(3):241-9.
16. Stagnaro-Green A, Abalovich M, Alexander E, Azizi F, Mestman J, Negro R, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid. 2011;21(10):1081-25.
17. Azizi F, Hedayati M. Thyroid function in breast-fed infants whose mothers take high doses of methimazole. J Endocrinol Invest. 2002;25(6):493-6.
18. Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, et al. Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? J Clin Endocrinol Metab. 2007;92(1): 203-7.
19. Chang DL, Leung AM, Braverman LE, Pearce EN. Thyroid testing during pregnancy at an academic Boston Area Medical Center. J Clin Endocrinol Metab. 2011;96(9):E1452-6.
20. Thangaratinam S, Tan A, Knox E, Kilby MD, Franklyn J, Coomarasamy A. Association between thyroid autoantibodies and miscarriage and preterm birth: meta-analysis of evidence. BMJ. 2011;342:d2616.
21. Lee YL, Ng HP, Lau KS, Liu WM, O WS, Yeung WS, et al. Increased fetal abortion rate in autoimmune thyroid disease is related to circulating TPO autoantibodies in an autoimmune thyroiditis animal model. Fertil Steril. 2009;91(5 Suppl):2104-9.
22. Andersen SL, Olsen J, Laurberg P. Foetal programming by maternal thyroid disease. Clin Endocrinol (Oxf). 2015;83(6):751-8.
23. Mandel SJ, Cooper DS. The use of antithyroid drug sin pregnancy and lactation. J Clin Endocrinol Metab. 2001;86(6):2354-9.
24. Azizi F. The safety and efficacy of antithyroid drugs. Expert Opin Drug Saf. 2006;5(1):107-16.
25. Nicholas WC, Fischer RG, Stevenson RA, Bass JD. Single daily dose of methimazole compared to every 8 hours propylthiouracil in the treatment of hyperthyroidism. South Med J. 1995;88(9):973-6.
26. Kallner G, Vitols S, Ljunggren JG. Comparison of standardized initial doses of two antithyroid drugs in the treatment of Graves' disease. J Intern Med. 1996;239(6):525-9.
27. Nakamura H, Noh JY, Itoh K, Fukata S, Miyauchi A, Hamada N. Comparison of methimazole and propylthiouracil in patients with hyperthyroidism caused by Graves' disease. J Clin Endocrinol Metab. 2007;92(6):2157-62.
28. Homsanit M, Sriussadaporn S, Vannasaeng S, Peerapatdit T, Nitiyanant W, Vichayanrat A. Efficacy of single daily dosage of methimazole vs. propylthiouracil in the induction of euthyroidism. Clin Endocrinol (Oxf). 2001;54:385-90.
29. He CT, Hsieh AT, Pei D, Hung YJ, Wu LY, Yang TC, et al. Comparison of single daily dose of methimazole and propylthiouracil in the treatment of Graves' hyperthyroidism. Clin Endocrinol (Oxf). 2004;60(6):676-81.
30. Nakamura H, Miyauchi A, Miyawaki N, Imagawa J. Analysis of 754 cases of antithyroid drug-induced agranulocytosis over 30 years in Japan. J Clin Endocrinol Metab. 2013;98(12):4776-83.
31. Watanabe N, Narimatsu H, Noh JY, Yamaguchi T, Kobayashi K, Kami M, et al. Antithyroid drug-induced hematopoietic damage: a retrospective cohort study of agranulocytosis and pancytopenia involving 50,385 patients with Graves' disease. J Clin Endocrinol Metab. 2012;97(1):E49-53.
32. Kobayashi S, Noh JY, Mukasa K, Kunii Y, Watanabe N, Matsumoto M, et al. Characteristics of agranulocytosis as an adverse effect of antithyroid drugs in the second or later course of treatment. Thyroid. 2014;24(5):796-801.
33. Russo MW, Galanko JA, Shrestha R, Fried MW, Watkins P. Liver transplantation for acute liver failure from drug induced liver injury in the United States. Liver Transpl. 2004;10(8):1018-23.
34. Bahn RS, Burch HS, Cooper DS, Garber JR, GreenleeCM, Klein IL, et al. The role of propylthiouracil in the management of Graves' disease in adults: report of a meeting jointly sponsored by the American Thyroid Association and the Food and Drug Administration. Thyroid. 2009;19(7):673-74.
35. Foulds N, Walpole I, Elmslie F, Mansour S. Carbimazole embryopathy: an emerging phenotype. Am J Med Genet A. 2005;132A(2):130-5.
36. Dosiou C, Barnes J, Schwartz A, Negro R, Crapo L, Stagnaro-Green A. Cost-effectiveness of universal and risk-based screening for autoimmune thyroid disease in pregnant women. J Clin Endocrinol Metab. 2012;97(5):1536-46.

Add the Next Generation Anti-diabetic for Better Control

GLYPTEN™ - M

Teneligliptin 20 mg and Metformin Hydrochloride 500 mg SR Tablets

Dual Action adds Life to β Cells

GLYPTEN™ - M FORTE

Teneligliptin 20 mg and Metformin Hydrochloride 1000 mg SR Tablets

Fortified Dual Action adds Life to β Cells

DIABÉTIX

A Division of

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.

2021

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Management of Diabetic End-stage Renal Disease: Role of Hemodialysis

H SUDARSHAN BALLAL

ABSTRACT

Diabetes mellitus is now the most common cause of end-stage renal disease (ESRD) all across the globe, including India. In view of the alarming rise in numbers, renal failure due to type 2 diabetes has been termed a "medical catastrophe of worldwide dimensions." When a patient develops uremic symptoms he needs renal replacement therapy. The renal replacement therapies available for all patients with ESRD are: hemodialysis, chronic ambulatory peritoneal dialysis (CAPD) and renal transplantation. Kidney transplantation is the best option for patients with diabetic ESRD. The 5-year survival of transplant patients of 75-85% is far superior to the 5-year survival rate of around 25% on dialysis.

Keywords: Diabetes mellitus, end-stage renal disease, renal replacement therapies, hemodialysis, CAPD, renal transplantation

Diabetes mellitus is now the most common cause of end-stage renal disease (ESRD) all across the globe, including India. It is estimated that 30-50% of patients being initiated on renal replacement therapy (RRT) have diabetes as the cause of their ESRD[1] and most of these patients have type 2 diabetes. In view of the alarming rise in numbers, renal failure due to type 2 diabetes has been termed a "medical catastrophe of worldwide dimensions".[2] This article will discuss the management of diabetic ESRD specifically related to type 2 diabetes.

RENAL REPLACEMENT THERAPY

When a patient's kidney function, as measured by the calculated glomerular filtration rate, has reached <10 mL/min (ESRD) or the patient develops uremic symptoms they need RRT.

The RRTs available for all patients with ESRD are:

- Hemodialysis
- Chronic ambulatory peritoneal dialysis (CAPD)
- Renal transplantation.

Though these modalities are available for all patients with ESRD, there are significant differences in the morbidity and mortality of any given modality between the diabetic and nondiabetic ESRD population. We will discuss some of these issues, specifically the modality of hemodialysis.

HEMODIALYSIS FOR DIABETIC ESRD

Although hemodialysis prevents death from uremia, the patient survival on hemodialysis is poor, especially for patients with diabetes, being approximately 20-25% at 5 years as compared to 40-50% for other causes of ESRD.[3] This is worse than many cancers. The survival of patients on maintenance hemodialysis in India seems dismal for both, diabetic and nondiabetic populations.[4]

The important contributors for mortality in the diabetic dialysis population are: Cardiovascular disease, adequacy of dialysis and nutritional status.

- **Cardiovascular disease (CVD):** CVD is the most common cause of death accounting for more than one-half of the cases.[5] The main reason for such a high mortality rate, which is of cardiovascular origin in the majority of cases is that the cardiovascular conditions of patients with diabetes are already severely impaired when they start RRT, as demonstrated by the high prevalence of coronary artery disease, stroke, peripheral occlusive disease and amputations. This also explains why patients who have diabetes and are on RRTs are at higher risk of developing *de novo* CVD, particularly ischemic heart disease,

Professor of Clinical Medicine
St. Louis University School of Medicine, USA
Manipal Academy of Higher Education, Manipal, India

which not only is more frequent but also has a more aggressive course than in nondiabetic patients. In view of this, aggressive measures to manage CVD need to be adopted in all diabetic patients even before they reach the stage of dialysis.

- **Adequacy of dialysis:** Adequacy of dialysis, which also plays an important role in CVD and nutrition (MIA or malnutrition inflammation atherosclerosis syndrome), is also a contributor to the poor outcome and diabetics, in particular, seem to be more sensitive than nondiabetics to inadequate dialysis.[6] The increase in mortality of these patients largely disappears if there is an improvement in the nutritional status as reflected by an increase in serum albumin and creatinine.[7] This is a major problem in India where for various reasons like financial constraints, lack of access and availability of good dialysis units causes most patients to have inadequate dialysis.[8] Whenever possible, it is very essential to monitor the adequacy of dialysis by using biochemical measures like urea reduction rates, Kt/V and clinical well-being of patients and to take measures to improve the adequacy of dialysis.
- **Nutrition in dialysis:** Nutrition in dialysis patients is closely linked to inadequate dialysis, which leads to anorexia and poor calorie and protein intake. This is reflected by poor serum albumin and creatinine levels, which are indicators for mortality in dialysis patients. The problems of diabetic gastroparesis and diabetic enteropathy compound the nutritional problems.

The help of a good dietician and measures to treat diabetic gastroparesis and enteropathy by motility agents, frequent small foods and appropriate use of broad-spectrum antibiotics to treat bacterial infections in diabetic enteropathy are needed to maintain adequate nutrition. It is to be noted that cisapride is best avoided in this population because of the risk of fatal arrhythmias.[9]

DIET IN DIABETIC PATIENTS ON DIALYSIS

The general recommendation for diet in dialysis patients is given in Table 1. The iron requirement of dialysis patients varies and will need to be addressed on a patient to patient basis. In general, water-soluble vitamins are routinely prescribed and calcitriol may be needed in some patients.

Table 1. Daily Dietary Recommendations for Dialysis Patients versus Nonuremics[a]

Factor	Nonuremic	HD	PD
Protein (g/kg)	0.8	1.2	1.2-1.5
Calories (sedentary; kcal/kg)	30	30[b]	30-40[b,c]
Protein (%)	15-20	15	15
Carbohydrate (%)	55-60	55-60[d]	55-60[c,d]
Fat (%)	20-30	Balance	Balance
Cholesterol (mg)	300-400	300-400	300-400
Polyunsaturated/Saturated fat ratio	2.0:1.0	2.0:1.0	2.0:1.0
Crude fiber (g)	25	25	25
Sodium (1 g = 43 mEq)	2-6 g	2 g + 1 g/LUO	2-4 g + 1 g/LUO
Fluids (L)	Ad lib 1 L/LUO	1 L + 1 L/LUO	1.0-2.5 L + 1 L/LUO
Potassium (1 g = 25 mEq)	2-6 g	2 g + 1 g/LUO	4 g + 1 g/LUO
Calcium (g)	0.8-1.2	Diet +1.2	Diet + 1.2
Phosphorus (g)	1.0-1.8	0.6-1.2	0.6-1.2
Magnesium (g)	0.35	0.2-0.3	0.2-0.3

[a]All intakes calculated on the basis of normalized body weight (i.e., the average body weight of normal persons of the same age, height and sex as the patient).

[b]These levels of caloric intake are rarely attained in practice.

[c]Includes glucose absorbed from dialysis solutions.

[d]Carbohydrate intake should be decreased in patients with hypertriglyceridemia.

HD = Hemodialysis; PD = Peritoneal dialysis; LUO = Liters of urine output per day.

BLOOD SUGAR CONTROL IN DIABETIC DIALYSIS PATIENTS

There are certain special problems about blood sugar control in dialysis patients.

Altered Insulin Metabolism

In uremic patients (both diabetic and nondiabetic), insulin secretion by the β-cells of the pancreas is reduced and the responsiveness of peripheral tissues (e.g., muscle) to insulin is depressed. On the other hand, the rate of insulin catabolism (renal and extrarenal) is decreased, and therefore, the half-life of any insulin present in the circulation is prolonged. All of these abnormalities are only partially corrected after institution of maintenance dialysis therapy.

Increased Sensitivity to Insulin

In diabetic dialysis patients treated with exogenous insulin, the importance of reduced insulin catabolism overrides the impact of insulin resistance; when exogenous insulin is administered, its effect may be intensified and prolonged. Thus, smaller than usual doses should be given.

Insulin Therapy

Tight control of sugar is sometimes difficult to achieve in diabetic dialysis patients. Nevertheless, good glucose control is worthwhile with split doses of insulin preferably. The "amount of insulin" per day required for patients receiving maintenance hemodialysis is usually small; optimum control of glycemia is achieved by administration of long-acting insulin at two separate times during the day (split dosing) and by supplementing with regular insulin for meals as needed. The proportions of long-acting and regular insulin, as well as the total insulin doses vary widely among different patients. Hypoglycemia is quite common in diabetic dialysis patients usually due to reduced insulin catabolism and reduced intake or food and/or poor absorption.

A fasting serum glucose of <140 mg/dL and a postprandial value <200 mg/dL is a reasonable goal to achieve.

Oral Hypoglycemic Agents

Lack of clinical studies on use of oral hypoglycemic agents (OHAs) in dialysis patients restricts the use of these agents.

Nevertheless, these agents are useful adjuncts in the treatment of diabetics and are used by many nephrologists. The safety of sulfonylureas depends on their mode of metabolism and their half-life. Use of short-acting agents primarily metabolized by the liver is, in general, safer in dialysis patients. Acetohexamide, chlorpropamide and tolazamide are excreted to a large extent in the urine. These drugs should not be used in dialysis patients because their half-lives will be greatly prolonged in the absence of renal function, possibly resulting in severe and prolonged hypoglycemia. The excretion of glyburide is 50% hepatic, and prolonged hypoglycemia has been reported using this drug in dialysis patients. Metabolism of glipizide, tolbutamide and gliclazide is almost completely hepatic. Consequently, the last three drugs should be considered if an OHA is desired. Many drugs frequently used in dialysis patients either antagonize (phenytoin, nicotinic acid, diuretics) or enhance (sulfonamides, salicylates, warfarin, ethanol) the hypoglycemic action of sulfonylureas.

Metformin, a biguanide, is associated with increased incidence of lactic acidosis in dialysis patients and should not be used. Acarbose inhibits α-glucosidase in the enteric mucosa and moderates postprandial hyperglycemia. It may prove to be a useful adjunct to other diabetic medications in diabetic patients.

Troglitazone and other thiazolidinediones sensitize the target tissues to insulin and may be of help in obese, type 2 diabetics with insulin resistance. However, the use of this class of drugs may be associated with the risk of severe hepatotoxicity.

In general, insulin use is preferable in diabetic dialysis patients but judicious use of appropriate OHAs can be done.

Specific problems of hemodialysis in diabetic patients:

- Difficulty in creating and maintaining a vascular access because of severe peripheral vascular disease (PVD) in older diabetic patients.
- Inability to tolerate volume shifts giving rise to hypotension during hemodialysis because of autonomic neuropathy and CVD.
- Risk of infection.
- Progression of diabetic retinopathy.

In view of all these problems, meticulous planning and appropriate management should start in the predialysis period well before dialysis is anticipated and would involve a special diabetic team consisting of an Ophthalmologist, Vascular Surgeon, Podiatrist, Endocrinologist, Cardiologist, Neurologist and Dietician to help the nephrology team in keeping

the patient as fit as possible even before they reach dialysis.

TIMING OF DIALYSIS IN DIABETIC ESRD

In general, most nondiabetic patients are initiated on dialysis when the creatinine clearance is <10 mL/min.

In diabetic patients, dialysis may have to be initiated at creatinine clearance even >15 mL/min.[9] The reasons for this being:

- Renal functions deteriorate rapidly in this group
- Hypertension is very difficult to control with severe renal failure
- Most patients have CVD with volume overload
- Uremic symptoms may manifest earlier than non-diabetic patients.

In spite of these recommendations, dialysis is usually started as an emergency in most Indian patients because of uremia, pulmonary edema or severe hyperkalemia because of poor awareness, financial constraints and lack of facilities for dialysis.[4,8]

ROLE OF CAPD

CAPD is another modality of treatment in diabetic ESRD. Though it has its advantages and disadvantages, the following factors decide the modality of dialysis:

- Comorbid conditions
- Family and home support
- Financial support
- CVD and PVD leading to poor vascular access for dialysis
- Hemodynamic stability
- Availability of hemodialysis centers.

CAPD is 30-50% more expensive than hemodialysis in India and is generally used for patients who do not have access to hemodialysis, have severe chronic heart failure (CHF), hemodynamic instability, poor vascular access and are not candidates for transplantation. The patient and the family should be motivated and have adequate financial support. Table 2 gives the comparison between the two modalities of dialysis.

Table 2. Dialysis Modalities for Diabetics

Modality	Advantages	Disadvantages
Hemodialysis	Very efficient	Risky for patients with advanced cardiac disease
	Frequent medical follow-up (in center)	Multiple arteriovenous access surgeries often required; risk of severe hand ischemia
	No protein loss to dialysate	High incidence of hypotension during dialysis session
		Predialysis hyperkalemia
		Prone to hypoglycemia
CAPD	Good cardiovascular tolerance	Peritonitis, exit site and tunnel infection risks similar to those in nondiabetic dialysis patients
	No need for arteriovenous access	Protein loss to dialysate
	Good control of serum potassium	Increased intra-abdominal pressure effects (hernias, fluid leaks, etc.)
	Good glucose control, particularly with use of intraperitoneal insulin; less severe hypoglycemia	Schedule not convenient for helper if one is required (e.g., for a patient with physical disability like blindness, stroke, etc.)
CCPD	Good cardiovascular tolerance	Protein loss to dialysate
	No need for arteriovenous access	
	Good control of serum potassium	
	Good glucose control with use of intraperitoneal insulin	Very very expensive
	Good for patients with disability	
	Peritonitis risk slightly less than for CAPD	

CAPD = Continuous ambulatory peritoneal dialysis; CCPD = Continuous cycling peritoneal dialysis.

SURVIVAL ON HEMODIALYSIS AND PERITONEAL DIALYSIS

There have been conflicting data about the survival of patients on CAPD compared to hemodialysis. Initial data from Michigan suggested an advantage for CAPD.[10] However, most studies after adjustment for comorbid condition, have not found a statistically significant survival difference between the two modalities.[11]

TRANSPLANTATION

Kidney transplantation is the best option for patients with diabetic ESRD. The 5-year survival of transplant patients of 75-85%, though less than that of nondiabetic ESRD, is still far superior to the 5-year survival rate of around 25% on dialysis.[3,12] Though in general healthier patients go on to transplant and sicker patients remain on dialysis the survival rates are better, even when these are factored in. Transplantation is also associated with a better quality-of-life and high degree of rehabilitation.

The pre- and post-transplant care of diabetic patients is generally similar to that of nondiabetics. However, in view of the high prevalence of CVD in this population, meticulous attention has to be paid to screen these patients for CVD prior to the transplantation.[13]

RECOMMENDATIONS FOR TREATMENT OF DIABETIC ESRD PATIENTS

Kidney transplant remains the best option of RRT for patients with diabetic ESRD in all suitable candidates. Recommendations for those not suitable for transplantation -

CAPD is recommended for patients with:

- Poor vascular access because of PVD
- Severe CVD with hemodynamic instability during hemodialysis
- Nonavailability of hemodialysis centers
- Good family and financial support
- Motivated patients.

Hemodialysis is the treatment for all the rest which is the treatment available for the vast majority of patients with diabetic ESRD in India who are not candidates for transplantation. In view of the multiple associated comorbid conditions, a multidisciplinary approach is needed to prevent and manage the complications of vascular diseases, malnutrition and retinopathy in diabetic dialysis patients.

REFERENCES

1. Ballal HS. Diabetic Nephropathy: Indian Scene, Scientific Proceedings, 1st National Conference in Prevention of Chronic Kidney Disease in India. February 2005.
2. Ritz E, Rychlík I, Locatelli F, Halimi S. End-stage renal failure in type 2 diabetes: A medical catastrophe of worldwide dimensions. Am J Kidney Dis. 1999;34(5): 795-808.
3. United States Renal Data System. Excerpts from the USRDS 2003 annual data report: Atlas of end stage renal disease in the United States. Am J Kidney Dis. 2004;42(Suppl 5): S1-S226.
4. Rao M, Juneja R, Shirly RB, Jacob CK. Haemodialysis for end-stage renal disease in Southern India - a perspective from a tertiary referral care centre. Nephrol Dial Transplant. 1998;13(10):2494-500.
5. Brunner FP, Selwood NH. Profile of patients on RRT in Europe and death rates due to major causes of death groups. The EDTA Registration Committee. Kidney Int Suppl. 1992;38:S4-15.
6. Collins AJ. How can the mortality rate of chronic dialysis patients be reduced? Semin Dial. 1993;6:102.
7. Lowrie EG, Lew NL, Huang WH. Race and diabetes as death risk predictors in hemodialysis patients. Kidney Int Suppl. 1992;38:S22-31.
8. Kher V. End-stage renal disease in developing countries. Kidney Int. 2002;62(1):350-62.
9. Tzamaloukas AH, Friedman EA. Diabetes. In: Daugirdas JT, Blake PG, Ing TS (Eds.). Handbook of Dialysis. 3rd Edition, Philadelphia: Lippincott, Williams & Wilkins; 2001. p. 453.
10. Nelson CB, Port FK, Wolfe RA, Guire KE. Comparison of continuous ambulatory peritoneal dialysis and hemodialysis patient survival with evaluation of trends during the 1980s. J Am Soc Nephrol. 1992;3(5):1147-55.
11. Jaar BG, Coresh J, Plantinga LC, Fink NE, Klag MJ, Levey AS, et al. Comparing the risk for death with peritoneal dialysis and hemodialysis in a national cohort of patients with chronic kidney disease. Ann Intern Med. 2005;143(3):174-83.
12. Locatelli F, Pozzoni P, Del Vecchio L. Renal replacement therapy in patients with diabetes and end-stage renal disease. J Am Soc Nephrol. 2004;15 Suppl 1:S25-9.
13. Scandling JD. Kidney transplant candidate evaluation. Semin Dial. 2005;18(6):487-94.

■■■■

Empower Diabetes Patient

GLYCIPHAGE®
Metformin 250 mg Tablets, 500 mg & 850 mg Press Tablets

GLYCIPHAGE SR®
Metformin 500 mg, 850 mg & 1000 mg Sustained Release Tablets

GLYCIPHAGE®-G 1mg 2mg
Metformin SR 500 mg + Glimepiride 1 mg / 2 mg

GLYCIPHAGE®-G 1mg 2mg FORTE
Metformin SR 1000 mg + Glimepiride 1mg / 2 mg

GLYCIPHAGE-G® 0.5
Metformin SR 500mg + Glimepiride 0.5mg

GLYCIPHAGE®-VG
Metformin SR 500 mg + Voglibose 0.2 mg + Glimepiride 1 mg / 2 mg Tablets

GLYPTEN
Teneligliptin 20 mg

GLYPTEN™ - M
Teneligliptin 20 mg and Metformin Hydrochloride 500 mg SR Tablets

GLYPTEN-M FORTE
Teneligliptin 20 mg and Metformin Hydrochloride 1000 mg SR Tablets

VILDAPHAGE™
Vildagliptin 50mg Tablets

VILDAPHAGE-M™
Vildagliptin and Metformin Hydrochloride 50mg/500mg Tablets

VILDAPHAGE-M Forte™
Vildagliptin and Metformin Hydrochloride 50mg/1000mg Tablets

Voliphage™ 0.2 mg / 0.3 mg
Voglibose 0.2 mg / 0.3 mg Tablets

Voliphage™-M 0.2 mg / 0.3 mg
Metformin SR 500 mg + Voglibose 0.2 mg / 0.3 mg Tablets

BENALGIS®
Benfotiamine 100 mg Tablets

Benalgis® Forte
Pregabalin 75 mg + Methylcobalamin 0.750 mg + Folic Acid 0.750 mg + Vitamin B_6 1.5 mg + Benfotiamine 7.5 mg

FOXSTAT™
Febuxostat 40 mg / 80 mg Tablets

DIAVIT™ PLUS

2021

DIABÉTIX
A Division of
FRANCO-INDIAN
PHARMACEUTICALS PVT. LTD.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Study of Demographic Profile, Comorbidities, Role of Hydroxychloroquine Prophylaxis and Outcomes of COVID-19 Positive Healthcare Workers at a Tertiary Care Center in Southern Rajasthan

MAHESH DAVE*, MANASVIN SAREEN†, YASH SHAH‡, SAHIL KHARBANDA†, ANIRUDDHA BURLI#

ABSTRACT

Background: In December 2019, a new respiratory tract infecting agent emerged in Wuhan city of China, known as the coronavirus. There are limited studies regarding coronavirus disease 2019 (COVID-19) in healthcare workers (HCWs). Therefore, the present study was aimed to determine the demographic profile, comorbidities, hydroxychloroquine as prophylaxis and outcomes of reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 HCWs. **Material and methods:** This study was an observational retrospective study carried out over a period of 10 months from 15th March, 2020 to 15th January, 2021 in 350 RT-PCR confirmed COVID-19 HCWs who were in home isolation or admitted in dedicated COVID hospital. **Results:** We observed that majority of HCWs were in the age group 20-39 years (66.58%), were males (69.14%) and from urban areas (72.86%). Only few had comorbidities (3.42%), took hydroxychloroquine as prophylaxis (5.71%) and mortality was 0.57%. About 46.29% of the HCWs were doctors and 28.40% of the doctors were from Medicine. **Conclusion:** From the present study, we conclude that HCWs affected by COVID-19 are mainly young adult male physicians from urban areas, without significant comorbidities. The outcome in COVID-19 positive HCWs is favorable due to better awareness, prompt diagnosis and treatment. The results of this study will be useful in knowing the most vulnerable section of HCWs.

Keywords: COVID-19, healthcare workers, hydroxychloroquine

In December 2019, a new respiratory tract infecting agent emerged in Wuhan city of China, known as the coronavirus. It was later named coronavirus disease 2019 (COVID-19). Full-genome sequencing and phylogenetic analysis indicated that 2019-nCoV is a form of beta-coronavirus which include human severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) viruses.[1] The World Health Organization (WHO) declared COVID-19 as a pandemic on 11th March, 2020, and from India, the first case was reported on 30th January, 2020 from Kerala. Transmission of the coronavirus is usually via respiratory droplets in closed environments and through close contact between people and touching contaminated surfaces, with incubation period of 2-14 days and a reproductive number noted in early studies as 2.2.[2] COVID-19 has various clinical presentations that range from asymptomatic to mild symptoms such as fever, myalgia, sore throat, cough and cold to severe symptoms like acute respiratory distress syndrome, myocarditis, acute renal failure and multi-organ failure.[3-5]

According to WHO, healthcare workers (HCWs) are defined as all people engaged in actions whose primary intent is to enhance health.[6] In this pandemic, to manage COVID-19, many people came together and worked

*Senior Professor and Unit Head
†Junior Resident (2nd Year)
‡Junior Resident (1st Year)
#Junior Resident (3rd Year)
Dept. of General Medicine, RNT Medical College, Udaipur, Rajasthan
Address for correspondence
Dr Manasvin Sareen
Junior Resident (2nd Year)
Dept. of General Medicine, RNT Medical College, Udaipur, Rajasthan
E-mail: manasvinsareen7@gmail.com

as HCWs. In our study, HCWs included consultants and postgraduates from clinical as well as nonclinical departments, interns, undergraduate students, nursing staff, nursing students, paramedical staff and lab technicians. HCWs have exposure to COVID-19 patients directly or indirectly or to the infectious materials. Secondary transmission from HCWs is a possibility among patients, family members and the community.

Therefore, the present study was aimed to determine the demographic profile (age, sex, residence), comorbidities, role of hydroxychloroquine as prophylaxis and outcomes of reverse transcription polymerase chain reaction (RT-PCR) confirmed COVID-19 HCWs who were in home isolation or admitted in dedicated COVID hospital, a tertiary care institute attached to RNT Medical College, Udaipur, Rajasthan over a period of 10 months (15th March, 2020 to 15th January, 2021).

AIMS AND OBJECTIVES

- To study the demographic profile (age, sex, residence) of COVID-19 positive HCWs.
- To study the comorbidities in COVID-19 affected HCWs.
- To study the role of hydroxychloroquine as prophylaxis in COVID-19 affected HCWs.
- To study the outcomes of COVID-19 positive HCWs.

MATERIAL AND METHODS

This study was an observational retrospective study which was carried out over a period of 10 months from 15th March, 2020 to 15th January, 2021 in 350 RT-PCR confirmed COVID-19 HCWs who underwent home isolation or were admitted in dedicated COVID hospital, a tertiary care center attached to RNT Medical College, Udaipur, Rajasthan. We have analyzed the demographic profile, associated comorbidities, role of hydroxychloroquine drug as prophylaxis and outcomes of these HCWs.

Inclusion Criteria

All RT-PCR confirmed COVID-19 positive HCWs who were in home isolation or admitted in wards and intensive care unit (ICU) of our dedicated COVID hospital, irrespective of age and gender were included. HCWs included consultants and postgraduates from clinical as well as nonclinical departments, interns, undergraduate students, nursing staff, nursing students, paramedical staff and lab technicians.

Exclusion Criteria

HCWs who did not give written consent for the study.

Methodology

HCWs who were suspected to be COVID-19 positive on the basis of their clinical history, contact history and travel history as per the Indian Council of Medical Research (ICMR) guidelines, underwent RT-PCR testing for COVID-19 and those who came out positive were admitted in COVID Dedicated Hospital (wards and ICU) or underwent home isolation and were enrolled in our study after written consent. The following parameters were used for our study:

- Demographic profile – which includes age-wise, sex-wise and area-wise distribution.
- Comorbidities – which include diabetes mellitus, hypertension, ischemic heart disease, chronic respiratory illness, malignancies and hypo-thyroidism.
- Number of HCWs taking hydroxychloroquine prophylaxis – which includes collecting information from the HCWs whether he or she had completed or was taking hydroxychloroquine as prophylaxis.
- Outcome was recorded in the form of recovery or deaths.
- Amongst the HCWs, we classified them into doctors, nursing staff, paramedical staff and lab technicians. We further divided the doctors department-wise to see the distribution of affected doctors in each and every department. This will further give us a better picture of the departments at risk of getting affected by COVID-19.

OBSERVATION AND RESULTS

Table 1 shows the demographic profile in the COVID-19 positive HCWs. Among the age groups, maximum HCWs were in the 20-39 years group (66.58%) followed by 40-59 years age group (30.00%). Regarding gender, males were predominantly affected (69.14%). The disease predominantly involved the urban population (72.86%).

Table 2 shows the association of comorbidities with COVID-19 positive HCWs. Out of 350 HCWs, 12 had comorbidities (3.42%). Among comorbidities, diabetes mellitus was observed in maximum HCWs (1.42%), followed by hypertension (0.57%), chronic respiratory illness (0.57%), ischemic heart disease (0.28%), malignancy (0.28%) and hypothyroidism (0.28%).

Table 1. Demographic Profile

Characteristics	HCWs (n = 350)	Percentage (%)
Age		
0-19 y	5	1.42
20-39 y	233	66.58
40-59 y	105	30.00
>60 y	7	2.00
Sex		
Male	242	69.14
Female	108	30.86
Residence		
Urban	255	72.86
Rural	95	27.14

Table 2. Comorbidities in COVID-19 Positive HCWs

Comorbidities	HCWs (n = 350)	Percentage (%)
Diabetes mellitus	5	1.42
Hypertension	2	0.57
Chronic respiratory illness	2	0.57
Ischemic heart disease	1	0.28
Malignancy	1	0.28
Hypothyroidism	1	0.28

Table 3. Number of HCWs Taking Hydroxychloroquine Drug as Prophylaxis

Hydroxychloroquine prophylaxis	HCWs (n = 350)	Percentage (%)
Yes	20	5.71
No	330	94.29

Table 3 shows that out of the 350 HCWs affected, 20 took hydroxychloroquine prophylaxis (5.71%).

Table 4 shows the outcome of COVID-19 positive HCWs. Out of 350 HCWs, 348 got discharged (99.42%).

Table 5 shows the distribution of COVID-19 positive HCWs. Out of 350 HCWs, maximum affected were doctors (46.29%) followed by nursing staff (37.14%), lab technicians (10.86%) and paramedical staff (5.71%). The table also shows the department-wise distribution of doctors. Among 162 doctors, maximum were from Medicine (28.40%) followed by Orthopedics (10.50%), Anesthesia (8.64%), Internship (8.64%), Pediatrics (7.40%), Surgery (6.80%), Obs and Gyne (6.17%), Radiodiagnosis (4.32%), Biochemistry (2.47%), ENT (2.47%) and others.

Table 4. Outcome of HCWs

Outcome	HCWs (n = 350)	Percentage (%)
Discharged	348	99.43
Death	2	0.57

Table 5. Distribution of COVID-19 Positive HCWs According to their Field

Subtypes	HCWs (n = 350)	Percentage (%)
Doctors	**162**	**46.29**
Medicine	46	28.40
Orthopedics	17	10.50
Anesthesia	14	8.64
Internship	14	8.64
Pediatrics	12	7.40
Surgery	11	6.80
Obs and Gyne	10	6.17
Radiodiagnosis	7	4.32
Biochemistry	4	2.47
ENT	4	2.47
Pathology	3	1.85
Anatomy	3	1.85
Microbiology	3	1.85
Physiology	3	1.85
PSM	3	1.85
Psychiatry	2	1.23
Ophthalmology	2	1.23
Radiotherapy	1	0.61
Dermatology	1	0.61
FMT	1	0.61
Dentist	1	0.61
Nursing staff	130	37.14
Paramedical staff	20	5.71
Lab technicians	38	10.86

DISCUSSION

The present study was an observational retrospective study which was done over a period of 10 months

(15th March, 2020 to 15th January, 2021) on 350 RT-PCR confirmed COVID-19 HCWs who underwent home isolation or were admitted in a dedicated COVID hospital attached to RNT Medical College, Udaipur, Rajasthan. These HCWs were analyzed in respect to demographic profile, comorbidities, role of hydroxychloroquine drug as prophylaxis and outcomes.

In the present study, we observed that COVID-19 affects all age groups. Out of 350 HCWs, maximum were from 20 to 39 years group (66.58%) followed by 40-59 years (30.00%), whereas the disease was less commonly seen in >60 years (2.00%) and 0-19 years (1.42%) age groups. Lai et al and Sikkema et al also observed similar results and calculated median age of COVID-19 positive HCWs as 36.5[7] and 49 years,[8] respectively. The possible explanation of higher COVID-19 positivity in the age group 20-59 years (96.58%) may be due to the fact that this age group of HCWs may be actively involved in management of this pandemic. Regarding gender, males were predominantly involved (69.14%). This may be because the majority of HCWs at our center are males and in the Indian society, males are more habituated in smoking, drinking alcohol, outdoor activities and tendency of removal of face masks frequently. The study done by Mahajan et al[9] found similar results (57%). This study also shows that the disease has a predominantly urban preponderance (72.86%). The possible explanation might be that the study was conducted at a tertiary care center, which in itself is in urban area.

In the present study, comorbidities were seen in 3.42% HCWs. Among comorbidities, diabetes mellitus was observed in maximum HCWs (1.42%), followed by hypertension (0.57%), chronic respiratory illness (0.57%), ischemic heart disease (0.28%), malignancy (0.28%) and hypothyroidism (0.28%). In contrast to our study, Mahajan et al[9] reported 19% comorbidities in COVID-19 positive HCWs. This significant difference in comorbidities may be due to the fact that the maximum HCWs in our study were in younger age groups. They also observed that hypertension and diabetes mellitus were the most common comorbidities, which resembles the present study.

The present study shows that only 5.71% of HCWs took hydroxychloroquine drug as prophylaxis as it was advocated to have a role in the early phase of the pandemic. But, the drug did not seem much efficacious, hence, HCWs stopped taking it as prophylaxis in the later half. Therefore, majority of the HCWs did not take hydroxychloroquine as prophylaxis. Jha et al[10] also stated that hydroxychloroquine did not have a role in prophylaxis. Multiple systematic reviews[11] also concluded that there is no pertinent data to support the use of hydroxychloroquine drug outside that of research, and there is lack of clinical data to actually support its efficacy.

Among the 350 COVID-19 positive HCWs, deaths occurred in only 2 HCWs (0.57%). Mahajan et al[9] and Lai et al[7] reported similar results in their studies (1%, 0.9%). This can be explained by several reasons. In our study, most of the HCWs were young adults which accounts for better immunity. Early symptoms were more easily noticed by HCWs which led to early diagnosis, treatment and better outcome. Also, the proper use of personal protective equipment (PPE) kits and face masks by them may be responsible for decreasing the severity of infection and death.

In the present study, out of 350 COVID-19 affected HCWs, maximum were doctors (46.29%) followed by nursing staff (37.14%), lab technicians (10.86%) and paramedical staff (5.71%). The study by Mahajan et al[9] showed involvement of 29% doctors, 26% nursing staff and 46% healthcare assistants and other staff. The result of the present study is contradictory to the above mentioned study. In the present study among HCWs, doctors were maximally affected (46.29%). This may be explained by the fact that doctors were the frontline warriors and were actively involved in the management of COVID-19 positive cases.

Amongst the 162 doctors affected, maximum were from Medicine department (28.40%), followed by Orthopedics (10.50%), Anesthesia (8.64%) and Internship (8.64%). The possible explanation of this higher involvement (28.40%) of doctors from Medicine department may be due to the fact that these doctors were actively and directly engaged in patient care in COVID-19 positive wards, ICU as well in severe acute respiratory illness (SARI) wards. In this pandemic, there were a lot of patients presenting with bilateral atypical pneumonias but their COVID-19 RT-PCR was repeatedly negative and they were admitted in various general medical wards, where improper use of PPE and exposure of these Medicine residents to highly suspected clinical COVID-19 patients might be one of the cause of higher involvement of doctors of this department. Orthopedicians are often involved due to operating on emergency cases of trauma without knowing the COVID-19 status of the patient. The surgeries are for longer hours and thus, increase the chances of exposure of the doctors. Anesthetists are involved in aerosol generating procedures like mechanical ventilation and noninvasive ventilation, which can lead to their increased chances of exposure.

Also, Interns are primarily affected because at our center, they are doing the job of sampling of COVID-19 suspect and positive cases, which leads to increased risk for them.

CONCLUSION

From the present study, we conclude that HCWs affected by COVID-19 are mainly young adult males from urban areas, without significant comorbidities. The outcome in COVID-19 positive HCWs is favorable due to better immunity, awareness, prompt diagnosis and treatment. We recommend that all HCWs as well as their family members and close contacts should be regularly tested for COVID-19 as they are the most precious resource for every country. Special attention needs to be paid to protect HCWs from cross infection from other HCWs. HCWs are at higher risk of being exposed to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and could potentially have a role in hospital transmission. Among HCWs, doctors are most prone to develop the infection, especially the ones from departments of Medicine, Orthopedics, Anesthesia and Interns.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382(13):1199-207.
3. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA. 2020;324(8):782-93.
4. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
5. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.
6. World Health Organization. The world health report 2006: working together for health. World Health Organization; 2006 Mar 23.
7. Lai X, Wang M, Qin C, Tan L, Ran L, Chen D, et al. Coronavirus disease 2019 (COVID-2019) infection among health care workers and implications for prevention measures in a tertiary hospital in Wuhan, China. JAMA Netw Open. 2020;3(5):e209666.
8. Sikkema RS, Pas SD, Nieuwenhuijse DF, O'Toole Á, Verweij J, van der Linden A, et al. COVID-19 in health-care workers in three hospitals in the south of the Netherlands: a cross-sectional study. Lancet Infect Dis. 2020, July 2, 2020.
9. Mahajan NN, Mathe A, Patokar GA, Bahirat S, Lokhande PD, Rakh V, et al. Prevalence and clinical presentation of COVID-19 among healthcare workers at a dedicated hospital in India. J Assoc Physicians India. 2020;68(12):16-21.
10. Jha S, Soni A, Siddiqui S, Batra N, Goel N, Dey S, et al. Prevalence of flu-like symptoms and COVID-19 in healthcare workers from India. J Assoc Physicians India. 2020;68(7):27-9.
11. Gbinigie K, Frie K. Should chloroquine and hydroxychloroquine be used to treat COVID-19? A rapid review. BJGP Open. 2020;4(2):bjgpopen20X101069.

■■■■

Measles Resurgence in DRC 8 Months After Epidemic Declared Over

A new measles outbreak has been reported in the Democratic Republic of Congo (DRC), 8 months after the epidemic was declared over by the authorities, stated medical charity Médecins Sans Frontières (MSF).

Over 13,000 measles cases have been reported in the country since January 1, in spite of the vaccination campaigns targeting millions of children across the country over the last 2 years. While the vaccine drive reduced the number of patients to a considerable extent, it could not cut the chain of transmission, MSF said.

From 2018 to 2020, over 4,60,000 children contracted measles and around 8,000 succumbed to the disease. Three-quarters of these were under 5 years old. Since the end of 2020, the country has started recording a rise in patients with measles, stated Anthony Kergosien, coordinator of MSF's emergency response team in Congo… (*Reuters*)

In Polymicrobial Infections

℞ **BRAKKE® Tab**

(Ofloxacin 200 mg + Ornidazole 500 mg)

BRAKKEs the chain of Aerobes and Anaerobes

For Intestinal Homeostasis

℞ **Lactisyn®**

Lyophilized *Saccharomyces boulardii*

The Most Studied and Only Scientifically Proven Probiotic...

Delicious Orange Flavour

2021

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

An Observational Study on Incidence of Ischemic Mitral Regurgitation Following First-time Acute Coronary Syndrome

S SARAVANAMOORTHY*, N VIJAYAKUMAR†, R UMARANI‡

ABSTRACT

Aims and objectives: To study the incidence of ischemic mitral regurgitation (IMR) following first episode of acute coronary syndrome (ACS) and to study the correlation between IMR and infarct location. **Methods:** Patients admitted in coronary care unit (CCU) of Rajah Muthiah Medical College and Hospital (RMMCH) during the period of January 2019 to March 2019 were screened. After satisfying the inclusion and exclusion criteria, 48 patients were enrolled in the study. The demographic details, risk factors for coronary artery disease (CAD), clinical findings, ECG findings, course in hospital, outcomes (till 10 days from admission) were recorded in a specially designated proforma. All these patients underwent ECHO imaging and the incidence of IMR was evaluated. **Results:** Out of 48 patients enrolled in our study, 25% (n = 12) of patients were found to have IMR. Among the patients with IMR following ACS, 75% had inferior wall myocardial infarction (IWMI) and 25% had anterior wall myocardial infarction (AWMI). **Conclusion:** Mild functional IMR following ACS is a very common finding on echocardiographic analysis. It was found to be more likely in elderly, diabetics and dyslipidemics. Patients with IWMI with right ventricular extension are more prone for IMR.

Keywords: Mitral regurgitation, ischemic mitral regurgitation, acute coronary syndrome

Mitral regurgitation (MR) is a well-known complication of myocardial infarction. It can occur either in patients with long-standing coronary artery disease (CAD) or in the setting of acute myocardial ischemia.

Ischemic mitral regurgitation (IMR) is a frequent complication of acute myocardial infarction, with a variable presentation depending on the severity of MR and the integrity of the subvalvular apparatus. While most cases are asymptomatic or have mild dyspnea, rupture of chordae tendineae or papillary muscles are catastrophic complications that may rapidly lead to cardiogenic shock and death. Echocardiography is the definite diagnostic modality, allowing quantification of the severity of MR and the structural abnormalities within the subvalvular apparatus.

In our study, we studied the profile of patients with IMR following an acute coronary syndrome (ACS) in whom the valve leaflets were structurally normal.

AIMS AND OBJECTIVES

- To study the incidence of IMR following first episode of ACS.
- To study the correlation between IMR and infarct location.

Inclusion Criteria

- Patients admitted in CCU for the first time with a diagnosis of ACS.

Exclusion Criteria

- Previous history of ACS/heart failure.
- Organic mitral valve diseases (rheumatic heart disease [RHD], mitral valve prolapse syndrome [MVPS], autoimmune diseases).
- History of mitral valve surgery.

*Final Year PG
†Assistant Professor
‡Professor
Dept. of General Medicine
Rajah Muthiah Medical College and Hospital,
Annamalai University, Chidambaram, Tamil Nadu
Address for correspondence
Dr S Saravanamoorthy
Final Year PG, Dept of General Medicine
Rajah Muthiah Medical College and Hospital,
Annamalai University, Chidambaram, Tamil Nadu

METHODS

Patients admitted in coronary care unit (CCU) of Rajah Muthiah Medical College and Hospital (RMMCH) during the period of January 2019 to March 2019 were screened. After satisfying the inclusion and exclusion criteria, 48 patients were enrolled in the study. The demographic details, risk factors for CAD, clinical findings, ECG findings, course in hospital, outcomes (till 10 days from admission) were recorded in a specially designated proforma. All these patients underwent echocardiographic imaging and the incidence and severity of MR were noted. The presence and degree of MR were evaluated using the proximal isovelocity surface area method. The ejection fraction was measured using the Simpson's method. Statistical analysis was done using the SPSS software. Figure 1 depicts an ECHO image showing IMR.

RESULTS AND ANALYSIS

- Incidence of IMR in patients with first episode ACS in our hospital was 25%.

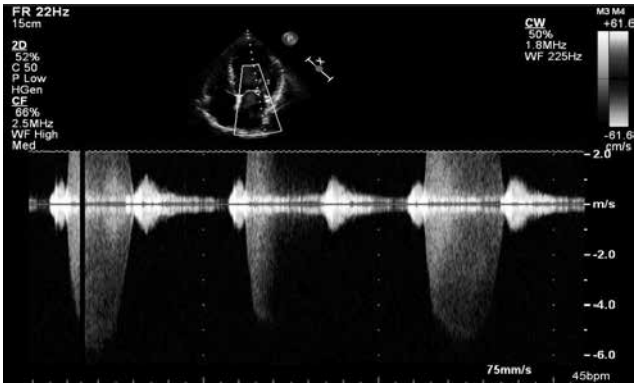


Figure 1. ECHO image showing IMR (continuous wave Doppler).

Table 1. Patient Characteristics

Variables		MR		Pearson Chi-square	P value
		Present	Absent		
Age	<60 years	3	20	3.346	0.067
	>60 years	9	16		
Dyslipidemia	Present	12	34	0.658	0.417
	Absent	0	2		
Diabetes mellitus	Present	10	15	6.211	0.013*
	Absent	2	21		
Systemic hypertension	Present	3	12	0.356	0.551
	Absent	9	24		
BMI	Under weight	2	5	4.726	0.094
	Normal Weight	3	21		
	Over weight	7	10		
Smoking	Present	3	7	0.247	0.616
	Absent	9	29		
Type of MI	IWMI	3	9	1.133	0.287
	IWMI with RV extension	6	12		
	AWMI	3	15		
Level of cardiac enzymes	Normal	3	6	0.247	0.613
	Increase	9	30		
Killip class	I	1	9	3.656	0.299
	II	6	8		
	III	3	10		
	IV	2	9		

*Statistically significant ($p < 0.05$).

- All patients with MR (n = 12) had dyslipidemia.
- Incidence of IMR in patients with diabetes mellitus was higher (n = 10) than the incidence of IMR in nondiabetic patients (n = 2), which was statistically significant (p = 0.013).
- Systemic hypertension, body mass index (BMI), smoking, level of cardiac enzymes had less effect on incidence of IMR (Table 1).

DISCUSSION

- IMR was found in 25% of ACS patients in our study population, which is in accordance with older studies.
- It was found to be higher in older age group, diabetics, dyslipidemics and IWMI with right ventricular extension patients, which was consistent with previous studies.

CONCLUSION

Mild functional IMR following ACS is a very common finding on echocardiographic analysis. It was found to be more likely in elderly, diabetics and dyslipidemics.

SUGGESTED READING

1. Tcheng JE, Jackman JD Jr, Nelson CL, Gardner LH, Smith LR, Rankin JS, et al. Outcome of patients sustaining acute ischemic mitral regurgitation during myocardial infarction. Ann Intern Med. 1992;117(1):18-24.
2. Lehmann KG, Francis CK, Dodge HT. Mitral regurgitation in early myocardial infarction. Incidence, clinical detection, and prognostic implications. TIMI Study Group. Ann Intern Med. 1992;117(1):10-7.
3. Lamas GA, Mitchell GF, Flaker GC, Smith SC Jr, Gersh BJ, Basta L, et al. Clinical significance of mitral regurgitation after acute myocardial infarction. Survival and Ventricular Enlargement Investigators. Circulation. 1997;96(3):827-33.
4. Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation: long-term outcome and prognostic implications with quantitative Doppler assessment. Circulation. 2001;103(13):1759-64.
5. Kisanuki A, Otsuji Y, Kuroiwa R, Murayama T, Matsushita R, Shibata K, et al. Two-dimensional echocardiographic assessment of papillary muscle contractility in patients with prior myocardial infarction. J Am Coll Cardiol. 1993;21(4):932-8.
6. Recusani F, Bargiggia GS, Yoganathan AP, Raisaro A, Valdes-Cruz LM, Sung HW, et al. A new method for quantification of regurgitant flow rate using color Doppler flow imaging of the flow convergence region proximal to a discrete orifice. An in vitro study. Circulation. 1991;83(2):594-604.
7. Utsunomiya T, Ogawa T, Doshi R, Patel D, Quan M, Henry WL, et al. Doppler color flow "proximal isovelocity surface area" method for estimating volume flow rate: effects of orifice shape and machine factors. J Am Coll Cardiol. 1991;17(5):1103-11 .
8. Enriquez-Sarano M, Miller FA Jr, Hayes SN, Bailey KR, Tajik AJ, Seward JB. Effective mitral regurgitant orifice area: clinical use and pitfalls of the proximal isovelocity surface area method. J Am Coll Cardiol. 1995;25(3):703-9.
9. Bonhorst D, Guerreiro S, Fonseca C, Cardim N, Macedo F, Adragão P. Real-life data on heart failure before and after implantation of resynchronization and/or defibrillation devices - the Síncrone study. Rev Port Cardiol. 2019;38(1):33-41.
10. Song L, Brezden-Masley C, Ramanan V, Ghugre N, Barfett JJ, Chan KKW, et al. Serial measurements of left ventricular systolic and diastolic function by cardiac magnetic resonance imaging in patients with early stage breast cancer on trastuzumab. Am J Cardiol. 2019;123(7):1173-9.

■■■■

CDC Updates Guidance on Travel for Fully Vaccinated People

The CDC has issued updated guidance on travel for individuals who are fully vaccinated.

In line with recent studies looking into the effects of vaccination in real-world scenario, the agency recommends that fully vaccinated people can travel at low risk to themselves. A person is fully vaccinated 2 weeks after getting the last recommended dose of the vaccine. The agency states that fully vaccinated people can travel within the United States and do not require COVID-19 testing or self-quarantine after travel if they continue to take COVID-19 precautions while traveling, including wearing a mask, avoiding crowds, social distancing and washing hands frequently… (*CDC*)

Identifying mixed images is a challenge...

So with the mixed infections

In Mixed Skin Infections

℞ **SURFAZ-SN®**
Cream

(Clotrimazole 1% + Beclomethasone Dipropionate 0.025% + Neomycin Sulphate 3500 Units / gm)

For Various Types of Fungal Infections

℞ **SURFAZ®**
Cream
Solution
Dusting Powder

(1% Clotrimazole)

In the Management of Superficial and Systemic Fungal Infections

℞ **SURFAZ-O®**

(Fluconazole 150 mg Tablets)

In Fungal Infections with Inflammation

℞ **SURFAZ-B®**
Cream

(Clotrimazole 1 % + Beclomethasone Dipropionate 0.025 %)

2021

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Correlation of Paroxysmal and Persistent Cardiac Arrhythmias with Clinical and Echocardiographic Parameters in Patients of Rheumatic Fever and Rheumatic Heart Disease

SARAH ALAM*, MU RABBANI†, MS ZAHEER‡, MUHAMMAD UWAIS ASHRAF#, S HASAN AMIR#

ABSTRACT

Introduction: Acute rheumatic fever (ARF) is a multi-system disease caused by an abnormal immunological response after Group A β-hemolytic streptococcus (GABHS) infection. Arrhythmias, atrial fibrillation (AF) occurring in patients of rheumatic heart disease (RHD) are associated with increased risk of stroke. In the Framingham Heart Study, patients with RHD and AF had a 17-fold increased risk of stroke compared with age-matched controls, and the attributable risk was 5 times greater in those with nonrheumatic AF. **Material and methods:** A total of 92 patients of ARF and RHD from Medicine OPD, Medicine IPD, CCU, Cardiology OPD, Pediatrics OPD, Pediatrics IPD of a tertiary care hospital in North India were recruited in this study. A detailed history, physical examination and routine investigations were carried out. Ambulatory 24-hour Holter recordings were obtained in a standard fashion with 3-channel PC card recorders in all patients. **Results:** Of the 92 patients studied, 84 had RHD and 8 had rheumatic fever (RF). Maximum number of patients was in the age group 31-40 years. On echocardiography, range of left atrial diameter was 32-81 mm with mean of 50.45 ± 11.27 mm. Thirteen patients were found to have paroxysmal AF detected on Holter monitoring. Thirty-nine patients were found to have pauses detected on Holter monitoring. Out of these, 25 patients were found to have pauses >2.5 seconds. Forty-eight had episodes of paroxysmal supraventricular tachycardia (PSVT) detected on Holter. Seventy-two patients were found to have premature ventricular contractions (PVCs) on ambulatory ECG monitoring. Twenty-five patients had Holter detected episodes of bigeminy; 29 patients had episodes of nonsustained ventricular tachycardia (NSVT) detected on Holter. The association of arrhythmias with age was evaluated. Pauses, PSVT, AF and NSVT were found to have a significant association with advanced age. Severity of mitral stenosis was significantly associated with presence of AF and PVCs. Severity of mitral regurgitation was significantly associated with AF. Eight patients had ARF and all patients were in New York Heart Association (NYHA) Class I. The PR interval was prolonged in 2 patients and was within normal limits in 6 patients. Pauses >1.5 seconds were detected in 2 patients. The duration of the longest pause was 1.60 seconds. **Conclusion:** RHD is a significant health problem in our region. It commonly affects young patients, compromising the workforce of a country. Only more symptomatic, severe cases belonging to higher functional classes report to hospital. Around one-third of patients are already in AF when they first seek treatment. Even in those patients who are in sinus rhythm, various arrhythmias can be detected on Holter monitoring.

Keywords: Acute rheumatic fever, arrhythmias, atrial fibrillation, rheumatic heart disease, echocardiography

*Senior Resident
Dept. of Endocrinology
All India Institute of Medical Sciences (AIIMS), New Delhi
†Professor
Centre for Cardiology
‡Professor
#Assistant Professor
Dept. of Medicine
JN Medical College, AMU, Aligarh, Uttar Pradesh
Address for correspondence
Dr Muhammad Uwais Ashraf
Assistant Professor
Dept. of Medicine
JN Medical College, AMU, Aligarh, Uttar Pradesh
E-mail: uwaisashraf@gmail.com

Acute rheumatic fever (ARF) is a multi-system disease caused by an abnormal immunological response after Group A β-hemolytic streptococcus (GABHS) infection. In 30-50% of cases, recurrent episodes of rheumatic fever (RF) may lead to chronic rheumatic heart disease (RHD), with progressive and permanent damage of the cardiac valves. The associated cardiac morbidity of RF with possible sequelae of heart failure, development of atrial fibrillation (AF), systemic embolism, transient ischemic attacks, strokes, endocarditis, the need for interventions

including cardiac surgery and impaired quality-of-life, and shortened life expectancy, impose a heavy burden and has major implications for the individual.

Arrhythmias, AF occurring in patients of RHD are associated with increased risk of stroke. In the Framingham Heart Study, patients with RHD and AF had a 17-fold increased risk of stroke compared with age-matched controls, and the attributable risk was 5 times greater in those with nonrheumatic AF. Holter monitoring is one of the most effective noninvasive clinical tools in the diagnosis and assessment of cardiac symptoms, prognostic assessment or risk stratification of various cardiac populations and in the evaluation of many cardiac therapeutic interventions. Data are limited regarding prevalence of arrhythmias in RHD patients and Holter monitoring is not part of their routine diagnostic work-up. The present work aims to study cardiac arrhythmias by Holter monitoring in patients of RF and RHD.

MATERIAL AND METHODS

This was an open-label, cross-sectional, hospital-based study. A total of 92 patients of ARF and RHD from Medicine OPD, Medicine IPD, CCU, Cardiology OPD, Pediatrics OPD, Pediatrics IPD of a tertiary care hospital in North India were recruited in this study. A detailed history and physical examination were carried out. Investigations carried out included, complete hemogram, blood urea, serum creatinine, urine analysis, liver function test, chest X-ray, electrocardiography (ECG), echocardiography and Doppler study. In patients of RF, additional investigations carried out were erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serological examination for streptococcal antibodies (antistreptolysin-O, antideoxyribonuclease B), throat culture or rapid antigen test for Group A streptococcus.

Ambulatory 24-hour Holter recordings were obtained in a standard fashion with 3-channel PC card recorders in all patients. All Holter recorders were subsequently analyzed using specialized software. All results were then visually analyzed to correct for artefact and any erroneous analysis.

STATISTICAL ANALYSIS

All statistical data were analyzed by using SPSS software version 20. Continuous variables were expressed as mean ± standard deviation (SD, Gaussian distribution) or range while proportions were expressed as percentages. Chi-square test was used for comparison of categorical variables between the groups, while unpaired *t*-test for independent samples was used for comparing continuous variables between two groups. Values of $p < 0.05$ were considered statistically significant.

RESULTS

Of the 92 patients studied, 84 had RHD and 8 had RF. Maximum number of patients was in the age group 31-40 years. Mean ± SD of age of RHD patients was 34.52 ± 14.47 years (range 13-76 years). Median age was 35 years.

Twenty-eight patients (33.33%) were males and 56 (66.67%) were females. Among the 56 females, 26.8% were seen in 31-40 years age group and around 8% were seen in more than 50 years age group. The most common valvular lesion in RHD patients was mitral stenosis seen in 73 (86.9%) patients, followed by mitral regurgitation seen in 64 (76.2%) patients. Almost equal number of patients had aortic regurgitation and tricuspid regurgitation, which was seen in 25 (29.8%) and 24 (28.6%) patients, respectively. Aortic stenosis was seen in 3 (3.54%) patients. None of the patients had tricuspid stenosis or involvement of pulmonary valve.

On echocardiography, range of left atrial diameter was 32-81 mm with mean of 50.45 ± 11.27 mm. Maximum mitral valve area was 4.40 cm^2 and minimum was 0.60 cm^2 with mean of 1.41 ± 1.15 cm^2. Range of ejection fraction was 18-76% with mean of 58.79 ± 10.44% (Table 1).

Figure 1 depicts scatter diagram showing plot of age and left atrial diameter on Echo of RHD patients.

Among the 53 patients who had sinus rhythm on baseline ECG, 13 patients were found to have paroxysmal AF detected on Holter monitoring. Out of 84 RHD patients, 39 patients were found to have pauses detected on Holter monitoring. Out of these 39, 25 patients were found to have pauses >2.5 seconds. Among 39 patients who had pauses detected on Holter monitoring, 26 had chronic AF. Presence of pauses was strongly associated with AF ($p < 0.001$). Among 13 patients who had pauses and were in sinus rhythm, 2 were found to have paroxysmal AF (Table 2).

Table 1. Echocardiography Findings

	Minimum	Maximum	Mean	SD
LA diameter (mm)	32.00	81.00	50.45	11.27
MVA (cm^2)	0.60	4.40	1.41	1.15
EF (%)	18.00	76.00	58.79	10.44

LA = Left atrial; MVA = Mitral valve area; EF = Ejection fraction.

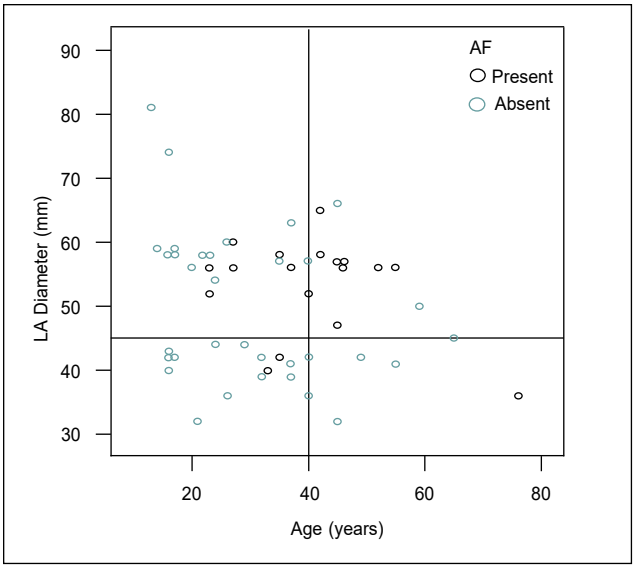


Figure 1. Scatter diagram showing plot of age and left atrial diameter on Echo of RHD patients.

Table 2. Presence of Atrial Fibrillation in Relation to Pauses on Holter Monitoring

		Atrial fibrillation		Total
		Present	Absent	
Pause	Present	26	13	39
	Absent	5	40	45
Total		**31**	**53**	**84**

Out of 84 patients, 48 had episodes of paroxysmal supraventricular tachycardia (PSVT) detected on Holter. Seventy-two patients were found to have premature ventricular contractions (PVCs) on ambulatory ECG monitoring. Twenty-five patients had Holter detected episodes of bigeminy and 29 patients had episodes of nonsustained ventricular tachycardia (NSVT) detected on Holter (Table 3).

The association of arrhythmias with age was evaluated. Pauses, PSVT, AF and NSVT were found to have a significant association with advanced age. There was an appreciable increase in these arrhythmias after the age of 40 years. Association of arrhythmias with increasing New York Heart Association (NYHA) class was found to be significant for pauses, PSVT, AF, couplets, bigeminy and trigeminy. Severity of mitral stenosis was significantly associated with presence of AF and PVCs. Severity of mitral regurgitation was significantly associated with AF. Severity of tricuspid regurgitation was found to have significant association

Table 3. Arrhythmias Seen in RHD Patients

Arrhythmia	No. of patients, n (%)
Pauses	39 (46.7)
PSVT	48 (57)
AF	31 (37)
Paroxysmal AF	30 (35.7)
PVC	72 (86)
Couplets	52 (62)
Bigeminy	25 (30)
Trigeminy	17 (20)
NSVT	29 (35)

Table 4. Association of Arrhythmias with Different Parameters

Parameter	Association	P value
Age	Yes	<0.001
NYHA class	Yes	0.032
Severity of MS	Yes	0.007
Severity of MR	No	0.110
Severity of TR	No	0.06
Severity of AS	No	0.596
Severity of AR	No	0.209

MS = Mitral stenosis; MR = Mitral regurgitation; TR = Tricuspid regurgitation; AS = Aortic stenosis; AR = Aortic regurgitation.

with presence of bigeminy and NSVT. No association was found between severity of aortic stenosis/aortic regurgitation and cardiac arrhythmias. Arrhythmias significantly associated with left atrial diameter >45 mm were pauses, AF, PVCs, bigeminy, trigeminy and NSVT (Table 4).

Paroxysmal AF was found to have a statistically significant association with advanced age, higher NYHA functional class and severity of mitral stenosis.

In our study, 8 patients had ARF. All patients were in 11-20 years age group. Mean ± SD of age of RHD patients was 13.25 ± 1.17 years with range of 12-15 years. Out of 8 patients in the RF group, 5 were females and 3 were males. Fever was the commonest clinical manifestation seen, being present in 7 (87.5%) patients. Among the major manifestations, polyarthritis and carditis were the commonest, both being present in 6 (75%) patients. One patient had chorea. None of the

patients had erythema marginatum or subcutaneous nodules. Two out of 8 patients gave prior history of sore throat infection 1-5 weeks before disease onset. Six out of 8 patients had mild mitral regurgitation, which was confirmed on echocardiography.

No other valvular involvement was seen. All patients were in NYHA Class I. The PR interval was prolonged in 2 patients and within normal limits in 6 patients. No advanced degree atrioventricular block was observed. None of the patients had junctional rhythm. Two patients had ventricular premature contractions in 24-hour ECG. In none of the patients, ventricular couplets were present and no ventricular runs were detected. Pauses >1.5 seconds were detected in 2 patients. The duration of the longest pause was 1.60 seconds. No patient had AF, PSVT or ventricular tachycardia.

DISCUSSION

Rheumatic heart disease is the world's most common acquired cardiovascular disease. Worldwide, this disease is the leading cause of heart failure in children and young adults, resulting in disability and premature death and severely affecting the workforce in the developing nations. Because secondary prevention can prevent adverse outcomes, early echocardiography-based identification of silent RHD (showing no clinical signs) with minimal valve lesions by active surveillance programs might be of major importance. In the present study, the commonest valvular lesion among RHD cases was combined mitral stenosis with mitral regurgitation, seen in 22 (26.2%) RHD cases, which was similar to the findings of Joseph et al and Melka A where this pattern was seen in 25.4% cases. However, other studies have reported mitral regurgitation to be the commonest valvular presentation in RHD cases. The differences in the pattern of involvement of valvular lesion could be possibly due to the difference in the age of subjects in various studies.

The mean left atrial diameter in our study was 50.45 ± 11.27 mm which was similar to the findings of Banerjee et al who found it to be 54.25 ± 1.48 mm. In current study, AF was present in 31 (37%) RHD patients on baseline ECG. Other studies have found rates ranging between 5.9% and 40%. Paroxysmal AF was detected on Holter in 13 out of 53 patients who had sinus rhythm on baseline ECG. This finding of 24% in our study was similar to the findings of 27% by Karthikeyan et al and 22.2% by Ramsdale et al.

PVCs occurred in 72 (85.7%) RHD patients, with couplets in 52 (62%) patients, bigeminy in 25 (29.7%) and trigeminy in 17 (20.2%) patients. This was similar to the findings of Ramsdale et al who found PVCs in 87.3% patients in a study done in Liverpool, UK. In our study, pauses were found in 39 (46.7%) patients detected on Holter monitoring. In a study done by Uebis et al to study asystolic pauses in 100 patients having AF by Holter monitoring, pauses longer than 2 seconds occurred in 57% of patients, but longer than 4 seconds only in 6 cases. They also found that a statistically higher frequency was seen in patients with permanent (78.3%) than in those with paroxysmal (24.5%) AF, and in patients with rheumatic valve disease (82.4%) in comparison with the rest (54.3%). They noted asystoles of up to 4 seconds duration in AF can be regarded as "normal" and longer asystoles must be anticipated particularly in patients with rheumatic valvular disease. It is only here that permanent pacemaker therapy appears to be indicated.

Pauses, PSVT, AF and NSVT were found to have a significant association with advanced age and were found to be more common in patients over 40 years of age. Paroxysmal arrhythmias were also found to be more common in advanced age by Ramsdale et al. Significant association of arrhythmias was found with increasing NYHA class for pauses, PSVT, AF, couplets, bigeminy and trigeminy. The possible explanation could be that patients who are having paroxysmal arrhythmias are more symptomatic and thus belong to higher NYHA functional class. Besides, the presence of arrhythmias not only indicates chronicity and severity of lesions but could also be contributing factor for higher NYHA functional class. In our study, subclinical AF detected on Holter was associated with increasing age, higher NYHA functional class and severe mitral stenosis. In our study, presence of PVCs was associated with severity of mitral stenosis. Also, AF was found to be strongly associated with severity of mitral stenosis. Similar findings were noted in earlier studies. Presence of AF was also associated with severity of mitral regurgitation. This may be due to the reason that majority of patients in our study had combined mitral stenosis and mitral regurgitation. A study done by Diker et al noted that the highest frequency of AF in RHD occurs in those with mitral stenosis, mitral regurgitation and tricuspid regurgitation in combination.

In patients of ARF, prior history of sore throat infection 1-5 weeks before disease-onset was found in 2 out of 8 cases and has ranged between 14% and 45.9% among cases in other studies. This wide variation in infection rates could be because of differing immunity

status and living conditions among patients in different parts of the world. Cases with sore throat reported at schools and villages should be immediately referred to health centers for confirmation. PR prolongation in many ARF patients has been a well-known finding since 1920.

In the present study, a pause >1.5 seconds on ECG was detected in 2 patients. The duration of the longest pause was 1.60 seconds. In the study by Karacan et al, on standard ECG, the frequency of the first-degree atrioventricular block was found to be 21.9%. ECG at 24 hours detected three additional and separate patients with a long PR interval. Mobitz type 1 block and atypical Wenckebach periodicity were determined in one patient (1.56%) on 24-hour ECG. Lower incidence of conduction abnormalities in our study could be due to small number of cases in our study. However, our results point towards the need of further Holter-based studies in patients of ARF. The prevalence of rhythm and conduction abnormalities may be much higher than determined on standard ECG.

CONCLUSION

Rheumatic heart disease is a significant health problem in our region. It commonly affects young patients, compromising the workforce of a country. Only more symptomatic, severe cases belonging to higher functional classes report to hospital. Around one-third of patients are already in AF when they first seek treatment. Even in those patients who are in sinus rhythm, various arrhythmias can be detected on Holter monitoring. Detection of paroxysmal AF on Holter can identify high-risk patients in which anticoagulation can be started and may prevent morbidity and mortality from stroke in such patients. Very few cases of RF report to hospital. Rhythm and conduction can be seen in RF patients also, although they are less common as compared to RHD patients. Very few Holter-based studies exist in literature to detect arrhythmias in patients of RHD and RF. Our study provides new insights as such a study has not been conducted previously in our region. More such studies are needed in future, so that high-risk patients can be identified and strategies can be formulated to improve outcomes in such patients.

SUGGESTED READING

1. Smith MT, Zurynski Y, Lester-Smith D, Elliott E, Carapetis J. Rheumatic fever - identification, management and secondary prevention. Aust Fam Physician. 2012; 41(1-2):31-5.
2. Delunardo F, Scalzi V, Capozzi A, Camerini S, Misasi R, Pierdominici M, et al. Streptococcal-vimentin cross-reactive antibodies induce microvascular cardiac endothelial proinflammatory phenotype in rheumatic heart disease. Clin Exp Immunol. 2013;173(3):419-29.
3. White H, Walsh W, Brown A, Riddell T, Tonkin A, Jeremy R, et al. Rheumatic heart disease in indigenous populations. Heart Lung Circ. 2010;19(5-6):273-81.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22(8):983-8.
5. Kennedy HL. The history, science, and innovation of Holter technology. Ann Noninvasive Electrocardiol. 2006;11(1):85-94.
6. Hegazy RA, Lotfy WN. The value of Holter monitoring in the assessment of pediatric patients. Indian Pacing Electrophysiol J. 2007;7(4):204-14.
7. Jackson SJ, Steer AC, Campbell H. Systematic Review: Estimation of global burden of non-suppurative sequelae of upper respiratory tract infection: rheumatic fever and post-streptococcal glomerulonephritis. Trop Med Int Health. 2011;16(1):2-11.
8. Carapetis JR. Acute rheumatic fever. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J (Eds.). Harrison's Principles of Internal Medicine. 18th Edition, New York: The McGraw-Hill Companies; 2012. pp. 2752-7.
9. Marijon E, Ou P, Celermajer DS, Ferreira B, Mocumbi AO, Jani D, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med. 2007;357(5):470-6.
10. Joseph N, Madi D, Kumar GS, Nelliyanil M, Saralaya V, Rai S. Clinical spectrum of rheumatic Fever and rheumatic heart disease: a 10 year experience in an urban area of South India. N Am J Med Sci. 2013;5(11):647-52.
11. Melka A. Rheumatic heart disease in Gondar College of Medial Sciences Teaching Hospital: socio-demographic and clinical profile. Ethiop Med J. 1996;34(4):207-16.
12. Fadahunsi HO, Coker AO, Usoro PD. Rheumatic heart disease in Nigerian children: clinical and preventive aspects. Ann Trop Paediatr. 1987;7(1):54-8.
13. Banerjee T, Mukherjee S, Ghosh S, Biswas M, Dutta S, Pattari S, et al. Clinical significance of markers of collagen metabolism in rheumatic mitral valve disease. PLoS One. 2014;9(3):e90527.
14. Chockalingam A, Gnanavelu G, Elangovan S, Chockalingam V. Clinical spectrum of chronic rheumatic heart disease in India. J Heart Valve Dis. 2003;12(5):577-81.
15. Karthikeyan G, Ananthakrishnan R, Devasenapathy N, Narang R, Yadav R, Seth S, et al. Transient, subclinical atrial fibrillation and risk of systemic embolism in patients with rheumatic mitral stenosis in sinus rhythm. Am J Cardiol. 2014;114(6):869-74.

16. Ramsdale DR, Arumugam N, Singh SS, Pearson J, Charles RG. Holter monitoring in patients with mitral stenosis and sinus rhythm. Eur Heart J. 1987;8(2):164-70.
17. Uebis R, Merx W, Fritzsche V. Asystolic pauses in atrial fibrillation. Incidence, dependence on the underlying disease and significance for pacemaker therapy. Dtsch Med Wochenschr. 1985;110(30):1157-60.
18. Moreyra AE, Wilson AC, Deac R, Suciu C, Kostis JB, Ortan F, et al. Factors associated with atrial fibrillation in patients with mitral stenosis: a cardiac catheterization study. Am Heart J. 1998;135(1):138-45.
19. Diker E, Aydogdu S, Ozdemir M, Kural T, Polat K, Cehreli S, et al. Prevalence and predictors of atrial fibrillation in rheumatic valvular heart disease. Am J Cardiol. 1996;77(1):96-8.
20. Arora R, Subramanyam G, Khalilullah M, Gupta MP. Clinical profile of rheumatic fever and rheumatic heart disease: a study of 2,500 cases. Indian Heart J. 1981;33(6):264-9.
21. Clarke M, Keith JD. Atrioventricular conduction in acute rheumatic fever. Br Heart J. 1972;34(5):472-9.
22. Hoffman TM, Rhodes LA, Pyles LA, Balian AA, Neal WA, Einzig S. Childhood acute rheumatic fever: a comparison of recent resurgence areas to cases in West Virginia. W V Med J. 1997;93(5):260-3.
23. Karacan M, Işıkay S, Olgun H, Ceviz N. Asymptomatic rhythm and conduction abnormalities in children with acute rheumatic fever: 24-hour electrocardiography study. Cardiol Young. 2010;20(6):620-30.

■■■■

Mental Illness Linked to Worse COVID-19 Outcomes, Including Death

A large meta-analysis suggests that pre-existing mental illness is linked with worse COVID-19 outcomes, including death.

The meta-analysis included 16 studies involving 6,34,338 COVID-19 patients. A total of 68,023 (10.7%) patients had been diagnosed with a mental disorder prior to testing positive for COVID-19. In the studies providing data about types of mental disorders, 43% of patients had mood disorders and 16% had schizophrenia, schizotypal disorder and delusional disorders. A model including all 16 studies, but not fully adjusted, showed that prediagnosis with mental disorders was associated with a significant increase in the risk for severe COVID-19 and mortality. The findings were published online in *Psychiatry Research*… (*Medscape*)

Pfizer Says Its Vaccine is Over 91% Effective After 6 Months

The Pfizer-BioNTech vaccine continued to be highly effective against COVID-19 after 6 months, suggest long-term results from a trial.

Follow-up data from the final-stage trial involving 46,307 individuals suggests that the vaccine was 91.3% effective in preventing symptomatic cases starting 1 week after the second dose until about 6 months. In the US alone, the vaccine had an efficacy rate of 92.6%. The companies also provided some of the initial data on how the vaccine might handle the B.1.351 variant that was first identified in South Africa. Nine of the 800 participants in that country contracted COVID-19, including 6 infected with B.1.351 variant. However, all of them were in the placebo group, thus suggesting that the vaccine was effective against the variant… (*NDTV – Bloomberg*)

Children Likely at the Forefront in Spread of COVID-19 Variants

Public health officials in the United States have expressed concern over the sharp new rise in COVID-19 cases in children.

The surge seems to be pushed by increased circulation of the more contagious variants, at a time when children and adolescents are returning to in-person activities like sports, classes, etc. In the previous surges, children did not play a major role in transmitting the infection. When diagnosed with COVID-19, their symptoms were mild or even absent, and it was noted that they were not usually the first cases in households or clusters. But now, as variants have started dominating, and seniors are gaining protection with the help of vaccines, the pattern may be changing. Infectious disease experts are on the vigil to see if COVID-19 will start spreading in a manner more similar to influenza, where children become infected first and take the infection home… (*Medscape*)

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Tropical Spastic Paraparesis Management with Herbal Neurogenic: A New Hope

AVINASH SHANKAR*, AMRESH SHANKAR†, ANURADHA SHANKAR‡

ABSTRACT

Tropical spastic paraparesis (TSP), a disease of the nervous system, is caused by human T-lymphotropic virus type 1, thus also known as HTLV-1 associated myelopathy. It is common among females of age group 30-50 years. In spite of advancement in diagnostic procedures, i.e., CT scan, MRI, etc., its treatment with α-interferon, steroids, antiviral drugs, neuro-vitamin supplementation, physiotherapy fails to ensure cure or improve quality-of-life except transient pain relief with analgesics and muscle relaxants. Thus, a therapeutic regime composite consisting of a proven herbal neurogenic has been evaluated. **Objective of the study:** To assess the herbal neurogenic and immune boosting composite in ensuring clinical relief and improving quality-of-life in patients deterred from various medicenters without any relief. **Material and methods:** Sixty-three diagnosed and already treated cases of tropical spastic paraparesis, attending the Centre for Critical Care, National Institute of Health and Research, Warisaliganj (Nawada), Bihar, were selected, interrogated, examined clinically, assessed and analyzed for their previous investigation reports, therapy taken and their effect. Irrespective of their clinical severity, all patients were advocated the prescribed regime and were followed for 2 years post-therapy for which patients were given a follow-up card to record the changes. **Result:** Approximately 88.9% patients had Grade I clinical response while rest 11.1% had Grade II clinical response without any untoward effect or any withdrawal during post-therapy 2 years follow-up. **Conclusion:** The present regime constituting intravenous calcium gluconate, intravenous methylcobalamin + pyridoxine + niacin, self-blood (2 mL) and intramuscular betamethasone 2 mg, capsule cholecalciferol 60K, syrup herbal neurotonic proved its worth in the management of TSP even in chronic and long-term treated cases.

Keywords: Tropical spastic paraparesis, human T-lymphotropic virus type 1, CT, MRI, herbal neurogenic, quality-of-life

Tropical spastic paraparesis (TSP), a chronic and progressive clinical condition affecting the nervous system, remained of obscure etiopathogenesis for long, but nowadays, an important association of this condition has been established with human retrovirus (Human T-cell lymphotropic virus type 1), thus this condition is also termed as HTLV-1 associated myelopathy (HAM).

As per World Health Organization (WHO) estimate, worldwide 10-20 million people are carrying HTLV-1 and 5% of them are affected with TSP in the age group of 30-50 years.

TSP is very common in Latin America, the Caribbean Basin, sub-Saharan Africa and Japan, but these days, incidence of this clinical state is increasing even in India.

Common presentation of the clinical condition is:

- Gradual weakening and stiffening of lower extremity
- Radiating back pain down to legs
- Burning and pricking sensation (paresthesia)
- Urinary and bowel function disturbances
- Erectile dysfunction in males
- Inflammatory skin condition, like dermatitis or psoriasis
- Rarely may present with eye inflammation, arthritis and muscle inflammation.

The common mode of transmission of this virus is through:

- Breastfeeding

*Chairman
National Institute of Health and Research, Warisaliganj (Nawada), Bihar
†Director (Hon)
Aarogyam Punarjeevan, Patna, Bihar
‡Ex-Director, Centre for Indigenous Medicine and Research and Senior Research Fellow, Regional Institute of Ayurveda, Itanagar, Arunachal Pradesh
Address for correspondence
Dr Avinash Shankar
Chairman
National Institute of Health and Research
Warisaliganj (Nawada), Bihar
E-mail: dravinashshankar@gmail.com

- Sharing infected needles during intravenous drug use
- Sexual activity
- Blood transfusions.

In spite of advancement in diagnostics (computed tomography [CT] scan and magnetic resonance imaging [MRI]) and its established etiopathogenesis, till date, no established therapeutic regime has ensured its reversal but only symptomatic relief through α-interferon, intravenous immunoglobulin, antiviral drugs and muscle relaxants is available.

Signs and symptoms vary but may include slowly progressive weakness and spasticity of one or both legs, exaggerated reflexes, muscle contractions in the ankle and lower back pain. Other features may include urinary incontinence and minor sensory changes, especially burning or prickling sensations and loss of vibration sense.

Considering the poor quality-of-life with present therapeutics, a clinical study was planned to evaluate the clinical efficacy of proved neurogenic herbal composite with neuromodulator at National Institute of Health and Research and Centre for Research in Indigenous Medicine.

OBJECTIVE OF THE STUDY

To evaluate the clinical efficacy and safety profile of herbal neurogenic with neuromodulator in TSP.

Duration of Study

January 2014 to December 2018.

MATERIAL AND METHODS

Material

Proved and treated cases of TSP without any clinical response, attending the Centre for Critical Care, National Institute of Health and Research, Warisaliganj (Nawada), Bihar were considered for evaluation of the herbal neurogenic constituting therapeutic regime.

Methods

Patients of spastic paraparesis diagnosed by myelogram, CT and MRI were interrogated thoroughly for the onset, duration and evolution of the disease, family history of neurological illness, history of extramarital sexual exposure, abortion, blood transfusions, dietary choices with emphasis on strict vegetarianism, *Lathyrus sativus* use, socioeconomic status, housing, sanitary conditions, treatment taken and their response. A detailed general examination and a meticulous neurological assessment were done.

Based on clinical presentation, patients were classified as summarized in Table 1.

Patients were investigated for hemoglobin concentration, total and differential leukocyte count, erythrocyte sedimentation rate (ESR), peripheral smear, fasting and postprandial blood sugar, renal and liver function tests and serological test for syphilis. Common presentation of TSP is summarized in Table 2.

All patients underwent conventional myelography, CT and MRI scans. The serum samples of all the patients were tested for HTLV-1 antibodies by the Serodia technique. All patients presenting with this crippling disease were advised and administered the following therapeutic regime after due awareness counseling and encouragement:

- Injection calcium gluconate 1 amp every 15th day intravenous, very slow
- Injection methylcobalamin + pyridoxine + niacinamide + pantothenic acid + betamethasone every week

Table 1. Clinical Presentation-based Classification

Severity Grade	Characteristics
Mild	Patients presenting with back pain, tingling and numbness in the leg
Moderate	Patient presenting with back pain, tingling and numbness, tendency to fall, heaviness in the lower extremity, leg weakness
Severe	Back pain, gait disturbance, stumbling, leg weakness, hyperreflexia and extensor plantar reflex, overactive bladder, constipation and sexual dysfunction

Table 2. Common Presentation of Tropical Spastic Paraparesis

Disturbances	Symptoms	Signs
Motor	Gait disturbance, tendency to fall, stumbling and leg weakness	Spastic paraparesis, weakness hyperreflexia lower limb, clonus, extensor plantar reflex
Sensory	Pain, numbness at lumbar level and backache	Feet paresthesia, loss of light touch sensory level at lower thoracic level
Autonomic	Urinary dysfunction, constipation, sexual dysfunction	Neurogenic or overactive bladder, diminished peristalsis, erectile dysfunction

- Injection self-blood + betamethasone 2 mg every 10th day intramuscular
- Capsule vitamin D_3 60K every week orally
- Syrup herbal neurogenic 10 mL every 12 hours/ Capsule herbal neurogenic 1 cap every 12 hours
- Active and passive exercise of the extremity
- Diet: High protein vegetarian diet.

Herbal composite neurogenic capsule 500 mg or syrup 5 mL constitutes 100 mg each of *Acorus calamus* (rhizome), *Nardostachys jatamansi* (flower), *Herpestis monniera* (leaf), *Convolvulus pluricaulis* (flower) and *Cassia acutifolia* (seed).

Patients were assessed for improvement in tone and power of the muscle, tingling and numbness, gait and autonomic function (passage of stool and urine) for which patients were given a follow-up card to mention date of achievement and any untoward manifestation experienced. Patients were advised to visit the center on any unusual manifestation or contact on helpline for needful redresses. To adjudge the safety profile of the regime practiced, basic bio-parameters were repeated every month for first 3 months and then every 3 months.

Based on the clinical outcome and safety profile therapeutic response was graded as Table 3.

RESULT

Sixty-three identified, diagnosed and treated patients of TSP were considered for the study and out of them, majority (30/63) were in the age group 30-35 years with female dominance (Table 4 and Fig. 1) and all were from rural background. The community representation is depicted in Figure 2.

Majority of the patients was nonvegetarian and none had any history of taking *Lathyrus sativus* (Fig. 3).

The age of onset of clinical presentation varied from 20 to 40 years and duration of illness from 1 to 12 years (Fig. 4). Symptoms at the onset were difficulty

Table 3. Grade of Therapeutic Response

Clinical Grade	Characteristics
Grade I	Complete recovery of power and tone without any residual neurological deficit and adversity
Grade II	Improvement in power and tone with residual paresis and sensory deficit without any adversity
Grade III	No alteration in status

Table 4. Distribution of Patients as per Age and Sex

Age group (years)	Number of patients		
	Male	Female	Total
30-35	02	28	30
35-40	04	12	16
40-45	-	06	06
45-50	-	11	11

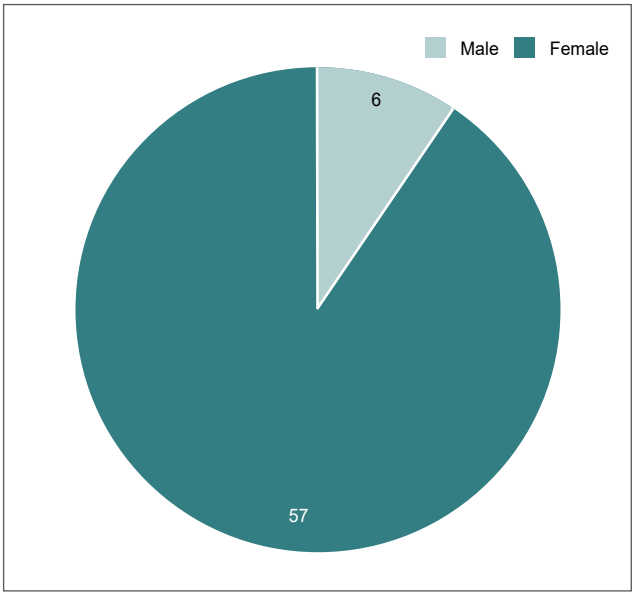


Figure 1. Pie diagram showing distribution as per sex.

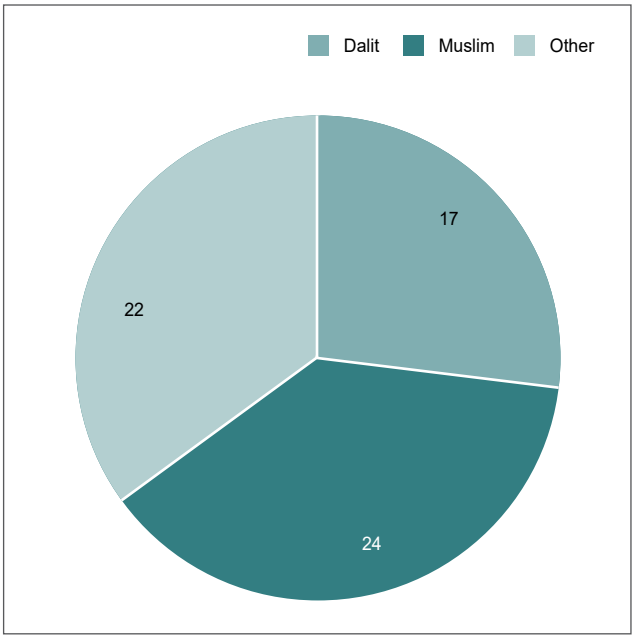


Figure 2. Pie diagram showing distribution of patients as per community.

in walking, stiffness of legs, back pain, weakness of legs, leg pain and urinary discomfort (Table 5) while presentation at our center included disturbed gait, leg stiffness, back pain, leg pain, urinary discomfort, urinary retention, tingling and numbness and erectile dysfunction in males (Table 5).

No history of blood transfusion, abortion, delivery or surgery prior to onset of the disease was evident but serum samples tested positive for HTLV-1 in 49 cases out of 63 (Fig. 5). In addition, all the bio-parameters (hepatic, hematological and renal profile) were normal. No patients were positive for tuberculosis, any sexually transmitted disease. In terms of clinical severity, out of 63 patients, 13 were of moderate and 50 were of severe status (Fig. 6).

Patients had taken treatment with α-interferon, muscle relaxants, neuro-vitamin supplementation at various medicare centers without any positive therapeutic outcome (Table 6). Symptomatic relief started from 4th week of therapy and by 24th week, all had symptomatic relief (Fig. 7).

The minimum and maximum duration of therapy required for complete reversal of clinical presentation

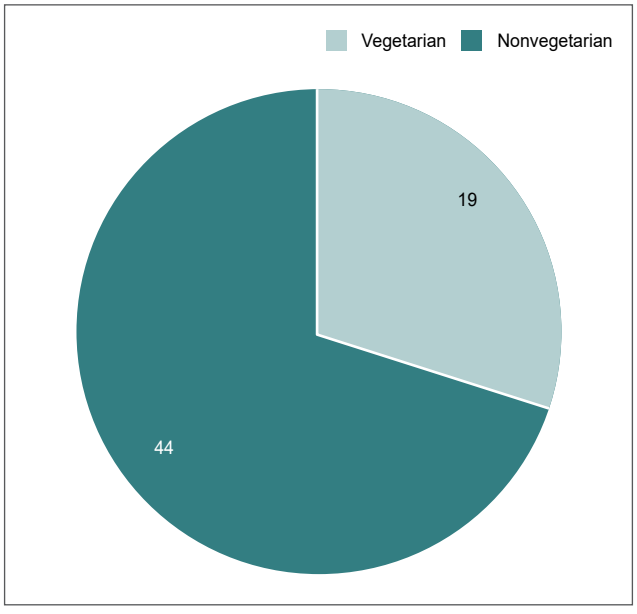


Figure 3. Pie diagram showing distribution of patients as per dietary status.

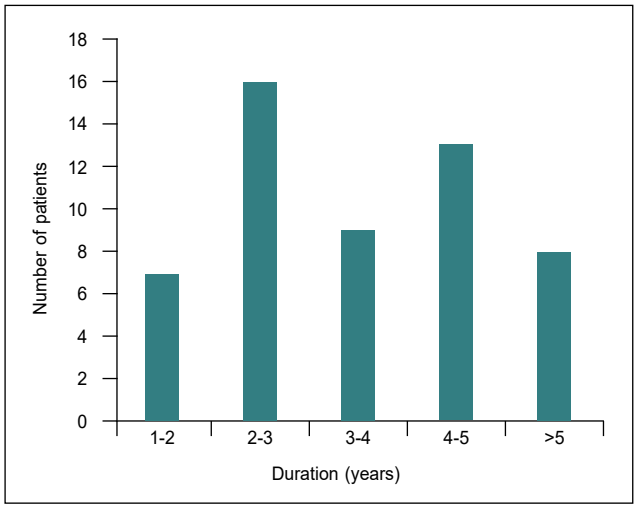


Figure 4. Bar diagram showing distribution of patients as per duration of illness.

Table 5. Distribution of Patients as per their Clinical Presentation

Clinical presentation	Number of patients
Difficulty in walking	63
Leg stiffness	63
Back pain	43
Weakness of the legs	63
Leg pain	63
Tingling and numbness	63
Gait disturbance	50
Urinary discomfort	50
Sexual weakness	06
History of surgery, abortion and blood transfusion	None

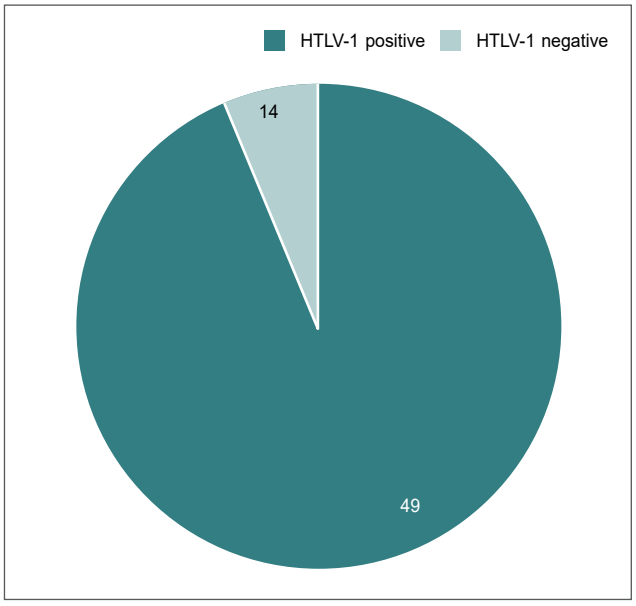


Figure 5. Pie diagram showing HTLV-1 status of the patients.

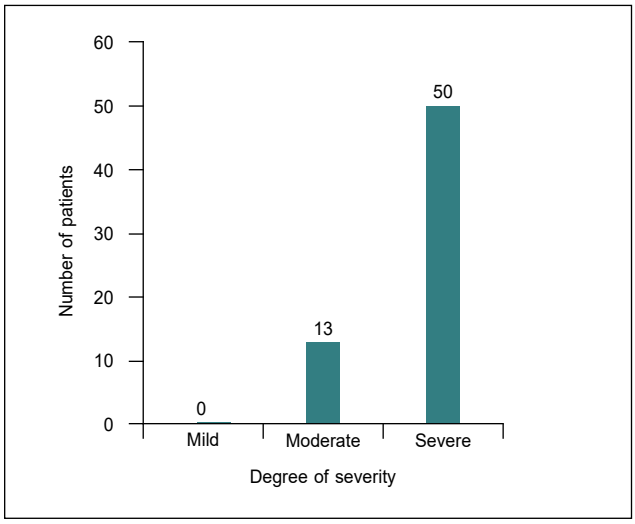


Figure 6. Bar diagram sowing clinical severity of illness.

Table 6. Treatments Taken in Past

Therapy taken	Number of patients
α-interferon	43
Antiviral drug	49
Muscle relaxants	63
Neuro-vitamin supplement	63
Active and passive exercise	63

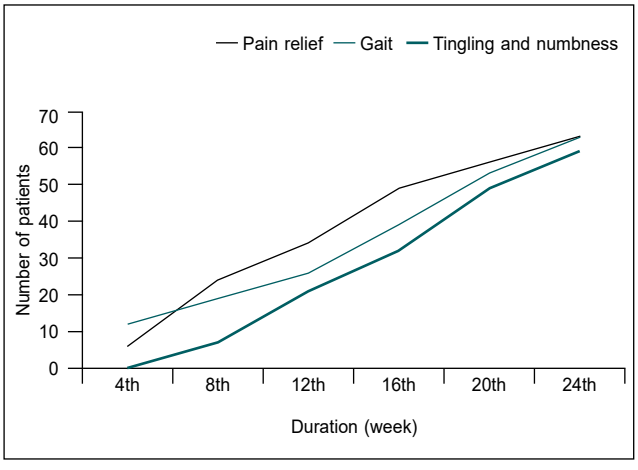


Figure 7. Graph showing duration required for improvement in presentation.

(both symptom and sign) was 9 months and 2 years, respectively. In all, 56 patients achieved Grade I clinical improvement and 7 achieved Grade II improvement (Fig. 8). No patients had shown any adversity, recurrence of presentation or any alteration in bio-parameters in 2 years of post-therapy follow-up (Table 7).

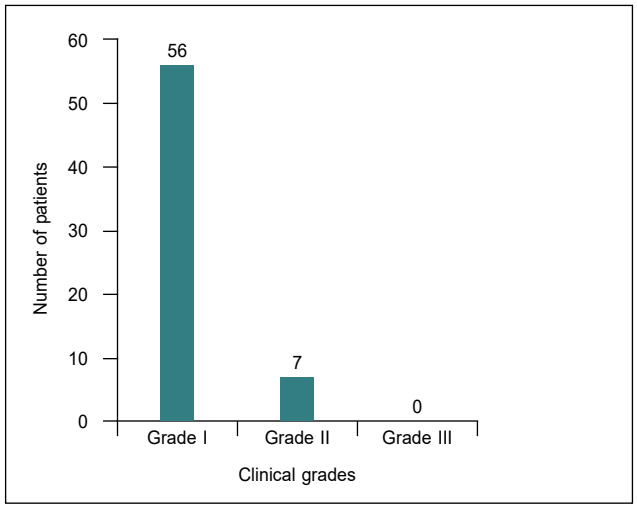


Figure 8. Bar diagram showing grades of clinical response.

DISCUSSION

Tropical spastic paraparesis is becoming a common neurological disorder in India though it is common in different parts of the world including Jamaica, Martinique, Seychelles, Colombia and Japan. While it was considered as a neurological disorder of obscure etiology, these days, it is proved to be caused by HTLV-1. In spite of advancement in diagnostics like CT, MRI, cerebrospinal fluid (CSF) and serum for HTLV-1 antigen, the therapeutics used, i.e., α-interferon, muscles relaxant and neuro-vitamin supplement, fail to ensure cure or improve quality-of-life, except for transient symptomatic relief.

The current study showed clinical supremacy in terms of marked improvement in pain, sensation and gait of the already treated patients with other regime and achieving Grade I clinical response in 88.9% patients and Grade II in rest 11.1%. No patients had any withdrawal or drug adversity in 2 years post-therapy follow-up. This clinical efficacy can be explained considering the pathogenesis and causation due to HTLV-1 infected T cells (Fig. 9).

Self-blood with betamethasone intramuscular induces antibody formation against the released toxin and ensure their neutralization, while betamethasone, acting as anti-inflammatory agent, reduces neural edema, which is synergized by intravenous calcium administration.

Methylcobalamin, pyridoxine, niacin and pantothenic acid support neural cells in its normal neural conduction and a herbal neurogenic, by its neurogenic activity helps in restoration of neural viability and vitality which combinely ensure relief in pain, neuropathic

Table 7. Outcome of the Study

Particulars	**Number of patients**								
Duration in months	**1**	**2**	**3**	**4**	**5**	**6**	**9**	**12**	**24**
Clinical relief	6	24	34	44	56	63	63	63	63
Back pain	14	24	32	45	63	63	63	63	63
Tingling numbness	12	19	26	39	53	63	63	63	63
Pain in legs	12	21	24	37	48	63	63	63	63
Autonomic disturbance	–	–	19	30	42	50	63	63	63
Gait	–	4	14	22	32	50	63	63	63
Post-therapy bio-parameters									
Hepatic profile:									
SGOT (<35 IU)	63	63	63	63	63	63	63	63	63
SGPT (<35 IU)	63	63	63	63	63	63	63	63	63
Alkaline phosphatase (<100)	63	63	63	63	63	63	63	63	63
Renal parameters									
Blood urea (<26 mg%)	63	63	63	63	63	63	63	63	63
Serum creatinine (<1.5 mg%)	63	63	63	63	63	63	63	63	63
Urine									
Albumin-Negative	63	63	63	63	63	63	63	63	63
RBC-Negative	63	63	63	63	63	63	63	63	63
Hematological									
Hemoglobin (>10 gm%)	52	58	59	63	63	63	63	63	63
Clinical grade									
Grade I									56
Grade II									07
Grade III									

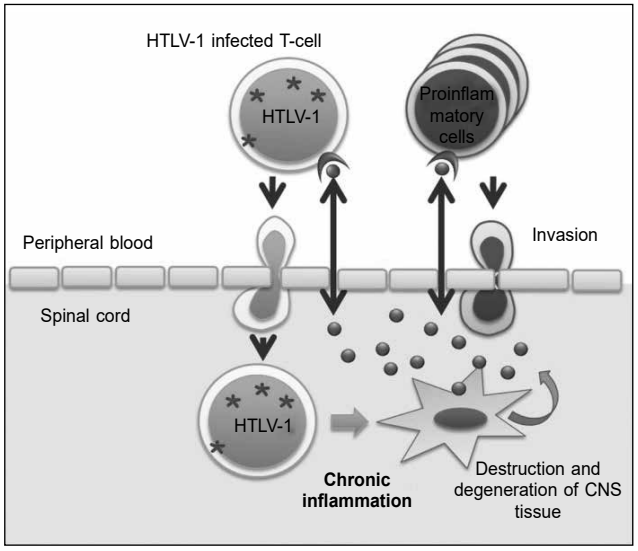


Figure 9. Pathogenesis and causation due to HTLV-1 infected T cells.

manifestation, gait and autonomic function and provide better quality-of-life to all.

CONCLUSION

Present regime constituting calcium gluconate intravenous, methylcobalamin + pyridoxine + niacin intravenous, self-blood (2 mL) and betamethasone 2 mg intramuscular, capsule cholecalciferol 60K, syrup herbal neurogenic proved its worth in the management of TSP even in chronic and long-term treated cases.

SUGGESTED READING

1. World Health Organization (WHO). Report of the scientific group on HTLV-1 and diseases, Kagoshima, Japan, December, 1988. Virus Diseases, Human T-lymphotropic virus type 1, HTLV-1. Wkly Epidemiol Rec. 1989;64:382-3.

2. Orland JR, Engstrom J, Fridey J, Sacher RA, Smith JW, Nass C, et al; HTLV Outcomes Study. Prevalence and clinical features of HTLV neurologic disease in the HTLV Outcomes Study. Neurology. 2003;61(11):1588-94.
3. Blattner WA, Gallo RC. Epidemiology of human retroviruses. Leuk Res. 1985;9(6):697-8.
4. Oomman A, Madhusoodanan M. Tropical spastic paraparesis in Kerala. Neurol India. 2003;51(4):493-6.
5. Román GC. The neuroepidemiology of tropical spastic paraparesis. Ann Neurol. 1988;23 Suppl:S113-20.
6. Arango C, Concha M, Zaninovic V, Corral R, Biojo R, Borrero I, et al. Epidemiology of tropical spastic paraparesis in Columbia and associated HTLV-1 infection. Ann Neurol. 1988;23 Suppl:S161-5.
7. Richardson JH, Newell AL, Newman PK, Mani KS, Rangan G, Dalgleish AG. HTLV-I and neurological disease in South India. Lancet. 1989;1(8646):1079.
8. Gessain A, Barin F, Vernant JC, Gout O, Maurs L, Calender A, et al. Antibodies to human T-lymphotropic virus type-I in patients with tropical spastic paraparesis. Lancet. 1985;2(8452):407-10.
9. Rubin M. Tropical spastic paraparesis/HTLV-1–associated myelopathy (TSP/HAM). Merck Manual. October, 2016. Available at: http://www.merckmanuals.com/professional/neurologic-disorders/spinal-cord-disorders/tropical-spastic-paraparesis-htlv-1%E2%80%93associated-myelopathy-tsp-ham.
10. Tropical spastic paraparesis information page. National Institute of Neurological Disorders and Stroke. Available at: https://www.ninds.nih.gov/Disorders/All-Disorders/Tropical-Spastic-Paraparesis-Information-Page. Accessed on Dec 7, 2017.
11. Iwasaki Y. Pathology of chronic myelopathy associated with HTLV-I infection (HAM/TSP). J Neurol Sci. 1990;96(1):103-23.
12. Izumo S, Umehara F, Osame M. HTLV-1 associated myelopathy. Neuropathology. 2000;20:565-8.
13. Osame M. Pathological mechanisms of human T-cell lymphotropic virus type I-associated myelopathy (HAM/TSP). J Neurovirol. 2002;8(5):359-64.
14. Lezin A, Olindo S, Oliere S, Varrin-Doyer M, Marlin R, Cabre P, et al. Human T lymphotropic virus type I (HTLV-I) proviral load in cerebrospinal fluid: a new criterion for the diagnosis of HTLV-I-associated myelopathy/tropical spastic paraparesis? J Infect Dis. 2005;191(11):1830-4.
15. Matsuzaki T, Nakagawa M, Nagai M, Usuku K, Higuchi I, Arimura K, et al. HTLV-I proviral load correlates with progression of motor disability in HAM/TSP: analysis of 239 HAM/TSP patients including 64 patients followed up for 10 years. J Neurovirol. 2001;7(3):228-34.
16. De Castro-Costa CM, Araújo AQ, Barreto MM, Takayanagui OM, Sohler MP, da Silva EL, et al. Proposal for diagnostic criteria of tropical spastic paraparesis/HTLV-I-associated myelopathy (TSP/HAM). AIDS Res Hum Retroviruses. 2006;22(10):931-5.
17. Bagnato F, Butman JA, Mora CA, Gupta S, Yamano Y, Tasciyan TA, et al. Conventional magnetic resonance imaging features in patients with tropical spastic paraparesis. J Neurovirol. 2005;11(6):525-34.
18. Scadden DT, Freedman AR, Robertson P. Human T-lymphotropic virus type I: Disease associations, diagnosis, and treatment. Waltham, MA: UpToDate; February 16, 2016. Available at: http://www.uptodate.com/contents/human-t-lymphotropic-virus-type-i-disease-associations-diagnosis-and-treatment.
19. Sandbrink F. Tropical myeloneuropathies treatment & management. January 2015. Available at: http://emedicine.medscape.com/article/1166055-treatment.
20. Arimura K, Nakagawa M, Izumo S, Usuku K, Itoyama Y, Kira J, et al. Safety and efficacy of interferon-alpha in 167 patients with human T-cell lymphotropic virus type 1-associated myelopathy. J Neurovirol. 2007;13(4):364-72.
21. Croda MG, de Oliveira AC, Vergara MP, Bonasser F, Smid J, Duarte AJ, et al. Corticosteroid therapy in TSP/HAM patients: the results from a 10 years open cohort. J Neurol Sci. 2008;269(1-2):133-7.
22. Taylor GP, Goon P, Furukawa Y, Green H, Barfield A, Mosley A, et al. Zidovudine plus lamivudine in human T-lymphotropic virus type-I-associated myelopathy: a randomised trial. Retrovirology. 2006;3:63.

■■■■

New Risk Factors Tied to Increased Risk of COVID-19 Identified in Study

Researchers have identified associations between certain lifestyle factors and an individual's risk of getting COVID-19 infection.

It is known that people with type 2 diabetes and a high body mass index (BMI) have an increased risk of hospitalizations and other severe complications related to COVID-19. They also have a greater risk of getting the symptomatic infection in the first place, reported a recent study published in the journal *PLoS One*. Investigators noted that those with positive COVID-19 test results had a greater likelihood of being obese or having type 2 diabetes. Those who tested negative had higher odds of having high levels of high-density lipoprotein (HDL) cholesterol and a healthy weight with a normal BMI… (*HT – ANI*)

Real is Rare

in the management of anemia

℞ **DEXORANGE®**

Syrup/Capsules/Paediatric Syrup

(Ferric Ammonium Citrate)

The Masterpiece in Hematinics

℞ In Anemia associated with

- Pregnancy & Lactation
- General Weakness
- Menorrhagia
- Chemotherapy Induced Anemia
- Nutritional & Iron deficiency
- Lack of Appetite
- Chronic Gastrointestinal Blood Loss
- Chronic Kidney Disease

FRANCO-INDIAN
PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

2021

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Herpes Zoster Ophthalmicus in Healthy 13-month Infant: An Unforeseen Scenario

DHAVALKUMAR S BANSODE*, SONIA P JAIN†, ABHAY DESHMUKH‡, PRATIKSHA MORESHWAR SONKUSALE#

ABSTRACT

Herpes zoster (HZ) as well as varicella are caused by varicella-zoster virus. It is uncommon in children. Cases have been reported in literature among all ages from neonate to old age. We report this case of HZ ophthalmicus in a healthy child born to healthy mother with a history of varicella infection in the third trimester (7th month of gestation). Early diagnosis and treatment reduce complications. Preconceptional varicella-zoster vaccine is also a matter of concern.

Keywords: Herpes zoster ophthalmicus, infant, varicella-zoster vaccine, varicella-zoster

Herpes zoster (HZ) and varicella are caused by the same virus, i.e., varicella-zoster virus.[1] Cases have been reported in medical literature from neonates to old age, but it is rare in immunocompetent children. Overall incidence of HZ is 3.4/1,000 people, whereas in children in the age group of 0-9 years and 10-19 years it is 0.74 and 1.38, respectively.[2] Herpes zoster ophthalmicus (HZO) is caused by varicella-zoster virus 3, i.e., human herpes virus 3.

Presented here is the case of a 13-month-old baby with HZO.

CASE REPORT

A 13-month-old, 7.5 kg, female child, born full-term, normal vaginal delivery, was brought with vesicular eruptions over right side of forehead, erythema and swelling over right upper eyelid since 4 days. It was accompanied with photophobia and watery discharge from the right eye. Cutaneous examination revealed multiple, tense, grouped vesicular lesions with erosions and yellow crust on erythematous base present over scalp, forehead extending to right periorbital region, nasal bridge and tip of nose (Fig. 1), suggesting involvement of nasociliary branch of the ophthalmic division of right trigeminal nerve, thus positive Hutchinson's sign. There was marked erythema and swelling of the right upper eyelid with difficulty in opening of right eye.

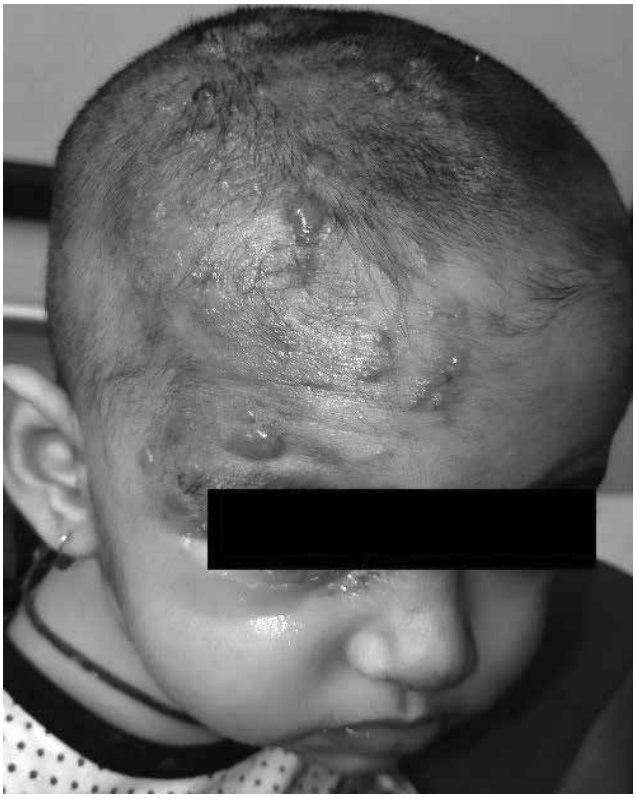


Figure 1. Vesicular eruption over right side of forehead, nose and tip of nose with marked erythema and swelling of right upper eyelid.

*Junior Resident
†Professor
Dept. of DVL
‡Assistant Professor, Dept. of Pathology
#Assistant Professor, Dept. of DVL
MGIMS, Sevagram, Wardha, Maharashtra
Address for correspondence
Dr Sonia P Jain
A-14, Dhanvantri Nagar, MGIMS, Sevagram, Wardha - 442 102, Maharashtra
E-mail: soniapjain@rediffmail.com

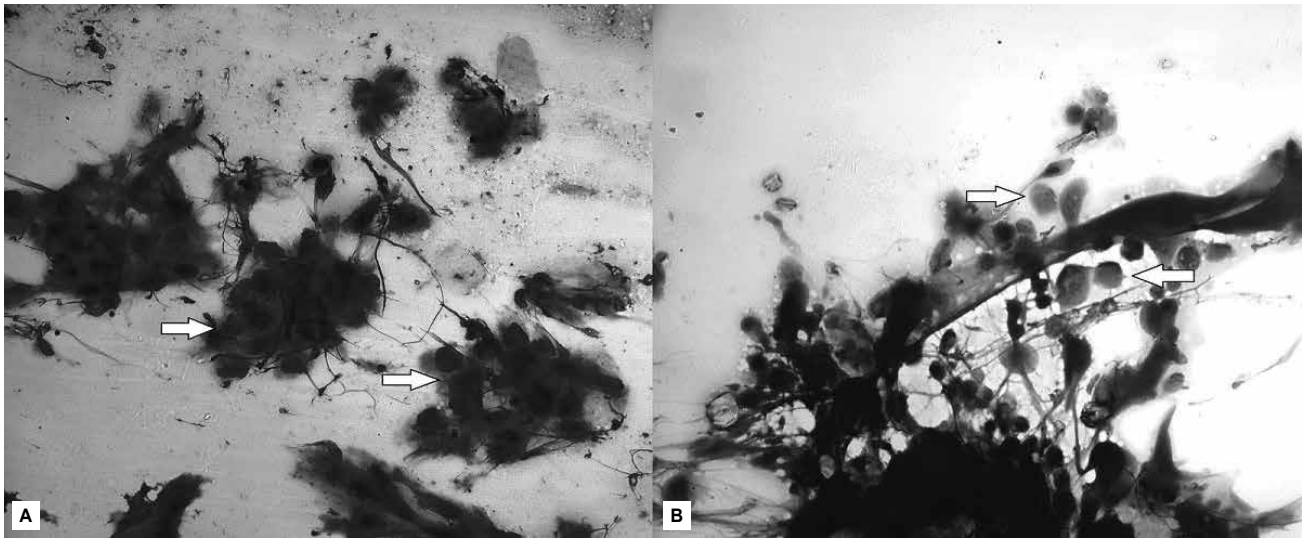


Figure 2. Smear showing presence of multinucleated giant cells (*white arrow*) (Giemsa, x400) **(A)** and acantholytic cells (*white arrow*) (PAP, x400) **(B)**.

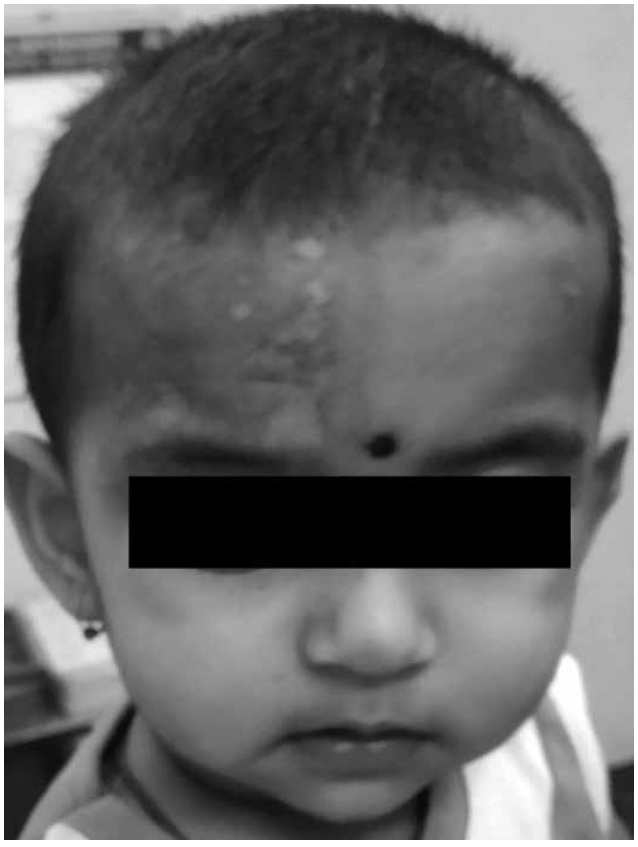


Figure 3. Complete resolution after 1 week of treatment.

On ophthalmic consultation, tobramycin eye drop twice and lubricating eye drop four times a day were started. Visual acuity was difficult to assess. Left eye was normal. There was no past history of varicella in the infant and neither was she vaccinated for varicella. Her mother had developed varicella infection during 7th month of gestation and was treated with tablet acyclovir five times a day for 7 days with other symptomatic drugs. Systemic examination and developmental milestones of the child were assessed by pediatrician and were normal. Child was irritable and so, was admitted. Treatment with injection acyclovir 75 mg intravenously three times a day for 7 days was initiated. Antibiotics were started to combat secondary bacterial superinfection. Topical mupirocin ointment and acyclovir eye drops were also added. Giemsa stained Tzanck smear showed presence of multinucleated giant cells, an epithelial cell containing numerous nuclei (Fig. 2A). Papanicolaou stained smear from scraping showed presence of acantholytic cells (Fig. 2B). Parents and child were also screened for human immunodeficiency virus (HIV) and both of them along with child came nonreactive for both HIV type I and II. Symptoms subsided remarkably within 1 week of treatment (Fig. 3). Right eye showed hyperemic conjunctiva with no other signs of ocular involvement.

DISCUSSION

Herpes virus is a neurotropic virus.[3] HZ occurs more commonly in elderly patients but is rare in childhood.[4] It has milder course with less residual damage in children than adults.[5] Varicella-zoster virus is responsible for both varicella and HZ.[1] Once a person suffers from varicella infection, the virus remains dormant in dorsal ganglion of spinal nerve root of spinal cord.[2] As immunity decreases, these virus reactivate to produce HZ.[2] If mother suffers from varicella infection in second-half of pregnancy, then there are higher chances

of the child suffering from HZ in 1st year of life.[6] Similar observation was seen in our case. Infantile HZ is due to intrauterine infection of varicella-zoster virus than postnatal.[6] Generally HZ occurs in children with immunodeficiency like malignancy or HIV infection, but it can also occur in immunocompetent individuals.[5] HZ affects eye in 10-20% cases.[4]

Hutchinson's sign is presence of vesicles on tip/side of nose which indicate involvement of nasociliary nerve of ophthalmic division of trigeminal nerve.[7] If Hutchinson's sign is positive, it means sight-threatening ocular changes can occur.[8] In our case, there was involvement of tip of nose.

In our case, there was history of maternal infection of varicella at the 28th week of gestation. Maternal varicella before 28 weeks of gestation increases chances of congenital varicella syndrome (CVS) in newborn and risk is negligible after 28 weeks of gestation. CVS includes multiple developmental defects like microcephaly, hydrocephaly, aplasia of brain, limb hypoplasia, Horner's syndrome, etc. In our case, mother suffered from varicella at 28 weeks of gestation; hence newborn did not suffer from CVS.

In our case, fetus was exposed to varicella in third trimester in intrauterine life but child developed HZO without developing clinical symptoms of varicella due to the presence of maternal antibody. This is similar to case reported by Van Aelst et al in a 2.5-year-old child.[9]

Varicella vaccine is live attenuated vaccine; so contraindicated in pregnancy and immunocompromised patients, but it can be given prior to conception.[10] Two doses are given 1 month apart. In our case, the mother had no history of varicella in past and there are no studies in literature where such cases are to be vaccinated with varicella vaccine before planning for pregnancy.

CONCLUSION

There are only few published reports on HZ ophthalmicus in immunocompetent children in Indian literature. We are reporting this case as rare pediatric case of HZO in an immunocompetent infant. This case report demonstrates that HZ ophthalmicus can occur in an immunocompetent child with a history of varicella infection to mother during late gestational months. Early diagnosis and treatment decrease fatal complications. Also, preconception vaccination of females not exposed to varicella-zoster virus in past is a matter of concern.

REFERENCES

1. Weller TH. Serial propagation in vitro of agents producing inclusion bodies derived from varicella and herpes zoster. Proc Soc Exp Biol Med. 1953;83(2):340-6.
2. Hope-Simpson RE. The nature of herpes zoster: a long-term study and a new hypothesis. Proc R Soc Med. 1965;58(1):9-20.
3. Savage MO, Moosa A, Gordon RR. Maternal varicella infection as a cause of fetal malformations. Lancet. 1973;1(7799):352-4.
4. Ragozzino MW, Melton LJ 3rd, Kurland LT, Chu CP, Perry HO. Population-based study of herpes zoster and its sequelae. Medicine (Baltimore). 1982;61(5):310-6.
5. Liesegang TJ. Herpes zoster ophthalmicus natural history, risk factors, clinical presentation, and morbidity. Ophthalmology. 2008;115(2 Suppl):S3-12.
6. Enders G, Miller E, Cradock-Watson J, Bolley I, Ridehalgh M. Consequences of varicella and herpes zoster in pregnancy: prospective study of 1739 cases. Lancet. 1994;343(8912):1548-51.
7. Frary J, Petersen PT, Pareek M. Hutchinson's sign of ophthalmic zoster. Clin Case Rep. 2019;8(1):219-20.
8. Zaal MJ, Völker-Dieben HJ, D'Amaro J. Prognostic value of Hutchinson's sign in acute herpes zoster ophthalmicus. Graefes Arch Clin Exp Ophthalmol. 2003;241(3):187-91.
9. Van Aelst S, Winters L, Janssen K, Laffut W, Thibaut K. A healthy 2.5-year-old boy with herpes zoster ophthalmicus as primary presentation. J Pediatric Infect Dis Soc. 2015;4(4):e160-2.
10. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report Prevention of Varicella Recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep Recomm. 2007;56(4):7.

Nurture Health Naturally

Enhance Immunity & Protect against Oxidative Stress

Choose the Natural Vitamin E

Natvie® 200IU 400IU

Natural Vitamin E (d-alpha Tocopherol) **Capsules**

Natvie® Gold

Natural Vitamin E (Tocotrienol – 100 mg) **Capsules**

Derived from

Non-GMO Soyabean oil

Natural Membrane Protector

2021

FRANCO-INDIAN PHARMACEUTICALS PVT. LTD.
20, Dr. E. Moses Road, Mumbai 400 011.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Metaplastic Carcinoma Breast with Chondroid Differentiation

M VISHNU PRIYA*, J THANKA†, RITHIKA RAJENDIRAN‡, P SURENDRAN#, LEENA DENNIS JOSEPH¥

ABSTRACT

Metaplastic carcinoma of breast, previously called as carcinosarcoma, is one rare form of breast cancer. It accounts for less than 1% of all primary breast tumors. It consists of both glandular and nonglandular components admixed with epithelial and mesenchymal tissues. This type of breast cancer usually resembles invasive ductal carcinoma clinically and radiologically. This is a case of a 65-year-old female with painful lump in left breast for 2 months. Lumpectomy of the same showed features of metaplastic carcinoma of breast with chondroid differentiation, which is a rare form of metaplasia with better prognosis than other forms. Immunohistochemistry was helpful in confirming the diagnosis. Overall survival is less with this form of carcinoma as compared to intraductal carcinoma of breast.

Keywords: Metaplastic, epithelial and mesenchymal, breast carcinoma, prognosis

Metaplastic breast carcinoma (MBC) is a rare heterogeneous group of invasive breast carcinomas. Previously termed as carcinosarcoma, it is characterized by differentiation of neoplastic epithelial cells towards squamous and/or mesenchymal looking elements. It accounts for only about 1% of all invasive breast carcinomas.[1] This rare histopathological variant of breast malignancy is reported for its correct identification and appropriate management.

CASE DETAILS

A 65-year-old female presented with chief complaints of a lump in left breast for past 2 months. The swelling was insidious in onset and was progressive in nature and associated with pain. There was no nipple discharge. There was no history of fever or trauma or weight loss. Her past medical history was unremarkable with no comorbidities. She had no family history of breast or ovarian cancer.

General physical and systemic examination was unremarkable. On examination, left breast was showing fullness over lower inner quadrant. Skin over swelling was normal and pinchable with no dimpling or ulceration. Nipple areola complex was normal. On palpation, there was a 2 × 1 cm lump felt over lower inner quadrant, hard in consistency, nontender and was moving with breast tissue. Right breast was normal. No palpable lymph nodes were noted in left and right axilla. All baseline investigations were normal. True-cut biopsy was done and was reported as benign breast tissue. After a complete pre-surgery workup, wide local excision under general anesthesia was done.

Histological examination was suggestive of metaplastic carcinoma with heterogeneous mesenchymal differentiation (chondroid) (Fig. 1). The tumor showed <10% of areas with glandular or tubular formation and with marked nuclear pleomorphism, irregular nuclear membrane, vesicular nuclei and prominent nucleoli (Figs. 2 and 3). Mitosis was increased (16/10 hpf) with a Nottingham grade of three. The surgical margins were free of tumor. The tumor conferred to pT1c pNx. By immunohistochemistry, tumor cells were triple negative (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor 2 [HER2]) and

*Post Graduate
Dept. of Pathology
Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu
†Professor
Dept. of Pathology
Sree Balaji Medical College and Hospital, Chennai, Tamil Nadu
‡Assistant Professor
Dept. of Pathology
#Dept. of General Surgery
¥Professor
Dept. of Pathology
Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu
Address for correspondence
Dr Leena Dennis Joseph
Professor (Pathology)
Sri Ramachandra Institute of Higher Education and Research, Chennai - 116, Tamil Nadu
E-mail: leenadj@gmail.com

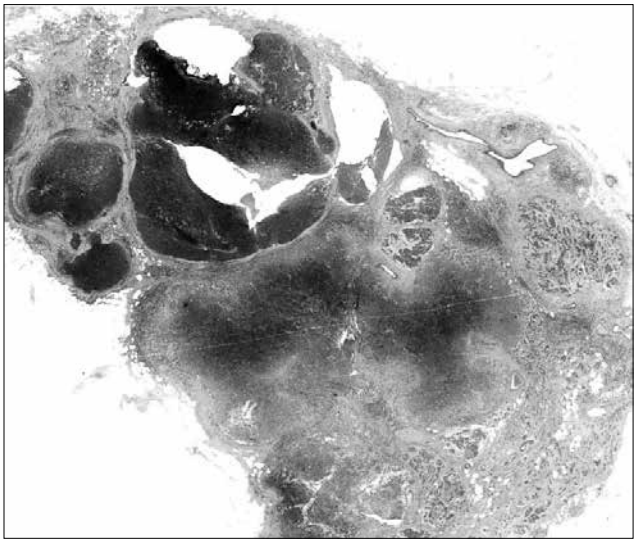


Figure 1. Breast tissue with multiple lobules of chondroid material (H&E x40).

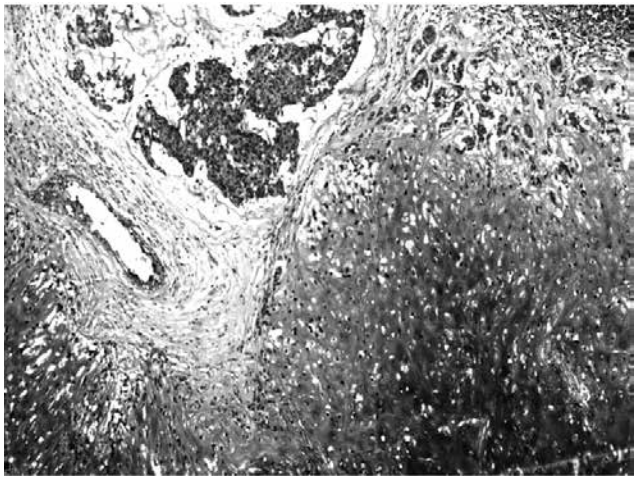


Figure 2. Invasive mammary carcinoma with <10% glandular formation and marked nuclear pleomorphism with chondroid differentiation (H&E x40).

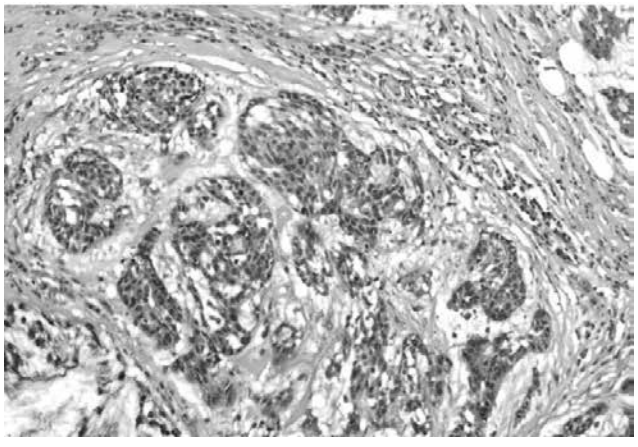


Figure 3. Higher magnification showing metaplastic carcinoma breast with chondroid differentiation (H&E x100).

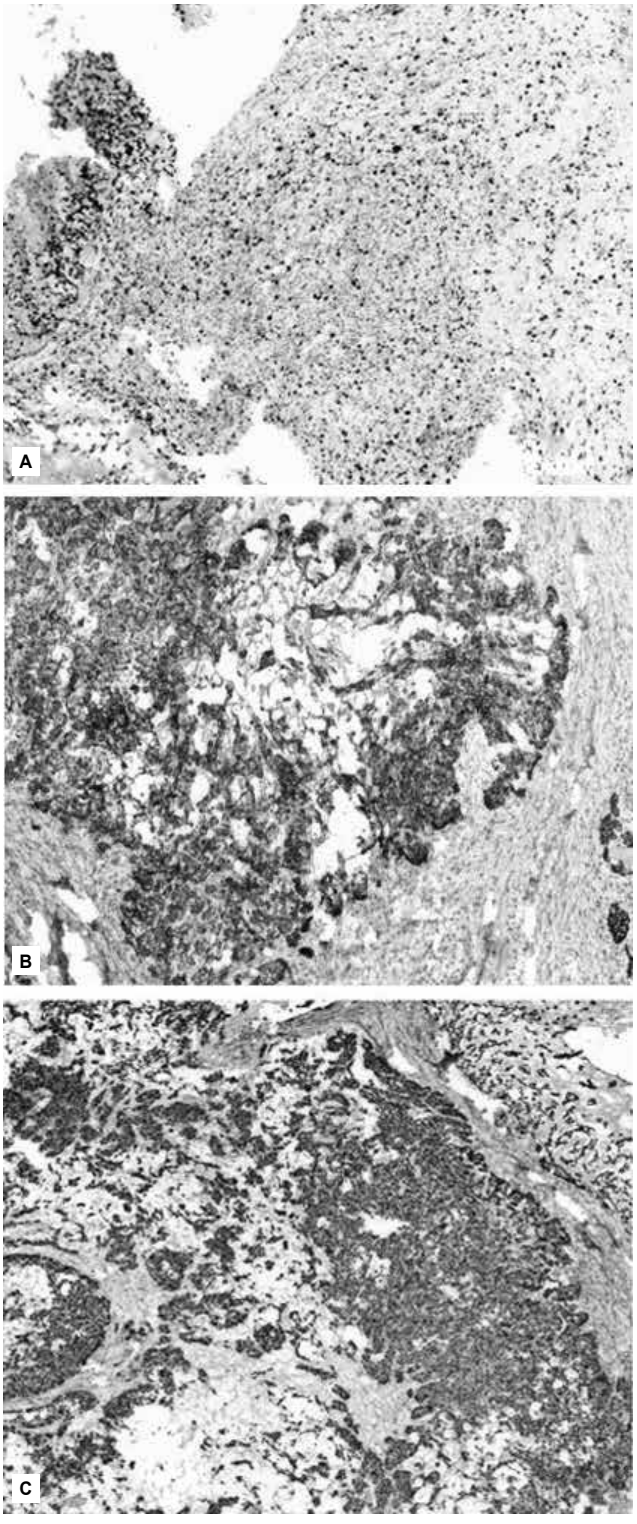


Figure 4. Immunohistochemistry showing Ki labeling index (**A**), CK positivity (**B**) and S-100 positivity (**C**).

p63 was negative. The tumor cells were strongly positive for S-100 and pan-cytokeratin (pan-CK). Ki-67 labeling index was 40% (Fig. 4). Postoperative period was uneventful.

DISCUSSION

Most of the benign and malignant tumors of breast originate from glandular epithelium.[1] In few instances, glandular epithelium differentiates into nonglandular mesenchymal tissue, known as metaplasia.[1] Metaplastic changes in breast include squamous cell, spindle cell and heterogeneous mesenchymal growth. Earlier it was known with different names like carcinosarcoma, sarcomatoid carcinoma, carcinoma with pseudosarcomatous metaplasia, carcinoma with pseudosarcomatous stroma, all of which are not recommended; rather it is known as metaplastic carcinoma not otherwise specified.

Metaplastic breast carcinoma is a rare, aggressive high-grade breast cancer. It accounts for <1% of all breast malignancy.[2] Most common age of presentation is around 48-59 years.[3] It presents as a rapidly growing mass with size usually larger than 2 cm^2. Clinically and radiologically more or less it resembles invasive ductal carcinoma (IDC).[4] On ultrasonogram, it may have high density with either circumscribed or irregular and/or spiculated margins. This may appear benign on mammogram.[3]

The cell of origin for MBC is not clear but many studies suggest that myoepithelial cells will differentiate along mesenchymal lines and produce matrix elements.[4] Epidermal growth factor receptor amplification is seen in around 28% of MBC.[4] P53 mutation is seen in 61% in MBC.[3,5] Presence of transitional areas and epithelial differentiation like tight junctions or desmosomes in heterogeneous sarcomatous component is supportive of a metaplastic process.[3] GATA3-regulated genes account for cell-to-cell adhesion, stem cell-like characteristics and epithelial to mesenchymal transition. Decreased expression of these GATA3-regulated genes make any tumor chemoresistant.[6] Like stem cells, tumor cells are positive for CD44 and negative for CD24.[7]

Histologically, MBC is a biphasic tumor containing ductal carcinoma admixed with areas of spindle, squamous, chondroid and osseous elements.[3] MBC with chondroid differentiation is a rare phenomenon.[8] Differential diagnoses include angiosarcoma, fibromatosis, pleomorphic carcinoma,[9] malignant phyllodes tumor, malignant adenomyoepithelial tumor with chondroid matrix and chondrosarcoma. With presence of benign chondroid tissue, chondrolipoma and pleomorphic adenoma are considered.[8] Thorough and extensive sampling is necessary for definitive diagnosis. Immunohistochemistry plays a vital role in confirming the diagnosis.

MBC also shows triple negativity in 90% cases, similar to infiltrating ductal carcinomas, because it is associated with poorly differentiated carcinomatous elements.[9] Chondroid cells are usually positive for pan-CK and S-100 and negative for epithelial membrane antigen (EMA).[5] Axillary lymph node metastasis in MBC is very uncommon. Rather, hematogenous route is preferred with most common distant site of metastasis being pleura, lung, liver and abdominal viscera.[9] Presence of axillary lymph node metastasis indicates a poor prognosis.[1,3]

Prognostic factors of MBC depend on tumor size >5 cm, histological type, degree of differentiation, type and degree of mesenchymal component, presence of axillary lymph node and distant metastasis.[1,9] Increased risk of local recurrence has been reported. Basically, MBC has poorer prognosis than other IDC, but MBC with chondroid differentiation exhibits better prognosis than other subtypes.

Surgical radical mastectomy is considered the mainstay of treatment. Conservative surgery with radiotherapy is followed for tumors <5 cm in size.[5] And total mastectomy followed by chemotherapy and radiotherapy is followed for tumors >5 cm in size with skin or chest wall involvement or >4 axillary lymph node metastasis. Since local recurrence and metastasis is more common, radiotherapy and chemotherapy play a vital role in treatment.[6] Clinical trials on role of targeted gene therapy following genetic profiling have been done.[4] Epidermal growth factor receptor inhibitors act as potent therapeutic agents.[6] Overall 5-year survival rate is around 43%.[1]

CONCLUSION

When a malignant breast tumor with chondroid elements is seen, metaplastic carcinoma with chondroid differentiation is essentially considered, even though epithelial component is minimal or even absent. Extensive sampling and immunohistochemistry will help in differentiating it from other tumors. Surgery with chemotherapy and radiotherapy is considered as most appropriate treatment. Disease-free survival and overall survival is less in metaplastic carcinoma as compared to IDC of breast.

REFERENCES

1. Bhosale SJ, Kshirsagar AY, Sulhyan SR, Jagtap SV, Nikam YP. Metaplastic carcinoma with predominant chondrosarcoma of the right breast. Case Rep Oncol. 2010;3(2):277-81.

2. Kumar M, Nigam JS, Khanna P, Arora A. Metaplastic carcinoma of the breast - Case report and review of literature. Int J Surg Open. 2020;24:43-6.
3. Schwartz TL, Mogal H, Papageorgiou C, Veerapong J, Hsueh EC. Metaplastic breast cancer: histologic characteristics, prognostic factors and systemic treatment strategies. Exp Hematol Oncol. 2013;2(1):31.
4. Shruti S, Siraj F. Matrix-producing metaplastic breast carcinoma - a rare tumor with heterologous elements. Ger Med Sci. 2017;15:Doc17.
5. Taghipour Zahir S, Javannejad M. Metaplastic breast carcinoma with chondroid differentiation: a rare variant of infiltrative carcinoma in a 38-year-old woman. BMJ Case Rep. 2017;2017:bcr2016217687.
6. Singh GK, Singh P, Bhowmik KT. Carcinosarcoma (metaplastic carcinoma) breast: a rare and aggressive primary - report of two cases with review of literature. Indian J Med Paediatr Oncol. 2018;39(3):400-4.
7. Oon ML, Thike AA, Tan SY, Tan PH. Cancer stem cell and epithelial-mesenchymal transition markers predict worse outcome in metaplastic carcinoma of the breast. Breast Cancer Res Treat. 2015;150(1):31-41.
8. Kim YJ, Shim HS, Lee H, Jung WH. Metaplastic carcinoma with extensive chondroid differentiation in the breast (chondroid carcinoma). Yonsei Med J. 2006;47(2):259-63.
9. Fernández Pérez MA, Viqueira Rodriguez I, Tello Royloa A, Martínez Guisasola J. Metaplastic breast carcinoma with unusual presentation: review of three cases. Breast Care (Basel). 2015;10(6):404-7.

■■■■

UK Regulator Found 30 Cases of Blood Clot Events Following Use of AstraZeneca Vaccine

The UK regulators have stated that 30 cases of rare blood clot events have been reported following the use of the AstraZeneca COVID-19 vaccine.

The Medicines and Healthcare products Regulatory Agency added that there were no such reports of clotting events after use of the Pfizer-BioNTech COVID-19 vaccine. The health officials maintained that the benefits of the vaccine in preventing COVID-19 still outweigh any possible blood clot risk.

While some countries have restricted the use of AstraZeneca vaccine, others have resumed its use, amid investigations into the reports of rare blood clot events.

The regulator had stated on March 18 that 5 cases of a rare brain blood clot had been reported among 11 million administered vaccine doses. Recently, it made it as 22 reports of cerebral venous sinus thrombosis, and 8 reports of other clotting events associated with low blood platelets from among 18.1 million doses administered… (*Reuters*)

No Approval for Sputnik V Vaccine in India Yet

An expert panel of the country's central drug authority has asked for additional information from Dr Reddy's Laboratories, which applied for EUA for the Russian COVID-19 vaccine, Sputnik V. The decision on the authorization was deferred till the next meeting.

The company had submitted the interim safety and immunogenicity data of the Gam-Covid-Vac combined vector vaccine from the county, in addition to the interim data from the ongoing Russian study. The Subject Expert Committee (SEC) on COVID-19 of the Central Drugs Standard Control Organisation (CDSCO) has recommended that the company must submit data regarding all immunogenicity parameters, unblinded data of serious adverse events and reverse transcriptase-polymerase chain reaction (RT-PCR) positive cases, and the causality analysis reported till now, for further evaluation… (*ET Healthworld – PTI*)

Covaxin Receives Approval for Trial of Booster Shot

The indigenous COVID-19 vaccine – Covaxin - will now be evaluated for a booster dose, which can be given 6 months following the second dose.

The Subject Expert Committee (SEC) that advises the Drugs Controller General of India (DCGI), has given approval for this and has recommended that Bharat Biotech must carry out the booster dose study only on Phase II trial participants after they have been given 6 μg of Covaxin. The participants have to be followed up for at least 6 months after the administration of the third dose. The approval for the booster dose study has come after Bharat Biotech requested amendments in the approved Phase II trial protocol, to permit administration of a booster dose 6 months after the second dose of the vaccine… (*ET Healthworld – TNN*)

Every citizen of India should have the right to accessible, affordable, quality and safe heart care irrespective of his/her economical background

HEART CARE FOUNDATION OF INDIA
A Not-For-Profit Organisation

Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

E-219, Greater Kailash, Part I, New Delhi - 110048 E-mail: heartcarefoundationfund@gmail.com Helpline Number: +91 - 9958771177

"No one should die of heart disease just because he/she cannot afford it"

About Sameer Malik Heart Care Foundation Fund

"Sameer Malik Heart Care Foundation Fund" it is an initiative of the Heart Care Foundation of India created with an objective to cater to the heart care needs of people.

Objectives

- Assist heart patients belonging to economically weaker sections of the society in getting affordable and quality treatment.
- Raise awareness about the fundamental right of individuals to medical treatment irrespective of their religion or economical background.
- Sensitize the central and state government about the need for a National Cardiovascular Disease Control Program.
- Encourage and involve key stakeholders such as other NGOs, private institutions and individual to help reduce the number of deaths due to heart disease in the country.
- To promote heart care research in India.
- To promote and train hands-only CPR.

Activities of the Fund

Financial Assistance

Financial assistance is given to eligible non emergent heart patients. Apart from its own resources, the fund raises money through donations, aid from individuals, organizations, professional bodies, associations and other philanthropic organizations, etc.

After the sanction of grant, the fund members facilitate the patient in getting his/her heart intervention done at state of art heart hospitals in Delhi NCR like Medanta – The Medicity, National Heart Institute, All India Institute of Medical Sciences (AIIMS), RML Hospital, GB Pant Hospital, Jaipur Golden Hospital, etc. The money is transferred directly to the concerned hospital where surgery is to be done.

Drug Subsidy

The HCFI Fund has tied up with Helpline Pharmacy in Delhi to facilitate patients with medicines at highly discounted rates (up to 50%) post surgery.

The HCFI Fund has also tied up for providing up to 50% discount on imaging (CT, MR, CT angiography, etc.)

Who is Eligible?

All heart patients who need pacemakers, valve replacement, bypass surgery, surgery for congenital heart diseases, etc. are eligible to apply for assistance from the Fund. The Application form can be downloaded from the website of the Fund. http://heartcarefoundationfund.heartcarefoundation.org and submitted in the HCFI Fund office.

Important Notes

- The patient must be a citizen of India with valid Voter ID Card/ Aadhaar Card/Driving License.
- The patient must be needy and underprivileged, to be assessed by Fund Committee.
- The HCFI Fund reserves the right to accept/reject any application for financial assistance without assigning any reasons thereof.
- The review of applications may take 4-6 weeks.
- All applications are judged on merit by a Medical Advisory Board who meet every Tuesday and decide on the acceptance/rejection of applications.
- The HCFI Fund is not responsible for failure of treatment/death of patient during or after the treatment has been rendered to the patient at designated hospitals.
- The HCFI Fund reserves the right to advise/direct the beneficiary to the designated hospital for the treatment.
- The financial assistance granted will be given directly to the treating hospital/medical center.
- The HCFI Fund has the right to print/publish/webcast/web post details of the patient including photos, and other details. (Under taking needs to be given to the HCFI Fund to publish the medical details so that more people can be benefitted).
- The HCFI Fund does not provide assistance for any emergent heart interventions.

Check List of Documents to be Submitted with Application Form

- Passport size photo of the patient and the family
- A copy of medical records
- Identity proof with proof of residence
- Income proof (preferably given by SDM)
- BPL Card (If Card holder)
- Details of financial assistance taken/applied from other sources (Prime Minister's Relief Fund, National Illness Assistance Fund Ministry of Health Govt of India, Rotary Relief Fund, Delhi Arogya Kosh, Delhi Arogya Nidhi), etc., if anyone.

Free Diagnostic Facility

The Fund has installed the latest State-of-the-Art 3 D Color Doppler EPIQ 7C Philips at E – 219, Greater Kailash, Part 1, New Delhi.
This machine is used to screen children and adult patients for any heart disease.

Free Education and Employment Facility

HCFI has tied up with a leading educational institution and an export house in Delhi NCR to adopt and to provide free education and employment opportunities to needy heart patients post surgery. Girls and women will be preferred.

Laboratory Subsidy

HCFI has also tied up with leading laboratories in Delhi to give up to 50% discounts on all pathological lab tests.

Help Us to Save Lives

The Foundation seeks support, donations and contributions from individuals, organizations and establishments both private and governmental in its endeavor to reduce the number of deaths due to heart disease in the country. All donations made towards the Heart Care Foundation Fund are exempted from tax under Section 80 G of the IT Act (1961) within India. The Fund is also eligible for overseas donations under FCRA Registration (Reg. No 231650979). The objectives and activities of the trust are charitable within the meaning of 2 (15) of the IT Act 1961.

Donate Now...

About Heart Care Foundation of India

Heart Care Foundation of India was founded in 1986 as a National Charitable Trust with the basic objective of creating awareness about all aspects of health for people from all walks of life incorporating all pathies using low-cost infotainment modules under one roof.

HCFI is the only NGO in the country on whose community-based health awareness events, the Government of India has released two commemorative national stamps (Rs 1 in 1991 on Run For The Heart and Rs 6.50 in 1993 on Heart Care Festival- First Perfect Health Mela). In February 2012, Government of Rajasthan also released one Cancellation stamp for organizing the first mega health camp at Ajmer.

Objectives

- Preventive Health Care Education
- Perfect Health Mela
- Providing Financial Support for Heart Care Interventions
- Reversal of Sudden Cardiac Death Through CPR-10 Training Workshops
- Research in Heart Care

Heart Care Foundation Blood Donation Camps

The Heart Care Foundation organizes regular blood donation camps. The blood collected is used for patients undergoing heart surgeries in various institutions across Delhi.

Committee Members

Chief Patron

Raghu Kataria

Entrepreneur

President

Dr KK Aggarwal

Padma Shri, Dr BC Roy National & DST National Science Communication Awardee

Governing Council Members

Sumi Malik
Vivek Kumar
Karna Chopra
Dr Veena Aggarwal
Veena Jaju
Naina Aggarwal
Nilesh Aggarwal
H M Bangur

Advisors

Mukul Rohtagi
Ashok Chakradhar

Executive Council Members

Deep Malik
Geeta Anand
Dr Uday Kakroo
Harish Malik
Aarti Upadhyay
Raj Kumar Daga
Shalin Kataria
Anisha Kataria
Vishnu Sureka
Rishab Soni

This Fund is dedicated to the memory of **Sameer Malik** who was an unfortunate victim of sudden cardiac death at a young age.

- HCFI has associated with Shree Cement Ltd. for newspaper and outdoor publicity campaign
- HCFI also provides Free ambulance services for adopted heart patients
- HCFI has also tied up with Manav Ashray to provide free/highly subsidized accommodation to heart patients & their families visiting Delhi for treatment.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Remitting Seronegative Symmetrical Synovitis with Pitting Edema: A Rare Case Report

VIRENDRA KR GOYAL*, JITESH AGGARWAL†, ROOTIK PATEL‡, MANAN DAVE‡

ABSTRACT

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare form of inflammatory arthritis which was first reported by McCarty et al in 1985. It usually affects elderly age group with a clinical presentation of symmetrical polyarthritis with pitting edema on the dorsum of hands and feet. Several studies consider RS3PE to be a form of polymyalgia rheumatica and even seronegative rheumatoid arthritis, but the clinical presentation and pathophysiologic mechanisms indicate that it can be a separate entity altogether. The joints involved frequently as developing stiffness include the metacarpophalangeal (MCP), proximal interphalangeal (PIP), wrist, shoulder, knee, ankle and elbows. RS3PE is a disease/syndrome characterized by an acute onset of polyarthritis with pitting edema, negative rheumatoid factor, absence of joint erosions on radiographs, synovitis suggested by USG/MRI, and a good response to low-dose steroids, with a sustained long-term response.

Keywords: Rheumatoid arthritis, RS3PE, synovitis, pitting edema, inflammatory arthritis

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a rare form of inflammatory arthritis which was first reported by McCarty et al in 1985. It usually affects elderly age group with a clinical presentation of symmetrical polyarthritis with pitting edema on the dorsum of hands and feet. The pathophysiology of RS3PE is not understood clearly. Several studies consider RS3PE to be a form of polymyalgia rheumatica (PMR) and even seronegative rheumatoid arthritis (RA), but the clinical presentation and pathophysiologic mechanisms suggest that it can be a separate entity altogether. The joints involved frequently as developing stiffness include the metacarpophalangeal (MCP), proximal interphalangeal (PIP), wrist, shoulder, knee, ankle and elbows.

*Professor and Head
†Assistant Professor
‡Senior Resident
Dept. of Medicine
American International Institute of Medical Sciences (AIIMS), Udaipur, Rajasthan
Address for correspondence
Dr Virendra Kr Goyal
Professor and Head, Dept. of Medicine
8 Faculty Quarters, AIIMS, Udaipur, Rajasthan - 313 001
E-mail: virendra601@yahoo.co.in

CASE REPORT

A 65-year-old female was referred to GBH General Hospital, Udaipur, Rajasthan on August 12, 2020, with the history of low-grade fever for 10 days followed by swelling over left knee, right hand and swelling over bilateral feet since 7 days. Patient also had a history of hysterectomy followed by radiotherapy about 20 years back, records of which were not available and nature of the illness is unknown.

On examination, left knee joint was red and swollen with increased local temperature. There was pitting edema of bilateral lower limbs and also over right hand (Fig. 1). Ultrasonography (USG) of the local parts showed effusion of the left knee joint with synovitis of the joint along with soft tissue edema over bilateral lower limbs and right hand. Arthrocentesis of the knee was done which showed inflammatory arthritis with cytology showing total counts of 6,400 with neutrophils 60%. Other findings included adenosine deaminase 19.8 U/mL, sugar 40 mg/dL, protein 4.5 g/dL (as the joint aspirate report did not have mononuclear cells predominance, the possibility of viral arthritis was ruled out), serum uric acid 4.0 mg/dL, negative rheumatoid factor (RF), normal anti-cyclic citrullinated peptide (anti-CCP) and normal antinuclear antibody (ANA), normal thyroid-stimulating hormone (TSH), anemia with hemoglobin of 7.8 g/dL, WBC 11 × 10^3 cells/mm^3 - $N_{85\%}$, $L_{20\%}$, elevated erythrocyte

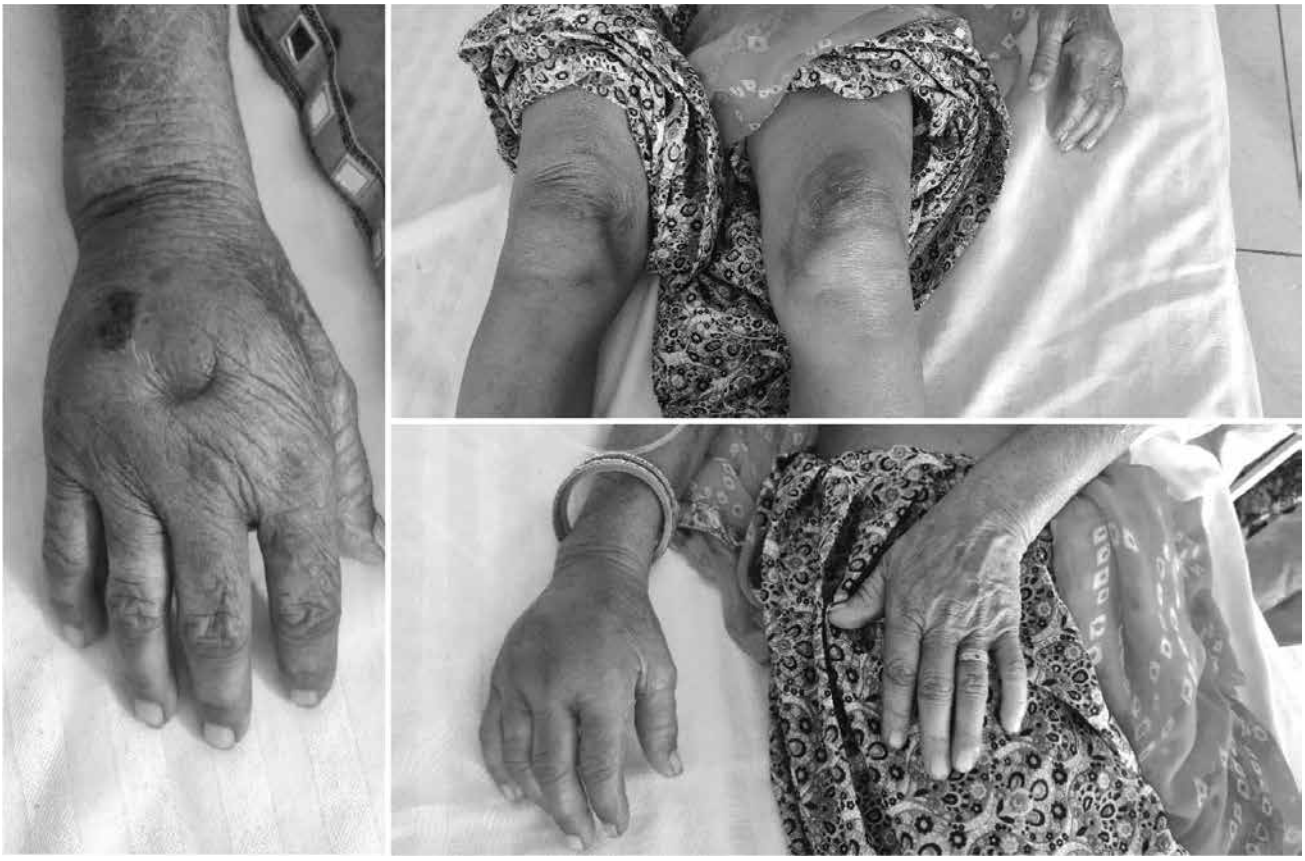


Figure 1. Pitting edema of right hand and swelling over left knee.

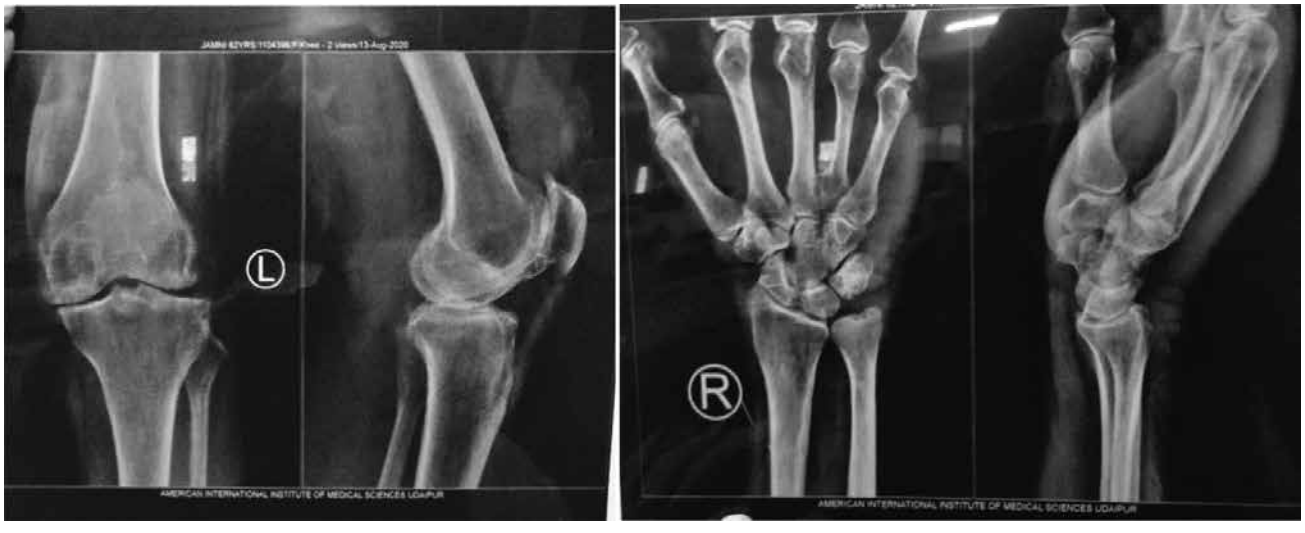


Figure 2. X-ray left knee showing osteoarthritic changes and X-ray right wrist showing soft tissue swelling.

sedimentation rate (ESR) of 111 mm/hr and elevated C-reactive protein (CRP) at 137 mg/L. All other viral markers - human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), anti-HCV (hepatitis C virus) - were negative. X-ray of the affected joints did not reveal any joint erosion. X-ray left knee showed osteoarthritic changes and X-ray right wrist showed soft tissue swelling (Fig. 2). USG of the abdomen showed cholelithiasis of 11 mm and minimal ascites. After ruling out all other causes, patient was started on prednisolone 30 mg. During her brief hospital stay, the patient started responding to treatment, her swelling started reducing and her pain subsided and she was discharged.

DISCUSSION

Remitting seronegative symmetrical synovitis with pitting edema syndrome is defined as seronegative symmetric polysynovitis and arthritis of the distal limbs, primarily the wrist, MCP, PIP and ankle joints with acute onset, together with pitting edema on the dorsum of the hands and feet. Olivé et al evaluated 27 cases with RS3PE retrospectively in 1997 and established the following diagnostic criteria for the disease:

- Clear pitting edema on both hands
- Polyarthritis with acute onset
- Age above 50
- Negative RF.

Nonobservation of erosive or degenerative change in joints and dramatic response to low-dose corticosteroid are characteristic. It is thought that pitting edema, which occurs in distal limbs, develops upon local reaction. RS3PE diagnosis in the presented case was based on the following: Female gender and age >50 years, symmetric pitting edema and sudden-onset polyarthritis, nonobservation of erosion on radiographs, and dramatic and rapid clinical and laboratory response to low-dose corticosteroid treatment within 1 week.

Associations with human leukocyte antigens (HLA) parvovirus B-19 infection malignancy, rheumatologic and autoimmune diseases and increased vascular endothelial growing factor (VEGF) levels have been cited in the etiopathogenesis.

Low-moderate elevation in sedimentation rate has been determined as a laboratory finding in the disease. RF and ANA are negative, while HLA-B7, B22 and B27 tissue antigens may be positive in some patients. Sedimentation rate was moderately increased in our case and RF was negative. Response of RS3PE to nonsteroidal anti-inflammatory drug (NSAID) treatment is not good. Russell et al reported in their series with 13 cases that the patients responded dramatically to 10 mg/day prednisolone treatment. It was found in different case series that remission was ensured in an average of 6-18 months with low-dose steroid treatment. Low-degree flexion contractures that developed on wrists and fingers may sometimes be permanent.

Despite the clear criteria, differential diagnosis of RS3PE is very difficult. Important differential diagnoses include amyloid arthropathy, psoriatic arthropathy, crystal arthropathy, rheumatoid arthritis (RA), late-onset spondyloarthropathies, Reiter syndrome and mixed connective tissue disease; they cause pitting edema on the hands and feet. Reiter syndrome is differentiated by asymmetric stiffness with conjunctivitis and urethritis and asymmetric pitting edema in lower limbs; late-onset spondyloarthropathies are differentiated by asymmetric pitting edema with sacroiliitis; and mixed connective tissue disease is differentiated by Raynaud's phenomenon and ANA positivity in high titer. While having very similar clinical and symptoms, it is distinguished from RS3PE with RF positivity and bone erosions.

RS3PE is most frequently confused with PMR since both are seronegative, are seen in older ages and respond to corticosteroids (Table 1).

Salvarani et al found pitting edema in 8% of the cases in their study examining 245 cases with PMR diagnosis.

Table 1. Comparing Three Polyarthritides Affecting the Elderly

	RA	RS3PE	PMR
Onset	Sudden or gradual	Usually sudden	Sudden
Sex	F>M	M>F	F>M
Age of onset	3rd to 5th decade	7th decade	7th decade
Synovitis	Usually severe	Severe	Mild
Pitting edema	Unusual	All (as per definition)	No
RF	Positive (80%)	Negative	Negative
HLA association	DR1,4	B7	DR3,4
Remission	Uncommon	Predictable (3-36 mo)	Common (2 y or more)
Response to low-dose steroids	Often incomplete	Dramatic	Dramatic

RA = Rheumatoid arthritis; RS3PE = Remitting seronegative symmetrical synovitis with pitting edema; PMR = Polymyalgia rheumatica; F = Female; M = Male; RF = Rheumatoid factor; HLA = Human leukocyte antigen.

Cantini et al argued that RS3PE may be a precursor or continuance of PMR since inflammation selects the same anatomic target in extra-articular synovial structures in magnetic resonance imaging (MRI) in PMR cases with pitting edema like RS3PE.

However, PMR is a disease mostly seen in women, requiring long-term steroid treatment and showing relapse and recurrence more frequently. In our case, although pain and limitation of motion in the knee joint and ankle joints were present, dramatic response to corticosteroid treatment in very low doses in a short time supports the diagnosis of RS3PE.

Cases diagnosed as RS3PE are observed to suffer from different rheumatologic diseases in the future, including RA, Sjögren's syndrome, spondyloarthropathy and PMR.

Although its diagnostic criteria are clear, RS3PE is a syndrome with a benign course, the differential diagnosis of which is very difficult, and it may lead to rheumatologic and neoplastic diseases. Correct recognition of these cases and patient follow-up after diagnosis are important.

RS3PE responds to relatively small doses of prednisolone. NSAIDs and hydroxychloroquine may provide an added advantage. There is very little role of the disease-modifying antirheumatic drugs (DMARDs). This remission is usually well-sustained. On the other hand, RS3PE with an underlying malignancy responds poorly and treatment of the underlying malignancy is needed as a primary step.

CONCLUSION

RS3PEis a disease/syndrome characterized by an acute onset of polyarthritis with pitting edema, negative RF, absence of joint erosions on radiographs, synovitis suggested by USG/MRI and a good response to low-dose steroids, with a sustained long-term response. A high-degree of suspicion and an early prompt diagnosis is required, as proper treatment results in a dramatic relief to the patient, while misdiagnosis results in a more intensive and expensive therapy, over a long period of time.

SUGGESTED READING

1. McCarty DJ, O'Duffy JD, Pearson L, Hunter JB. Remitting seronegative symmetrical synovitis with pitting edema. RS3PE syndrome. JAMA. 1985;254(19):2763-7.
2. Paik R. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): a case report and brief review. Int J Clin Rheumatol. 2019;14(4):127-9.
3. Sibilia J, Friess S, Schaeverbeke T, Maloisel F, Bertin P, Goichat B, et al. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): a form of paraneoplastic polyarthritis? J Rheumatol. 1999; 26(1):115-20.
4. Olivé A, del Blanco J, Pons M, Vaquero M, Tena X. The clinical spectrum of remitting seronegative symmetrical synovitis with pitting edema. The Catalán Group for the Study of RS3PE. J Rheumatol. 1997;24(2):333-6.
5. Perandones CE, Colmegna I, Arana RM. Parvovirus B19: another agent associated with remitting seronegative symmetrical synovitis with pitting edema. J Rheumatol. 2005;32(2):389-90.
6. Cimmino MA, Silvestri E, Garlaschi G. Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) as recurrence of aborted PMR. Ann Rheum Dis. 2001;60(3):303.
7. Arima K, Origuchi T, Tamai M, Iwanaga N, Izumi Y, Huang M, et al. RS3PE syndrome presenting as vascular endothelial growth factor associated disorder. Ann Rheum Dis. 2005;64(11):1653-5.
8. Cantini F, Salvarani C, Olivieri I, Benozzi L, Macchioni L, Nicolli L, et al. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome: a prospective follow up and magnetic resonance imaging study. Ann Rheum Dis. 1999;58(4):230-6.
9. Finnel JA, Cuesta IA. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome: a review of the literature and a report of three cases. J Foot Ankle Surg. 2000;39(3):189-96.
10. Russell EB, Hunter JB, Pearson L, McCarty DJ. Remitting, seronegative, symmetrical synovitis with pitting edema - 13 additional cases. J Rheumatol. 1990;17(5):633-9.
11. Salvarani C, Gabriel S, Hunder GG. Distal extremity swelling with pitting edema in polymyalgia rheumatica. Report on nineteen cases. Arthritis Rheum. 1996;39(1):73-80.

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Unusual Temporary Treatment for Mastoid Fistula

SUBRAMANIAM VINAYAK EASWERAN*, SARVESH NAYAK†, ARPANA HEGDE‡

ABSTRACT

Postauricular mastoid fistula is a rare complication of chronic suppurative otitis media. It could also occur after ear surgery as a complication and at times as a complication of congenital cholesteatoma. Usual treatment suggested in literature is surgery by closing the defect by using temporalis muscle rotation flap. This article is an out of the box thinking to temporarily treat a patient having mastoid fistula by using a prosthesis made in the dental department using acrylic in order to snugly fit in the postauricular defect area. Such a prosthesis could be made use of when a patient experiences giddiness if and when water enters the fistula tract while bathing, or if the patient wants to postpone the surgery due to some reason.

Keywords: Postauricular mastoid fistula, complication, acrylic prosthesis

Postauricular cutaneous mastoid fistula is a rare condition, as rare as only about 6 cases were reported in literature.[1] Mastoid fistula is a rare complication of chronic suppurative otitis media. This complication could be secondary to ear surgery, or a complication of congenital cholesteatoma.[2] Usual treatment in all referred literature is surgery using:

- Temporalis muscle rotational flap for closure of the defect.[1]
- Fascio-cutaneo-periosteal advancement flap with Burow's triangles.[2]

However, simple closure is often unsuccessful because of the necrotic skin edges.

This article is written as an out of the box thinking in the treatment of a postauricular mastoid fistula, which presented to us a case of complication of chronic suppurative otitis media.

CASE REPORT

A 65-year-old lady presented to us in the ENT OPD with a complication of chronic suppurative otitis media in the form of a postauricular mastoid fistula. She had uncontrolled diabetes and experienced giddiness while having bath as water was stimulating her labyrinth. Because of her comorbid condition and her debilitating giddiness, we tried helping her to buy time till she became fit for her surgery (which is the ideal treatment for a condition like this) by making a prosthesis that snugly fits in the fistula area and thus could help her overcome her giddiness, while having bath and preventing water entering the labyrinth.

The dentists initially approximated the depth of the sinus by measuring it using a match stick. Semi hot impression compound cake was molded over the match stick, which was inserted into the sinus. The impression was taken out and put into the bowl-containing wet dental stone (gypsum). Impression compound was removed after setting of dental stone by heating on to that impression cavity. Acrylic polymer and monomer were mixed and poured on a thin plate of acrylic over which water was poured and let to set.

After setting, the acrylic was taken out from the bowl by splitting of the set dental stone and checked for trying on the patient's sinus cavity. Figure 1 a and b show the prosthesis mold and Figure 1c shows the prosthesis *in situ*.

*Dept. of ENT, Pandit General Hospital, Church Road, Sirsi, Uttara Kannada, Karnataka
†Venkatesh Dental Clinic, Near Narashimha Temple, Pramankatta, Keni Road Mandi Bazar, Ankola, Karwar Dist, Karnataka
‡Dental Care Center, 1st floor, GP Center, Court Road, Sirsi, Karnataka
Address for correspondence
Dr Subramaniam Vinayak Easweran
Dept. of ENT
Pandit General Hospital
Church Road, Sirsi, Uttara Kannada - 581401, Karnataka
E-mail: vinoo121071@gmail.com

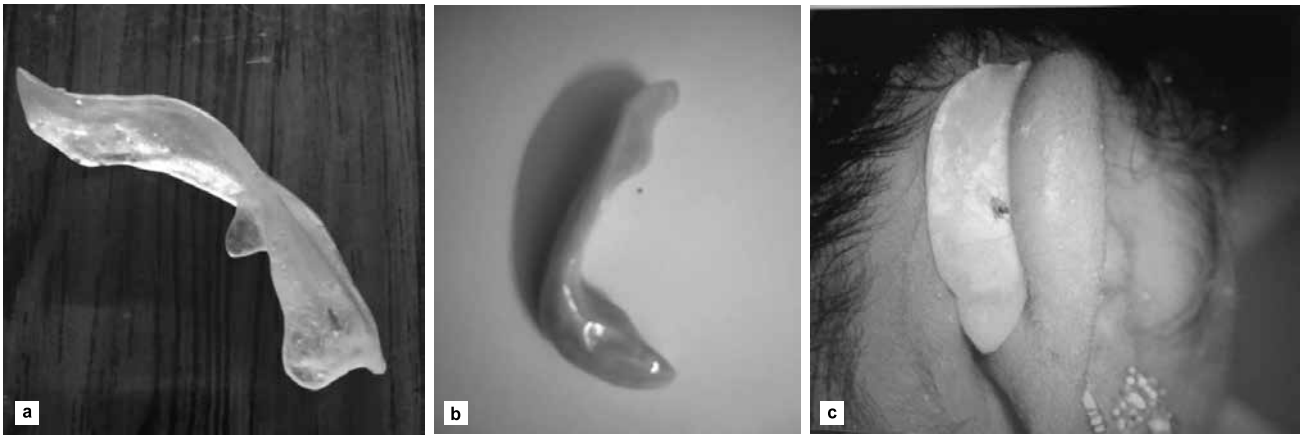


Figure 1. Prosthesis mold **(a and b)** and prosthesis *in situ* **(c)**.

DISCUSSION

We present here an unusual and temporary treatment of mastoid fistula. What makes this case a special one is that it has never been published in literature, and moreover it could be thought of as an ideal treatment for the patient who wants to buy time for surgery owing to the patient's comorbid conditions. At the same time, it can help the patient get rid of the debilitating giddiness, which is a consequence of the complication of chronic suppurative otitis media. However, surgery to close the fistula is the mainstay treatment of such a case.

CONCLUSION

We can keep this as a treatment option, though surgery is the main treatment. Such a treatment could be given a thought for patients who have comorbid conditions making them unfit for surgery and have other associated symptoms with regards to the disease condition per say, giving a choice to the patient to buy time till the patient could be made fit for surgery.

REFERENCES

1. Choo JC, Shaw CL, Chong Y C S. Postauricular cutaneous mastoid fistula. J Laryngol Otol. 2004;118(11): 893-4.
2. Olusesi AD, Opaluwah E. Postauricular advancement fascio-cutaneo-periosteal flap for closure of mastoid cutaneous fistula. Otolaryngol Pol. 2014;68(5): 276-80.

■■■■

Living with the Times: New Toolkit to Help Older Adults Maintain Well-being During Pandemic

A new toolkit, titled "Living with the Times" has been developed that carries illustrated posters with important messages for older adults on how to maintain well-being during the COVID-19 pandemic, while supporting those around them.

The posters have a unique design and require minimal reading skills. They are culturally diverse and are aimed at engaging these people in conversations and activities. The toolkit also provides information for facilitators of mental health and psychosocial support (MHPSS) on carrying out guided conversations with older adults with the help of these posters. The Inter-Agency Standing Committee (IASC) Reference Group on Mental Health and Psychosocial Support (MHPSS) in Emergency Settings (IASC MHPSS RG) and experts from various disciplines, including dementia, MHPSS in humanitarian settings, and aging and disability, have come together to develop this resource which targets the needs of older adults… (*WHO*)

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Stroke in Hanging: Ischemic or Thrombotic?

KA VIVEK*, N VIJAYAKUMAR†, R UMARANI‡

ABSTRACT

Hanging is among the most common methods of committing suicide in India, as reported in recent data published by National Crime Records Bureau. Neurological injury in such cases occurs due to compression of the neck. We present the case of a 52-year-old male who presented to the emergency with an alleged history of attempted suicide by hanging with nylon thread. Patient was started on supportive therapy, and 24 hours following admission, he became stable with normal blood pressure without any antihypertensive medications. However, on Day 3 of admission, he developed weakness of left upper limb and lower limb and deviation of angle of mouth to the left side. Repeat CT imaging of brain showed two hypodense foci in right caudate nucleus, head of adjacent internal capsule and a focus in right lentiform nucleus and posterior limb of internal capsule. MRI of brain, including MRA, showed an acute infarct with restricted diffusion in right lentiform nucleus, caudate nucleus, with filling defect in proximal M1 segment of right middle cerebral artery (MCA) suggestive of thrombus and attenuated signal was also noted in distal branches of right MCA. This case highlights the neurological complication following suicidal hanging and a structured approach to it.

Keywords: Suicidal hanging, neuroimaging, CT, MRI, stroke, hypoxia, thrombosis

Suicidal hanging is among the most common methods of committing suicide in India according to recent data published by National Crime Records Bureau, where neurological injury occurs due to compression of the neck. The neck is the target organ for hanging. Easy accessibility, rounded contours, minimum bony shields, the small diameter and unsafe location of the airway, vital blood vessels and spinal cord make it susceptible to life-threatening injuries by hanging, which has been practiced as a popular method of committing suicide since ancient times.

The jugular veins are the first structures to get compressed (force of 2 kg) followed by the carotid arteries (5 kg), causing cerebral edema and hypoxic brain damage, respectively. Compression of the airways needs greater force (15 kg), which can lead to severe hypoxia and death. Neurological outcomes in hanging vary from death, permanent hypoxic brain damage to complete recovery.

In the reviewed literature, the neuroimaging findings in hanging have consistently been described as bilateral hemorrhagic and/or ischemic lesions in the thalamus, cerebellum and other areas of the basal nuclei. Unilateral lesions seem to be a very rare event and to the best of our knowledge, very few cases have been reported.

We report a case of suicidal hanging where the patient survived an initial brain insult, but later developed a neurological deficit in the form of hemiplegia due to an infarct in the right lentiform nucleus, caudate nucleus and corona radiata. Patient recovered with supportive treatment. This case highlights the neurological complication following suicidal hanging and a structured approach to it.

CASE REPORT

A 52-year-old male presented to the emergency with an alleged history of attempted suicide by hanging with nylon thread. After few seconds of suspension, he fell down, and was rushed to the hospital. There was no history of seizure, bleeding from nostrils, eyes and mouth. There were no pre-existing comorbid conditions.

At the time of admission, patient was conscious and oriented. The pulse rate was 110/min, blood pressure

*Final Year Post Graduate
†Lecturer
‡Professor
Dept. of General Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamil Nadu
Address for correspondence
Dr KA Vivek
Final Year Post Graduate
Dept. of General Medicine, Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamil Nadu
E-mail: vivekasokan@gmail.com

was 170/100 mmHg, respiratory rate was 18/min and oxygen saturation by pulse oximeter was 98%. Local examination revealed one circumferential shallow abraded ligature mark over anterior aspect of the neck. There was no cyanosis or subconjunctival hemorrhages. Nasal mucosa, post pharyngeal wall and bilateral tympanic membrane were not congested. Neurological examination was normal except for bilateral extensor Babinski response. Fundus was normal. Both pupils were mid-dilated and responding to light. All biochemical investigations and baseline computed tomography (CT) imaging of brain was normal, and there were no fractures of the cervical spine. Patient was started on supportive therapy, and 24 hours following admission, patient became stable with normal blood pressure without any antihypertensive medications.

On Day 3 of admission, patient developed weakness of left upper limb and lower limb and deviation of angle of mouth to the left side. Neurological examination revealed hemiparesis of left upper limb and lower limb with a power of 3/5. Tone was increased, reflexes were diminished on both left upper limb and lower limb. Extensor plantar was present on the left side and right side plantar was not elicitable; left upper motor neuron (UMN) type of facial nerve palsy was also present.

Urgent repeat CT imaging of brain (Fig. 1a) showed two hypodense foci in right caudate nucleus, head of adjacent internal capsule and a focus in right lentiform nucleus and posterior limb of internal capsule.

Magnetic resonance imaging (MRI) of brain (Fig. 1b), including magnetic resonance angiography (MRA), showed an acute infarct with restricted diffusion in right lentiform nucleus, caudate nucleus, with filling defect in proximal M1 segment of right middle cerebral artery (MCA) suggestive of thrombus and attenuated signal was also noted in distal branches of right MCA. Magnetic resonance venography (MRV) had no evidence of venous thrombosis. Cardiac evaluation including echocardiogram was found to be normal.

Patient was treated with fluid restriction, mannitol, intravenous antibiotics, low molecular weight heparin, physiotherapy and other supportive measures. Patient gradually improved and was discharged on Day 9, with advice to continue physiotherapy.

DISCUSSION

The factors that contribute to death after suicidal hanging include pulmonary complications and neurological complications. *Pulmonary complications*

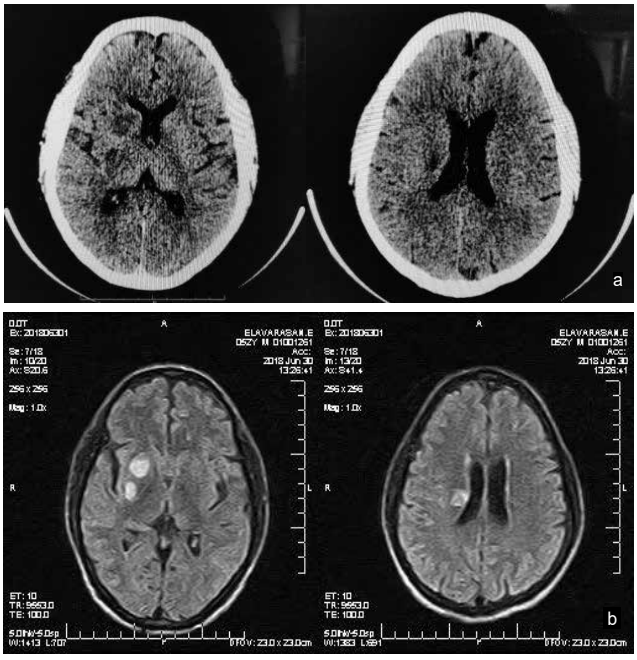


Figure 1 a and b. CT imaging of brain showing two hypodense foci in right caudate nucleus, head of adjacent internal capsule and a focus in right lentiform nucleus and posterior limb of internal capsule **(a)**. MRI showing acute infarct with restricted diffusion in right lentiform nucleus and caudate nucleus **(b)**.

include pulmonary edema and bronchopneumonia, secondary to aspiration. The edema may be due to a centrally mediated sympathetic discharge or due to negative intrathoracic pressure, which is generated as the person attempts to inspire through an obstructed airway. *Neurological complications* include transient hemiparesis, spinal cord syndromes, focal cerebral deficits, cerebral edema, various nerve palsies and larger infarctions. Other complications like hyperthermia, subarachnoid hemorrhage, pneumoperitoneum, ruptured esophagus may also occur. Some factors such as systolic blood pressure <90, Glasgow coma scale score ≤8, anoxic brain injury on CT scan and injury severity score >15 have been found to be significantly associated with mortality in hanging.

In suicidal hanging, there is slower development of *cerebral hypoxia and ischemia*, with both the events being strongly dependent on the materials, location and the method of suicide attempt. This cerebral hypoxia and ischemia can be attributed to the mechanical compression and obstruction of the airway and vasculature of the neck. Further, airway can be compromised by the upward displacement of the tongue and epiglottis, jugular vein occlusion by mild neck closure and vertebral artery occlusion by spinal

injury. These combined factors can easily lead to acute cerebral hypoxia. In rare instances, direct injury to the spinal cord and brainstem can also occur.

The most sensitive areas of hypoxic and ischemic damage are the cerebral cortex, border zones between arterial territories, Ammon's horn, Purkinje cells, particularly the basal ganglia. In the early stages, ischemic neuronal changes are demonstrated by cytotoxic edema (swelling of neurons, glia and endothelial cells) and failure of the sodium ion exchange pump. Sodium accumulates within the cell and water follows this movement to maintain the osmotic equilibrium. The venous hypertension and stasis of blood flow caused by the acute bilateral compression of the internal jugular veins result in hydrostatic transudation of intravascular contents and subsequently rapid occurrence of hypoxia and infarction.

Bilateral involvement is the common finding in hypoxic ischemic injury in suicidal hanging. However, unilateral involvement of brain in the form of hemiplegia due to thrombotic stroke can occur rarely. Traumatic thrombosis of internal carotid artery is reported as being caused by one of the four mechanisms:

- Injury to intrapetrous or cavernous part of the carotid artery during the basal skull fracture
- Injury to point of emergence of carotid artery from the cavernous sinus as a result of strain
- A direct blow to the neck or trauma to peritonsillar area by a foreign object carried in the month
- Stretching of the carotid artery by hyperextension and lateral flexion of neck.

The pathophysiology of thrombosis is due to adherence of platelets to the endothelium with subsequent aggregation, which releases thromboplastin leading to initiation of coagulation cascade.

The neuroimaging in hypoxic ischemic brain injury is often symmetrical, diffuse, low-density lesions found in the watershed areas of the brain. However, in thrombotic injury, the CT and MRI findings are consistent with the vascular territory of the vessels involved. MRA and MRV may show filling defects with attenuated signals.

CONCLUSION

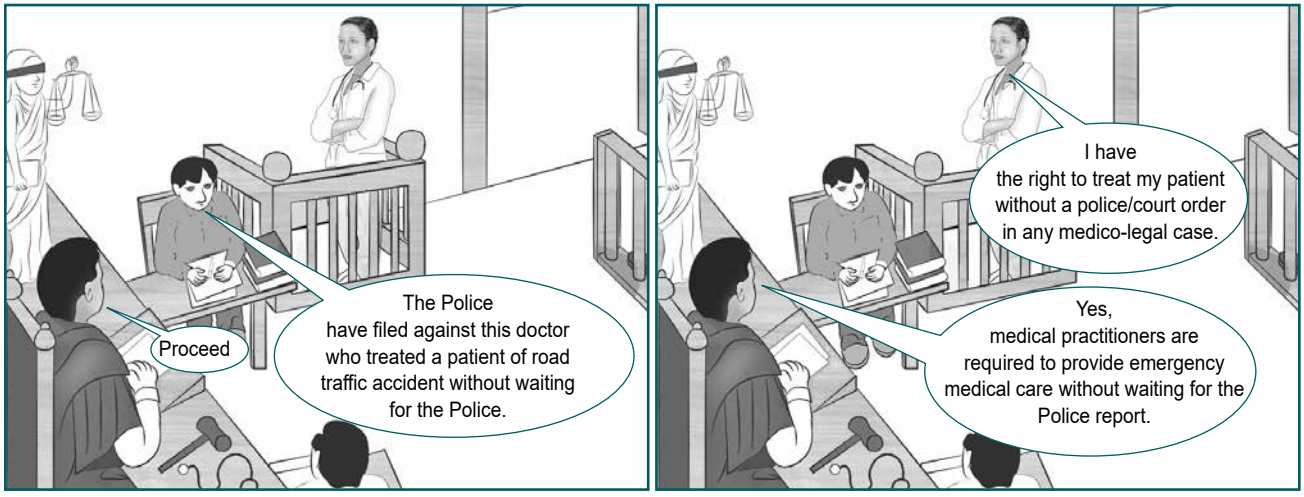
The mechanism of injury, pathophysiology, clinical features and neuroimaging are distinct and different in both cerebral hypoxic ischemic injury and traumatic thrombotic injury to the brain in patients with suicidal hanging. Detailed neurological examination daily to look for subtle changes in clinical features in the patient, repeated neuroimaging studies including MRA and MRV, would help in early diagnosis of thrombotic episodes in suicidal hanging and for early medical management, and if required, surgical management.

SUGGESTED READING

1. Garaci FG, Bazzocchi G, Velari L, Gaudiello F, Goldstein AL, Manenti G, et al. Cryptogenic stroke in hanging. A case report. Neuroradiol J. 2009;22(4):386-90.
2. Kumar S, Verma AK, Bhattacharya S, Rathore S. Trends in rates and methods of suicide in India. Egypt J Foren Sci. 2013;3(3):75-80.
3. Kodikara S. Uneventful recovery from suicidal hanging: a case report. Med Sci Law. 2006;46(1):89-91.
4. Salim A, Martin M, Sangthong B, Brown C, Rhee P, Demetriades D. Near-hanging injuries: a 10-year experience. Injury. 2006;37(5):435-9.
5. Matsuyama T, Okuchi K, Seki T, Higuchi T, Ito S, Makita D, et al. Magnetic resonance images in hanging. Resuscitation. 2006;69(2):343-5.
6. Kalita J, Mishra VN, Misra UK, Gupta RK. Clinicoradiological observation in three patients with suicidal hanging. J Neurol Sci. 2002;198(1-2):21-4.
7. Nemoto EM. Pathogenesis of cerebral ischemia-anoxia. Crit Care Med. 1978;6(4):203-14.
8. Kjos BO, Brant-Zawadzki M, Young RG. Early CT findings of global central nervous system hypoperfusion. AJR Am J Roentgenol. 1983;141(6):1227-32.
9. Narayanaswamy R, Sharma RK, Thakur M, Kansra U. Stroke secondary to attempted strangulation. Arch Med Health Sci. 2014;2(1):71-3.
10. Nakajo M, Onohara S, Shinmura K, Nakajo M, Amitani H, Munamoto T, et al. Computed tomography and magnetic resonance imaging findings of brain damage by hanging. J Comput Assist Tomogr. 2003;27(6):896-900.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Doctors are Required to Provide Emergency Medical Care without Waiting for the Police Report



Lesson: Doctors have the right to practice unencumbered in the best interest of patients even in medico-legal cases. In Pt. Parmanand Katara vs Union Of India & Ors on 28 August, 1989 AIR 2039, 1989 SCR (3) 997, the Supreme Court of India, in the context of medico-legal cases, has emphasised the need for rendering immediate medical aid to injured persons to preserve life and the obligations of the State as well as doctors in that regard. The Court observed: "Every doctor whether at a Government Hospital or otherwise has the professional obligation to extend his services with due expertise for protecting life. No law or State action can intervene to avoid/delay the discharge of the paramount obligation cast upon members of the medical profession."

Regulation 13 of the Code of Medical Ethics framed by the Medical Council of India also says that the patient must not be neglected. "A physician is free to choose whom he will serve. He should, however, respond to any request for his assistance in an emergency or whenever temperate public opinion expects the service…"

CASE SUMMARY

Mr P, a human rights activist, filed a writ petition in the Supreme Court under Article 32 of the Constitution of India on the basis of a newspaper report titled ''Law helps the injured to die". According to the story, a bystander picked up an injured scooterist who had been hit by a speeding car. He took the injured to the hospital nearby, but the doctors refused to attend to the victim and instead asked him to take the injured person to another hospital located, 20 km away, that was authorised to handle medico-legal cases.

The victim succumbed to his injuries before he could reach the hospital. Mr 'P' asked that every citizen brought to the hospital should be promptly administered treatment and the procedural criminal law should be allowed to operate after that. And, suitable compensation should be allowed in addition to any action taken for negligence in contravention of this directive.

SOME SALIENT COURT OBSERVATIONS

- The Counsel for Medical Council of India (MCI) stated that there is no prohibition in law justifying the attitude of the doctors as complained. The affidavit filed on behalf of the MCI mentioned 'Clause 10 - Obligations to the sick and Clause 13 – The patient must not be neglected' of the Code of Medical Ethics Regulations and further stated: "*… It should be the duty of a doctor in each and every casualty department of the hospital to attend such person first and thereafter take care of the formalities under the Criminal Procedure Code. The life of a person is far more important than the legal formalities.*"
- The affidavit filed on behalf of the Union of India on 3rd August, 1989 also said: "*There are no provisions in the Indian Penal Code, Criminal Procedure Code, Motor Vehicles Act, etc. which prevent Doctors from promptly attending seriously injured persons and*

accident case before the arrival of Police and their taking into cognisance of such cases, preparation of F.I.R. and other formalities by the Police."

- *"There can be no second opinion that preservation of human life is of paramount importance. This is so on account of the fact that once life is lost, the status quo ante cannot be restored, as resurrection is beyond the capacity of man."*
- *"Every doctor whether at a Government hospital or otherwise has the professional obligation to extend his services with due expertise for protecting life. No law or State action can intervene to avoid/delay the discharge of the paramount obligation cast upon members of the medical profession. The obligation being total, absolute and paramount, laws of procedure whether in statutes or otherwise which would interfere with the discharge of this obligation cannot be sustained and must, therefore, give way."*
- *"There is also no doubt that the effort to save the person should be the top priority not only of the medical professional but even of the Police or any other citizen who happens to be connected with the matter or who happens to notice such an incident or a situation."*
- The Court observed that there is an apprehension among doctors that he/she would be called as witness in medico-legal cases and also that they would be interrogated by the Police, which prevents them from helping such cases. It said, *"…, the policy, the members of the legal profession, our law courts and everyone concerned will also keep in mind that a man in the medical profession should not be unnecessarily harassed for purposes of interrogation or for any other formality and should not be dragged during investigations at the Police station and it should be avoided as far as possible. We also hope and trust that our law courts will not summon a medical professional to give evidence unless the evidence is necessary and even if he is summoned, attempt should be made to see that the men in this profession are not made to wait and waste time unnecessarily…"*
- *"We have no hesitation in saying that it is expected of the members of the legal profession which is the other honourable profession to honour the persons in the medical profession and see that they are not called to give evidence so long as it is not necessary… where the facts are so clear it is expected that necessary harassment of the members of the medical profession either by way of requests for adjournments or by cross examination should be avoided so that the apprehension that the men in the medical profession have which prevents them from discharging their duty to a suffering person who needs their assistance utmost, is removed and a citizen needing the assistance of a man in the medical profession receives it."*
- *"…if he finds that whatever assistance he could give is not sufficient really to save the life of the person but some better assistance is necessary-it is also the duty of the man in the medical profession so approached to render all the help which he could and also see that the person reaches the proper expert as early as possible."*

COURT ORDER

The Court ordered that the guidelines indicated in the 1985 decision of the Committee under the Chairmanship of the Director-General of Health Services should become operative.

1. *"Whenever any medico-legal case attends the hospital, the medical officer on duty should inform the Duty Constable, name, age, sex of the patient and place and time of occurrence of the incident, and should start the required treatment of the patient. It will be the duty of the Constable on duty to inform the concerned Police Station or higher police functionaries for further action. Full medical report should be prepared and given to the Police, as soon as examination and treatment of the patient is over. The treatment of the patient would not wait for the arrival of the Police or completing the legal formalities.*
2. *Zonalisation as has been worked out for the hospitals to deal with medico-legal cases will only apply to those cases brought by the Police. The medico-legal cases coming to hospital of their own (even if the incident has occurred in the zone of other hospital) will not be denied the treatment by the hospital where the case reports, nor the case will be referred to other hospital because the incident has occurred in the area which belongs to the zone of any other hospital. The same police formalities as given in para 1 above will be followed in these cases.*
3. *All Government Hospitals, Medical Institutes should be asked to provide the immediate medical aid to all the cases irrespective of the fact whether they are medico-legal cases or otherwise. The practice of certain Government institutions to refuse even the primary medical aid to the patient and referring them to other hospitals simply because they are medico-legal cases is not desirable. However, after providing the primary medical aid to the patient, patient can be referred to the hospital if the expertise facilities required for the treatment are not available in that Institution."*

REFERENCE

1. Pt. Parmanand Katara vs Union of India & Ors on 28 August, 1989; 1989 AIR 2039, 1989 SCR (3) 997.

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Medtalks with Dr KK Aggarwal

CMAAO Coronavirus Facts and Myth

Possible Mental Health Pandemic

Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases (NIAID) and a top White House COVID-19 advisor, is concerned how Americans will react once the pandemic is controlled. An American Psychological Association survey has noted high stress levels among people because of the pandemic. Hence, there are concerns about a possible mental health pandemic.

The survey has revealed the following:

- 61% of respondents reported experiencing undesired weight changes since the pandemic started.
- 67% reported changes in their sleep habits, with 35% reporting that they slept more while 31% slept less.
- 23% of the respondents reported drinking more alcohol to tackle stress.
- 47% reported that they delayed or canceled healthcare services because of the pandemic.
- 48% reported that their stress levels had increased. (*WebMD*)

UK COVID Variant More Deadly

The B.1.1.7 strain, first identified in Britain, is 30-100% more deadly than previous dominant variants. The strain is now found in over 100 other countries. Scientists have stated that it is about 40-70% more transmissible than previous dominant variants. In a UK study, published in *The BMJ*, infection with the new variant resulted in 227 deaths among 54,906 COVID-19 patients, compared to 141 deaths among the same number of patients matched for age, sex, sociodemographic background, date of infection, etc., who were infected with other variants. (*Mint*)

Data Suggest Vaccine 94% Effective in Preventing Asymptomatic Infection, Say Pfizer and BioNTech

Pfizer Inc and BioNTech SE stated that real-world data from Israel suggests that their COVID-19 vaccine is 94% effective in preventing asymptomatic infections. This would mean that the vaccine could significantly reduce transmission. The latest analysis of the data from Israel shows that the vaccine was 97% effective in preventing symptomatic disease, severe disease and death. This is in accordance with the 95% efficacy reported by the companies from the late-stage clinical trial in December. (*Reuters*)

Molnupiravir for Treatment of COVID-19

Interim phase 2 results from the oral experimental COVID-19 drug molnupiravir were presented at the Conference on Retroviruses and Opportunistic Infections (CROI) 2021 Annual Meeting. The drug led to significant reduction in the infectious virus in symptomatic patients who had tested positive for COVID-19 during the previous 4 days but were not hospitalized. After 5 days of treatment, none of the subjects who received molnupiravir had detectable virus, while 24% who received placebo did. (*Medscape*)

Mental Health Impact of COVID-19

A new survey looked at the mental health impact of COVID-19 globally. The findings revealed high rates of trauma and clinical mood disorders related to the pandemic. The survey was conducted by Sapien Labs in eight English-speaking countries and included 49,000 adults. About 57% of respondents reported having experienced some COVID-19–related adversity or trauma. About a quarter had clinical signs of or had a risk for a mood disorder. Just 40% of the respondents described themselves as succeeding or thriving. (*Medscape*)

Is One mRNA Vaccine Dose Enough for People Who have had COVID-19?

Individuals who have had COVID-19 may need only one dose of the Pfizer/BioNTech or Moderna vaccine to get the effect of two doses. The disease seems to prime the body to produce antibodies seen with the two-dose vaccine regimen, reported an exploratory study presented at the virtual Conference on Retroviruses and Opportunistic Infections. The study looked into the titer

levels of antibodies among patients who had COVID-19 and those who did not… (*Medpage Today*)

Is Pollen Driving COVID-19 Infection?

Some scientists have identified a pattern to the recurring waves of COVID-19 infection across the globe. They noted that as pollen levels increased in outdoor air across 31 countries, cases of COVID-19 increased. However, certain other studies point to the contrary, indicating that peaks in pollen seasons correspond to a decline in the spread of some respiratory viruses, such as COVID-19 and influenza. There's even some evidence that pollen may compete with the virus known to cause COVID-19 and may help prevent infection. (*Medscape*)

COVID-19 Vaccination in Immunocompromised

In a study with 436 COVID-naïve subjects who received a first dose of mRNA vaccine, a mere 17% attained detectable antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On the contrary, among immunocompetent individuals who were vaccinated, 100% attained detectable antibody levels. It was noted that individuals taking antimetabolites, **such as mycophenolate or azathioprine,** had about five times lesser odds of developing antibody responses (8.75% detectable antibody in those taking antimetabolites compared to 41.4% in those not taking them).

Considering these findings, the Centers for Disease Control and Prevention (CDC) guidelines for vaccinated individuals should be updated, warning immunosuppressed people that they still may be prone to COVID-19 following vaccination.

It is clear that immunosuppressed people need their second vaccine dose. Additionally, it is important for immunosuppressed people to understand that they are not necessarily immune after receiving the vaccine, and should consult with their providers about antibody testing. (*Medpage Today*)

Blood Type A Linked to COVID-19 risks

Blood type A has been found to be linked with a greater risk of severe COVID-19 in one recent study and with a higher risk of contracting the disease in another study. Dr James Szymanski of Montefiore Medical Center and Albert Einstein College of Medicine in New York City, co-author of one of the studies, stated that their study indicates that blood Group A may be associated with a greater risk, while the second study gives one possibility on the 'how' part. That study suggests that the receptor-binding domain (RBD) of the SARS-CoV-2 virus interacts with respiratory cells via the blood Group A antigen. (*Medscape*)

Child Vaccinations Required for Herd Immunity

Anthony Fauci, Director of the NIAID, stated that while it is not known what the magical point of herd immunity is, but if a major proportion of the population is vaccinated, it will be good. He added that children will have to be in that mix. He estimated that 70-85% of the population would need to be vaccinated or immune in order to attain herd immunity. (*WebMD*)

Changes to the Sebum Lipidome with COVID-19 Infection

In a study published by *Lancet EClinicalMedicine*, sebum samples were obtained from 67 hospitalized patients, 30 of whom were COVID-19 positive and 37 were negative. Lipidomics analysis detected 998 reproducible features. Lipid levels were depressed in COVID-19-positive individuals, suggesting dyslipidemia. (https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(21)00066-3/fulltext)

Variants may Escape Vaccines

Antibodies induced by the Moderna and Pfizer vaccines appear to be considerably less effective when it comes to neutralizing certain variants. A new study collected blood samples from 99 people who had been given one or two doses of either vaccine and evaluated the vaccine-induced antibodies against engineered virus that mimic 10 variants circulating across the globe. Five out of the 10 variants were highly resistant to neutralization, even when the study participants had received both doses of the vaccines, reported researchers in *Cell*. All of the five highly resistant variants had mutations in the spike [K417N/T, E484K and N501Y]. The proportion of neutralizing antibodies was found to decline 5- to 6-times against the variants discovered in Brazil. Neutralization declined 20- to 44-fold against the variant discovered in South Africa. It appears that vaccine-induced antibodies may find it harder to neutralize variants with E484K. (*Reuters*)

Older Individuals More Likely to Catch COVID Again

A new study suggests that older individuals who have recovered from COVID-19 cannot assume that they have immunity against a second attack. The study suggests that those below the age of 65 are less prone to reinfection. The study, conducted in Denmark, noted that those below 65 had nearly 80% protection for at least 6 months against contracting COVID a second

time. Contrary to that, those above 65 had only 47% protection. Authors of the study, published in the *Lance*t, say that it is important to take measures to protect elderly people, who also have an increased likelihood of death from COVID-19. The study confirms previous findings that reinfection is rare in younger, healthy people, but the elderly have a higher risk of catching the infection again. (*The Guardian*)

Women in 40s, 50s Who Survive COVID have Higher Odds of having Persistent Problems

Women in their 40s and 50s seem to have a higher risk of long-term problems following discharge from hospital after COVID-19. Several of them may suffer from months of lingering symptoms like fatigue, breathlessness and brain fog, noted two UK studies. In one study, 5 months following discharge, COVID-19 patients who were also middle-aged, white, female, and had other health problems including diabetes, lung or heart disease, had a higher likelihood of reporting long-COVID symptoms. A second study by the International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) revealed that women below 50 years of age were more likely to have worse long-term health outcomes compared to men as well as older participants, even in the absence of any underlying health conditions. (*Reuters*)

Kaleido Biosciences Says Its Experimental Oral Drug Reduces COVID-19 Recovery Time, Hospitalizations

Kaleido Biosciences has stated that in an early trial, its experimental oral treatment reduced recovery time and hospitalizations as well as emergency room visits among patients with mild-to-moderate COVID-19. KB109, the experimental treatment, decreased the number of hospitalizations, emergency room visits and urgent care visits by 51% in the study that included 350 patients, and by 62% among patients who had one or more comorbidities. This treatment is a targeted, synthetic glycan that works by changing the composition and metabolic output of gut microbes. (*Reuters*)

Pfizer and Moderna Vaccines Effective for Healthcare Workers

Data from healthcare workers in the United States and Israel have confirmed the effectiveness of the Pfizer and Moderna vaccines against COVID-19. The data are published in *The New England Journal of Medicine*.

Pooled data from employees from the University of California, San Diego and the University of California Los Angeles health systems suggest that during a system of aggressive testing, carried out during a spike in COVID-19 cases in the general population, **there was a dramatic decline in the rate of new infections among the staff, beginning the second week after the first dose of the vaccine was given.**

Testing revealed **new cases in 2.5% of those tested within the first week following the first dose, 1.2% in the second week, 0.7% in the third week, 0.4% during the week following the second dose and less than 0.2% during the second week following the second dose.**

In North Texas, workers were also vaccinated amid the largest COVID-19 surge in the region. Here, 2.61% of unvaccinated employees developed the infection compared to 1.82% of partially-vaccinated workers and 0.05% of fully-vaccinated employees. There was more than 90% reduction in the number of employees either in isolation or quarantine, thus preserving the workforce when it was needed the most during the surge. (*Medscape*)

SARS-CoV-2 Variants Detected in Animals

Veterinarians in Texas and the UK have identified infections with B.1.1.7 among dogs and cats. Animals in the UK study were also found to have heart damage. However, it is not clear if the damage was caused by the virus or was already there and was detected because of their infections.

Researchers at the Institut Pasteur, Paris noted that the B.1.351 and P.1 variants of concern, first detected in South Africa and Brazil, respectively, can infect mice. Thus, the virus seems to have a potential new host. Older versions of the virus couldn't infect mice as they could not bind to receptors on their cells. However, these two variants can.

Good: This will assist scientists conduct experiments in mice easily. Earlier, conducting an experiment with SARS-CoV-2 in mice needed the use of a special strain of mouse that was bred to carry human angiotensin-converting enzyme 2 (ACE2) receptors on their lung cells. Now, since the mice can contract the infection naturally, any breed can be used.

Bad: Virus could now have more and varied ways to spread. (*Medscape*)

Rituximab therapy has been found to be tied to more severe COVID-19 among patients with inflammatory rheumatic and musculoskeletal diseases in a study published in *The Lancet Rheumatology*.

From April 15 till November 20, 2020, investigators looked at data from 1,090 patients who had

inflammatory rheumatic and musculoskeletal diseases and suspected or confirmed COVID-19 from the French RMD COVID-19 cohort. Sixty three of these patients were treated with rituximab, particularly for rheumatoid arthritis (49%), antineutrophil cytoplasmic antibody-associated vasculitis (17%) and systemic sclerosis (11%). Of the 1,027 patients who were not given rituximab, a subgroup of 495 patients had diseases for which rituximab is a known treatment option. (*Lancet Rheumatology*)

Moderna and Pfizer-BioNTech Vaccines Effective in Real-world Settings at Preventing COVID Infections

The Moderna and Pfizer-BioNTech COVID-19 vaccines are proving to be highly effective for the prevention of symptomatic and asymptomatic infections under real-world settings. There has been a discussion whether vaccinated people can get asymptomatic infections and transmit the virus and the findings suggest that transmission may be highly unlikely. Virus variants were in circulation when the study by researchers at the CDC was conducted, but the vaccines still provided robust protection. In line with the clinical trial data, a two-dose regimen prevented 90% of infections by 2 weeks following the second dose. Following one dose, 80% of infections were prevented by 2 weeks. (*NY Times*)

COVID-19 Risk in Adult Congenital Heart Disease

Most adults with congenital heart disease (CHD) do not appear to have an increased risk of COVID-19 mortality; however, certain subgroups may have a high risk, reports an international study. Fever, dry cough and malaise seem to be the most common presenting symptoms. Sixty patients had no presenting symptoms but underwent testing on the basis of known exposure or an upcoming procedure. A total of 179 patients (17%) were hospitalized and 67 patients (6.4%) needed ICU admission, 36 of whom had to be intubated.

There were 24 COVID-19–related deaths, with a case/fatality rate of 2.3% (95% confidence interval [CI], 1.4-3.2%). This is in line with a reported cumulative world fatality rate of 2.2%. Mortality rates and severe course varied by CHD diagnosis and were found to be the highest in patients with Eisenmenger physiology (13%), cyanosis (12%) and pulmonary arterial hypertension (10%). The findings are published in the *Journal of the American College of Cardiology*. (*Medscape*)

New COVID Vaccines Needed within a Year

Around two-thirds of epidemiologists from across the globe state that we will need new or modified vaccines for COVID-19 within a year. A survey of 77 epidemiologists from 28 countries by the People's Vaccine Alliance, reported that about 66.2% predicted that the world has a year or even less before the available vaccines become ineffective against the variants.

Around one-third (32.5%) of the surveyed epidemiologists said that ineffectiveness would be seen in 9 months or less while 18.2% said it will be seen within 6 months or less. Around 88% of those surveyed said that persistently low vaccine coverage in many countries would increase the likelihood of emergence of vaccine-resistant mutations. (*Medscape*)

When variants of SARS-CoV-2 started surfacing in late 2020, there were concerns that they might elude the immune responses generated by previous infection or vaccination, thus making reinfection more likely or vaccination less effective.

NIAID researchers evaluated blood cell samples from 30 people who had recovered from COVID-19 before the virus variants emerged. It was noted that **CD8+ T-cell continued to remain active against the virus.**

The investigators explored if CD8+ T cells in the blood of recovered COVID-19 patients, who had been infected with the initial virus, could recognize the three key variants: B.1.1.7, B.1.351 and B.1.1.248.

Investigators noted that the SARS-CoV-2-specific CD8+ T-cell responses were largely intact and recognized virtually all mutations in the variants that were studied.

The T-cell response in convalescent individuals, and in individuals who have been vaccinated, do not seem to be affected by the mutations in these three variants, and should protect against emerging variants.

Optimal immunity to the virus needs strong multivalent T-cell responses besides neutralizing antibodies and other responses to protect against current SARS-CoV-2 strains as well as the emerging variants. (*NIH*)

Measles Vaccine as Base for Experimental COVID-19 Vaccine

Measles vaccine is among the safest and most effective vaccines. The vaccine has been shown to be safe in both children and adults, and provides long-term protection against the measles virus. It uses a live, weakened strain of the measles virus.

Researchers have used it to develop an experimental vaccine against SARS-CoV-2. They created and evaluated a series of measles-based vaccine candidates. The vaccines were developed by inserting genes for

different forms of the coronavirus spike protein into the measles vaccine genome.

The modified measles virus serves as a vehicle and carries the gene for the spike protein into the body. The cells are instructed to produce the coronavirus spike protein, thus prompting the immune system to produce antibodies. This guides the immune system to neutralize the virus when encountered.

The study findings have been published in the *Proceedings of the National Academy of Sciences*.

Researchers found the most promising vaccine candidate, which produced the highest levels of neutralizing antibodies against SARS-CoV-2 in rodents. The vaccine carried the gene for the stabilized prefusion version of the spike protein, which forms the basis for the available vaccines.

The new vaccine, named rMeV-preS, yielded neutralizing antibody levels in rodents higher than those seen in patients who have recovered from COVID-19. The vaccine also evoked a robust T-cell response.

Researchers also assessed if the vaccine would protect against SARS-CoV-2 infection. Using golden Syrian hamsters, they noted that the vaccine protected them from infection and also prevented viral replication in the lungs and nasal passages.

This new candidate may offer several advantages. The measles vaccine is known to be safe, effective, and long-lasting. Several experimental measles-based vaccines against other viruses are also being evaluated in clinical trials. The new vaccine could protect against both COVID-19 and measles. (*NIH*)

Super-spreader Events Driving Variants

Super-spreader events are pivotal to the survival and predominance of new variants.

If the transmission of the virus only occurs one person at a time, a new variant cannot gain dominance and will die out in the population by chance.

Even strong variants can die out if they are not by chance transmitted in a super-spreader event.

Early super-spreader events that infect over five people are critical to the survival of a variant, while super-spreader events that infect over 20 people are critical to its dominance.

Even a highly infectious new variant will need a super-spreader event to help it overtake a current variant. (*Reuters*)

Vaccines Effective Against New York Variant

Antibodies induced by the Pfizer/BioNTech and Moderna vaccines as well as the antibody therapy from Regeneron, can neutralize a coronavirus variant currently surging in New York.

The New York variant contains mutations E484K, S477N and D235G. Experts were concerned that the variant might diminish antibody efficacy. However, new results suggest that this potential problem is not a problem.

The mutations cause changes to the spike protein. The researchers exposed copies of the New York variant to blood obtained from individuals who had received either the vaccines or the antibody combination from Regeneron. Vaccine-induced antibodies were found to be highly effective at binding to the altered spike protein, and the Regeneron therapy was also a potent blocker of the virus, reported researchers. (*Reuters*)

Immune Response could Explain Rare Clots After AstraZeneca COVID-19 Vaccine

Rare but serious blood clots have been reported among some individuals who have received AstraZeneca COVID-19 vaccine. They appear to be similar to heparin-induced thrombocytopenia (HIT). Here, heparin incites the immune system to produce antibodies that activate platelets. Drugs apart from heparin can lead to clotting disorders resembling HIT, and it is suspected that in rare cases, this vaccine may act as another such trigger.

Four healthy individuals who got the AstraZeneca vaccine and developed clots appeared to have the same kind of antibodies that activate platelets and initiate clotting in HIT, noted researchers in a paper posted on Research Square.

Twenty individuals who were administered the vaccine but did not develop clots were found not to have these antibodies. (*Reuters*)

SARS-CoV-2 Neutralizing Antibody Responses and Duration of Immunity

Antibodies against SARS-CoV-2 may die out at different rates based on the severity of the infection. The researchers in a new study, followed 164 COVID-19 patients for up to 9 months following infection. Five distinct groups were identified based on patterns of neutralizing antibodies:

- Negative group - did not develop neutralizing antibodies at the 30% inhibition level. They comprised 12% of patients in the study.

- Rapid waning group comprised 27% of the study patients. They had varying early levels of antibodies from around 20 days of symptom onset, but they sero-reverted in less than 180 days.
- Slow waning group - 29% of the study subjects; they remained antibody-positive at 180 days following symptom onset.
- Persistent group comprising 32% of the study subjects. They had minimal antibody decline up to 180 days.
- Delayed response group comprising 2% of the subjects in the study. They had a marked increase in neutralizing antibodies during late convalescence (at 90 or 180 days after symptom onset).

In the study published in *Lancet Microbe*, the researchers stated that persistence of neutralizing antibodies had a link with disease severity and sustained levels of pro-inflammatory cytokines, chemokines and growth factors. T-cell responses did not have a clear link with the different patterns of neutralizing antibodies.

(*The Lancet Microbe*)

With input from Dr Monica Vasudev

The CDC and the WHO have Determined New Criteria for the Classification of Variants of SARS-CoV-2

The new designations include "variant of interest"; "variant of concern" and "variant of high consequence".

- *A variant of interest* is the one that has led to discrete clusters of infections in the United States or in other countries, or appears to be guiding a rise in cases. It carries gene changes indicating that it might be more transmissible or that may help it to evade immunity conferred by natural infection or vaccination. Treatments and tests may not work as well against it. The CDC is looking at three of these.
- *A variant of concern*, as proven through scientific research, is more contagious or leads to more severe disease. It may also diminish the effectiveness of treatments and vaccines. People, who had previously been infected with COVID-19, may become reinfected by the new strain. The CDC is looking at five of these.
- *A variant of high consequence* is the one that leads to more severe disease and increased hospitalizations. It leads to failure of medical countermeasures, such as vaccines, antiviral drugs, and monoclonal antibodies. None of the variants thus far fulfil this criteria. (*Medscape*)

How Much Physical Distance is Required to Safely Reopen Schools?

- A study, conducted in Massachusetts, published in the journal *Clinical Infectious Diseases*, noted that it did not make a difference to keep children 6 feet apart compared to half of that.
- Data over the last year have revealed that schools do not seem to be super-spreading environments.
- Any outbreaks that may have happened in schools were associated with exposures in the community or happened in schools in the absence of protective protocols.
- The nonrandomized study compared COVID-19 rates in 242 Massachusetts school districts. Some of them kept students 6 feet apart while others maintained 3-foot distance over a 16-week period between September 2020 and January 2021. Student case rates were found to be similar in districts with ≥3 feet versus ≥6 feet of distance between students after adjusting for rates of SARS-CoV-2 in the community.
- Among school staff, there were similar case rates in districts with ≥3 feet versus ≥6 feet of physical distancing.
- Study authors thus concluded that lower physical distancing policies can be adopted in schools with masking mandates.
- The CDC also now recommends that a 3-foot distance can be used in situations, where teachers are fully vaccinated with two doses of a COVID-19 vaccine.
- Physical distancing continues to be a part of the recommendations for schools, besides universal masking, hand hygiene, cohorting of students and teachers, and use of outdoor space when possible.
- How to achieve herd immunity to COVID when children are excluded from vaccination? At least 70% of the population is required to have immunity, either through vaccination or natural infection, in order to reach herd immunity.
- In the US, about 25% of the population is below 18 years of age. Considering the number of adults refusing vaccination, it would be difficult to attain herd immunity through vaccination unless children and teens are included.
- Pfizer has completed enrollment for a clinical trial for older children (age 12 and up) and Moderna is having a trial underway in adolescents. (*Medpage Today*)

HCFI Round Table Expert Zoom Meeting on "Covishield Vaccine Halted in Some European Countries: Evidence-based or Knee Jerk Reaction?"

13th March, 2021 (11 am-12 pm)

Participants: Dr KK Aggarwal, Dr Shashank Joshi, Dr Suneela Garg, Dr DR Rai, Mrs Upasana Arora, Ms Balbir Verma, Dr KK Kalra, Dr Ashok Gupta, Dr Anil Kumar, Ms Ira Gupta, Dr S Sharma

Consensus Statement of HCFI Expert Round Table

- If the reactogenicity is uncontrolled, inflammation is likely.
- Delayed local injection site reaction to vaccine is uncommon; they are likely due to T-cell–mediated hypersensitivity.
- Mantra: In susceptible high-risk (proinflammatory and/or procoagulative) individuals, reactogenic vaccines can trigger transient thromboinflammation, lasting for first few (up to 4) days.
- Muscle COVID vs. COVID disease: Vaccine-induced disease is nonpulmonary. In muscle COVID, nonreplicable dose of the gene is injected, whereas in COVID disease, the gene is replicable. Vaccine is a fixed-dose, whereas in the disease, the dose is variable. In vaccine, the acute inflammation lasts for up to 4 days, whereas in the disease, the inflammation lasts for 10 days or more.
- Individuals with microalbumin in urine, C-reactive protein (CRP) >1 and 6-minute walk text (MWT) <200 m are high risk.
- Acanthosis nigricans is procoagulative or prothrombotic state.
- This vaccine is going to be more reactogenic than mRNA vaccine.
- Reactogenicity is different from allergenicity and immunogenicity.
- Cases of disease enhancement are being seen. If vaccine is given in the presence of non-neutralizing antibodies, these patients may develop some degree of nonpulmonary disease enhancement presenting with high-grade fever and high CRP.
- Considering the large coverage of Covishield, the reported adverse drug reactions (ADRs) seem to be reasonably less. Direct cause-effect relationship has not been established.
- The Indian vaccination program perhaps has the largest pharmacovigilance database, but there is a need to simplify the system and make it single point reporting, harmonize the ADR reporting and make it hassle-free and digital.
- Maharashtra is in the second surge. In Maharashtra, the Vidharbha and Marathwada regions were less exposed during the first surge. There were gatherings, no masking and no physical distancing and total lack of adherence to COVID appropriate behavior protocol. In Amravati, Akola, clusters of cases were seen. Whole buildings were affected.
- There is an unusual strain, which is spreading rapidly, but it has good recovery and case fatality rate is very low. Testing frequency had dramatically come down. In Mumbai local trains, physical distancing is not possible and masking was scanty. Hence, double masking is being recommended.
- About 80% of cases in Maharashtra are asymptomatic. They do not home isolate despite stamp. In some districts, institutional quarantine is being done even for asymptomatic cases otherwise they become spreading points.
- Gut COVID is seen more; patients are coming with diarrhea. Sewage may be a source of infection.
- Contact tracing has been increased to 1:30.
- The positive signals are asymptomatic infection, faster recovery, younger age and lower death rates.
- Usually Maharashtra precedes the country; what is happening here, it is likely to happen in the rest of the country. Maharashtra is in the same stage as Europe was 2-3 months back. Rapid vaccination is the answer. Citizens have to take responsibility.
- Dissemination of findings of investigation of death after vaccine is important, whether related to the vaccine or not. Precautions to be taken by susceptible persons should be more widely disseminated.

Viral Vector Vaccines Don't Seem to Alter DNA

- Adenoviral vector vaccines have been in development for decades. However, only a few of them have been approved for use in humans.
- Adenoviruses are common cold viruses known to cause illnesses that range from cold-like symptoms to bronchitis, gastroenteritis and conjunctivitis.
- Most serotypes of adenovirus cause mild illness, while serotype 7 is linked with more severe illness. Older adults and immunocompromised individuals or those having pre-existing respiratory or cardiac disease may have worse illness.
- Since adenoviruses are so common, one problem with using them in vaccines is that people may

already have antibodies against them, which might overwhelm them before they can do their work.

- Researchers try to overcome this issue by using adenoviruses that humans are not likely to have encountered before.
- Five adenovirus vector vaccines for COVID-19 are in use across the globe.
- Each of them works on the same basic principle, while delivery platforms may differ. The AstraZeneca/Oxford vaccine uses the ChAdOx1 platform, which is based on a modified chimpanzee adenovirus.
- The Johnson & Johnson vaccine makes use of a proprietary AdVac platform, which constitutes a recombinant human adenovirus (adv26). It's the same platform that the company uses in its Ebola virus vaccine (approved in Europe) and its investigational Zika, respiratory syncytial virus (RSV) and human immunodeficiency virus (HIV) vaccines.
- Sputnik V uses recombinant human adenoviruses Ad26 and Ad5 for the first and second doses, respectively.
- China's CanSino vaccine uses recombinant human adenovirus Ad5.
- In the 1990s, study on adenoviruses for use in gene transfer therapy to treat diseases like cystic fibrosis began.
- Adenoviruses induced robust T- and B-cell immune responses, leading to quick viral clearance but this limited their purpose in gene therapy. But as adenoviral vectors induced a strong immune response, it made them key candidates for developing vaccines against infectious diseases.
- Scientists have therefore been working on adenoviral vector vaccines against several viruses, including Zika, RSV, HIV, influenza, dengue and Middle East respiratory syndrome (MERS). During the Ebola outbreaks in West Africa and the Democratic Republic of the Congo (DRC), two adenoviral vector vaccines were developed and deployed. Adenoviruses can also be genetically modified for targeting and eliminating cancer cells.
- The platform that is being used in the AstraZeneca/Oxford vaccine had been in clinical trials in humans for over a decade for several other diseases.
- Adenoviruses can be used almost like a plug-and-play system. The platform doesn't need to be changed but we may switch out the gene of interest for a particular disease.
- Earlier work has provided data on dosage and safety of adenoviral vector vaccines in humans.
- Safety data from several trials in humans showed that they are safe and incite good immune responses.
- Adenoviral vector vaccines seem to have similar side effects as other types of vaccines like flu shots, such as pain at the injection site, headache or mild fever.
- Adenoviruses deliver DNA that enters the cell nucleus.
- Unlike retroviruses such as HIV or lentiviruses, wild-type adenoviruses do not have the enzymatic machinery which is required for integration into the host cell's DNA. This makes them good vaccine platforms for infectious diseases.
- Engineered adenoviruses used in vaccines have been further debilitated by deleting chunks of their genome. Therefore, they are not able to replicate, further increasing their safety.
- The cell lines that are used for adenovirus vaccines are well characterized cell lines. They are nonintegrating, which means that there is no evidence in humans and multiple animal models of vector-borne DNA integrating into a host.

(*Medpage Today*)

Women and COVID vs. Women and Vaccine

- CDC: Side effects from the vaccines appear to be worse in women. For example, 63 out of 66 reported cases of anaphylaxis occurred in women.
- Men in acute disease suffer worse outcomes. Men appear to have three times greater likelihood of being admitted into the ICU compared to women.
- Men appear to be more vulnerable to severe outcomes from viral infections, as evidenced in severe acute respiratory syndrome (SARS) epidemic in 2003 and in MERS epidemic.
- Immune response seems to be stronger in women as compared to men. Is it related to the two X chromosomes with the hormones that women have more of? The answer is both.
- X chromosome is enriched for immune response genes.
- Before menopause, every immune cell in our bodies has receptors for estrogen and progesterone hormones. These hormones regulate the functioning of immune cells. They can turn the

responses on and off. This holds true for androgens as well, like testosterone in men. Testosterone is anti-inflammatory and turns off several initial antiviral, inflammatory types of immune responses that trigger and let the body detect that there is something foreign you need to mount a protective response.

- So, women have two X chromosomes allowing additional activation to protect against immune function and response, and they also have the hormones that turn on response to target the virus; and men have the hormone that turns off the ability to target the virus?
- In women, the responses that get turned on and help protect against a virus, **can become dangerous when they mount against one-self, as in** autoimmune diseases.
- In systemic lupus erythematosus (SLE), there are 9-to-1 women to men. That's where one starts attacking own DNA. In multiple sclerosis, one is attacking the lining of one's nerve fibers. About 80% of all autoimmune disease patients are women.
- Significantly more women suffer from long COVID compared to men.
- Anecdotal reports suggest that women with COVID-19 have reported changes to their menstrual cycles. The parts of the brain that are associated with induction of fever are also the parts that control the hormonal regulation of menstrual cycle. So, it is feasible to see a connection. The connection between the immune system and reproductive function is known.
- Many vaccine adverse events are mediated by inflammation. If women have more of the inflammatory responses which are required to protect you against infection, that could be accountable for the development of these types of adverse reactions.
- In 1993, Revitalization Act required inclusion of women in all clinical trials.
- In 1977, it was determined that women of reproductive ages should not be included in clinical trials. This was meant to protect pregnant women and their developing fetuses from any potential toxicological effects of drugs or in the case of vaccines, biologics. But eventually, women were completely excluded from clinical trials and we were not given autonomy to make a decision for themselves, to claim that they wanted or didn't want to be included.
- Government Accounting Office audit in 2016 of all NIH uncovered that now more women than men enroll in clinical trials.
- But what's not happening is that there is no separation of the outcome data from men and women and comparison of those data.
- So, publication of data from clinical trials often don't tell us whether a drug or whether a vaccine or an intervention worked equally well in men and women. Or if there were differences in adverse events. Usually that becomes known only after a drug or a vaccine or an intervention has come out in to the market.
- In COVID vaccines, women weren't really given the choice to participate. Pregnant women were not subjected to the vaccines by their own choice. And now, women are going to get the vaccine who are pregnant and have a higher risk of COVID and severe outcomes from COVID; they don't really know how the vaccine works in pregnancy. (*Medpage Today*)

Thrice-Weekly Antigen Test or Once-Weekly RT-PCR

Amount of virus: When an individual is initially infected with SARS-CoV-2 (Day 0), a minute amount of the virus starts replicating inside them until it becomes so abundant that it cannot be contained. The infected individual thus becomes infectious and can spread the virus to others. This transition to becoming infectious usually **occurs around Day 3. By about the 5th day,** infected individuals usually reach peak contagiousness. The person's immune system starts containing the situation, and from Day 5 onward, the amount of virus starts declining. After nearly a week of contagiousness, by about Day 9, the virus is repressed. Viral particles continue to remain for weeks or months but are no longer a threat to others.

Polymerase chain reaction (PCR) is a better test. It can potentially detect virus very slightly earlier, and for much longer. However, what is important is detecting contagious virus.

- In order to detect **contagious virus, antigen tests appear to work just** as well and do not detect virus that does not pose a threat.
- One may consider two screening strategies: once-weekly PCR or thrice-weekly antigen testing.
- Let us imagine Day 0 is Sunday. If a student gets infected at a weekend playdate, the virus starts replicating, but the level is lesser than the threshold

for detection if a PCR test is done on Wednesday. If the test results are received on Friday, they will be negative. This is true for how the student was on Wednesday; but false for Friday.

- The infectious student has a false reassurance; so do the classmates, teachers, parents, etc. The student stays in school. When the infected student is again tested on Wednesday, the results on Friday show it as positive. This time, it is true for Wednesday but false for Friday (considering contagiousness). After a week of being contagious in school, the student is now sent home to self-isolate and the classroom is quarantined.
- Now, due to false positives, another classroom ends up shutting down. The teacher had a distant infection from which she has recovered and is no longer a threat. But considering several classrooms now with positive tests, the school has an outbreak and shuts down.
- If the infected student had been assessed with thrice a week antigen testing, it would have been identified on Friday. The results would have come out immediately, say within 15 minutes. The student would have been advised to self-isolate at home, and close contacts would have been sent home to quarantine. The PCR-positive teacher would have tested negative with an antigen test. The class would not have had to quarantine, and there would not have been an impression of outbreak at the school.
- Daily antigen screening would be even better. If everyone is screened every day, positive cases can be detected (and isolated) before anyone gets exposed. But even in the absence of daily screening, antigen testing several times a week would allow early detection. (*Medscape*)

COVID-19 Vaccination for Patients with Rheumatic and Musculoskeletal Diseases

The American College of Rheumatology: Guidance on COVID-19 vaccination for patients with rheumatic and musculoskeletal diseases (RMDs)

- Decisions to be individualized, with regard to disease severity, comorbidities and treatments.
- Patients with underlying diseases should be given priority for vaccination.
- A patient with rheumatoid arthritis whose disease is controlled with hydroxychloroquine will probably have lesser risk than someone with severe vasculitis under treatment with intravenous cyclophosphamide or rituximab.
- Vaccination should be done when the underlying disease is well controlled, if possible. However, a theoretical risk for disease flare or worsening after vaccination still exists.
- No one vaccine preferred over another; patients should be given whatever is easily available.
- No need to delay vaccination for patients on hydroxychloroquine, sulfasalazine, leflunomide, apremilast or intravenous immune globulin.
- For patients treated with rituximab, vaccination should be scheduled to be started 4 weeks prior to the next rituximab dose. This recommendation is based on a study that demonstrated differences in response to influenza vaccination on the basis of timing of rituximab dose.
- Methotrexate should be withheld for a week after each dose of the vaccine. This recommendation was based on studies of pneumococcal and influenza vaccines.
- A similar recommendation has been made for JAK inhibitors, owing to concern about the effects of this drug class on interferon signaling that may lead to decreased vaccine response.
- Abatacept must be withheld for a week prior to and after the first dose of the vaccine. This recommendation was based on findings of a possible negative effect of this drug on the immunogenicity of the vaccine. Furthermore, the first dose tends to prime naive T cells; CTLA4 inhibits naive T-cell priming; and abatacept is a CTLA4-Ig construct.
- Intravenous cyclophosphamide is usually given at intervals of 2 or 4 weeks. The recommendation in this case was to give cyclophosphamide dosing a week after the vaccine doses, if possible.
- It was recommended that rituximab be administered 2-4 weeks following the second vaccine dose if possible, but only if the disease is controlled enough to allow such a delay. This recommendation was based on immune responses to other vaccines, and it may not be possible to fully generalize this to the COVID-19 vaccine. (*Medpage Today*)

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

72nd Annual Cardiology Conference

THROMBOLYSIS IN INTERMEDIATE RISK PULMONARY EMBOLISM: YES, I WILL LYSE

Dr Shibba Takkar Chhabra, Ludhiana

Submassive pulmonary embolism accounts for 20% of pulmonary embolism cases, with in-hospital mortality of 2-5%. Systemic thrombolysis should be reserved for high risk intermediate pulmonary embolism patients with clinical and hemodynamic deterioration in presence of low bleeding risks. Half dose thrombolysis as one time bolus can be considered with strenuous clinical monitoring. Catheter directed thrombolysis can be considered in patients with failed systemic thrombolysis, clinical deterioration and increased bleeding risks.

EXERCISE IS GOOD AND SAME IRRESPECTIVE OF GENDER

Dr M Jyotsna, Hyderabad

Regular physical exercise improves the cardiovascular health, both directly and indirectly, in both sexes. Exercise improves effects of the traditional risk factors for cardiovascular disease (CVD). In addition, exercise improves vascular endothelial function, vascular remodeling in favor of angiogenesis, improves cardiac preconditioning and decreases the sympathetic tone in both sexes. There are differences in the occurrence and prognosis of different CVDs in men and women. Not only there are physiological differences in the male and female heart, but also difference in the response to pressure overload. Men and women differ in exercise habits. Recommendations for exercise and physical activity by ACC/AHA guidelines 2019 are same for both sexes.

WHEN TO INTERVENE IN MYOCARDIAL BRIDGE?

Dr Vijayachandra Reddy Y, Chennai

Myocardial bridge is common, benign and rarely necessitates testing or intervention. Beta-blockers or calcium channel blockers are useful treatment options. Document ischemia before intervention by dobutamine stress echocardiography (DSE), DS-myocardial perfusion imaging (MPI), DS-diastolic fractional flow reserve (dFFR). Minimally invasive surgical unroofing (myotomy) can help in some patients. Coronary stenting is likely deleterious.

CORONARY INTERVENTION IN WOMEN

Prof (Dr) Lekha Adik-Pathak, Mumbai

- Interventions in women is no more a dilemma. All women should be diagnosed properly from their atypical symptoms.
- Noninvasive tests have poor sensitivity.
- Coronary angiography is a better alternative.
- Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) are useful.
- Society and family should consider for interventions for women.

CORONARY IMAGING IN CONTEMPORARY CLINICAL PRACTICE: IVUS IS THE WAY FORWARD

Dr Gary S Mintz, USA

From more than 100 randomized trials, meta-analyses and registries, there is overwhelming evidence that IVUS-guidance improves percutaneous coronary intervention (PCI) outcomes (death, myocardial infarction [MI], ST and repeat revascularization) in simple as well as complex patients and lesions. While there are specific situations in which IVUS-guidance is preferred (left main coronary artery [LMCA], chronic total occlusion [CTO], chronic kidney disease [CKD], etc.), there are also situations when OCT is preferred. However, in the vast majority of cases, IVUS and OCT can be used interchangeably. The argument is not IVUS vs. OCT, but intravascular imaging guidance vs. angiography-guided PCI.

BALLOON EXPANDABLE VS. SELF-EXPANDING VALVES

Dr Sengottuvelu G, Chennai

Transcatheter aortic valve implantation (TAVI) is a well-established treatment for severe symptomatic aortic stenois. Both balloon expandable and self-expanding valves are widely used. Balloon expandable valve was the first system used for TAVI and has unique advantages: ease of doing, good results with low gradients, minimal paravalvular leak (PVL), excellent safety profile with low permanent pacemaker implantation (PPI) rates, stroke and patient-prosthesis mismatch (PPM).

With increasing TAVI numbers and longevity of patients, future coronary access becomes very important and

clearly balloon expandable valves do not interfere with successful coronary cannulation as opposed to self-expanding valves.

SALT, NUTRITION AND HYPERTENSION

Dr T Govindan Unni, Thrissur

Understanding of the sodium handling by the human body is slowly changing. Role of skin and muscle as reservoirs for salt has been accepted. Long-term and short-term high salt intake elicit different response from human body. Spot sample of urine does not reflect daily salt intake. This understanding questions the findings of major epidemiological studies so far. Role of reduced potassium intake in 21st century diet is also important. The Dietary Approaches to Stop Hypertension (DASH) and Mediterranean diet are considered the best for preventing hypertension. Finally, role of gut microbiome is also increasingly discussed in the pathogenesis of hypertension.

PATHOPHYSIOLOGY AND MANAGEMENT OF SUBCLINICAL ATRIAL FIBRILLATION: KNOWNS AND UNKNOWNS

Dr Bernard Gersh, USA

- Undetected or silent atrial fibrillation (AF) is relatively common. It is associated with risk of stroke, related to AF burden and risk factors.
- Temporal relationship between both timing of AF and stroke is variable (>30 days in the majority). Whether oral anticoagulation (OAC) has overall benefit is being investigated in trials (ARTESIA, NOAH, Danish Loop). How much AF is too much is not known.
- In the interim – Treat if duration >24 hours, depending on risk factors and individualized risk assessment; Duration of 6-24 hours is a subject of ongoing trials; After cryptogenic stroke, generally treat if >30 seconds-2 mins of AF (recent trials may question this approach).
- Whether, when, whom and how to screen is the subject of ongoing studies.

PERIPARTUM CARDIOMYOPATHY – AN UPDATE

Dr Sarita Rao, Indore

The diagnosis of peripartum cardiomyopathy (PPCM) should be considered in any pregnant or postpartum woman with symptoms concerning for HF. An elevated brain natriuretic peptide (BNP) level should always be followed by an echocardiogram to assess for systolic dysfunction. Prompt treatment with medications tailored for pregnancy and lactation may prevent adverse outcomes. Limited studies suggest breastfeeding is safe. Acutely ill women should be managed by specialized multidisciplinary teams, and may require advanced heart failure therapies. Women considering a subsequent pregnancy should be counseled and monitored by physicians familiar with PPCM. Long-term follow-up is important, but the optimal duration of medications following recovery is unknown. Despite many advances in our understanding of PPCM, questions remain about the pathogenesis and complex interaction of genetics with the vascular and hormonal milieu of late pregnancy.

COMPLEX CORONARY INTERVENTION

Dr Amisha Patel, USA

High-risk PCI can be done safely in patients with severe aortic stenosis by doing balloon valvuloplasty followed by plaque modification with atherectomy.

BLOOD PRESSURE-LOWERING COMBINATION THERAPY: PUSHING THE BOUNDARIES FOR BETTER ADHERENCE, EFFICACY AND EFFICIENCY

Dr Mark Huffman, USA

Massive scale of hypertension burden requires a response that is effective and efficient, and combination therapy can help. Combination therapy serves as the backbone for many hypertension control programs around the world, including in the US, much like HIV, TB and malaria care. Triple-drug half-dose and quadruple-drug, quarter-dose combination therapies may be strategies to push the boundaries of simplifying treatment to improve adherence, efficacy and even efficiency.

INTERVENTIONS IN MALIGNANCY: CAN THE CATHETER DO SOME GOOD?

Dr Lijesh Kumar, Cochin

A catheter is a modern day scalpel and interventionist a modern day surgeon. As interventional radiologists, we deal with a wide gamut of clinical scenarios related to malignancy. Catheter based interventions in oncology range in scope across all organ systems and include a host of scenarios, where we contribute either to curative or palliative management. As the cancer burden increases across the world and India set to become the cancer capital, these services help these patients lead a dignified fulfilling life, especially in the setting of longer survival with better oncological treatment.

MASKED HYPERTENSION: IS IT TOO MUCH STRESS?

Dr SB Gupta, Mumbai

The prevalence of masked hypertension in patients with treated and well-controlled clinic BP is high. Masked hypertension is more common in patients with CKD and associated with lower estimated glomerular filtration rate (eGFR), proteinuria and cardiovascular target-organ damage. Nocturnal BP is increasingly recognized as a strong predictor of risk in many studies of ambulatory BP monitoring (ABPM). Clinic BP monitoring alone is not adequate to optimize BP control because many patients have an elevated nocturnal BP. The US Preventive Services Task Force concluded that ABPM is the diagnostic method of choice for detecting both outliers of white coat and masked hypertension.

THE EVIDENCE FOR THE UNIVERSAL BLOOD PRESSURE GOAL OF <130/80 MMHG IS STRONG

Dr Ashok Goyal, Jaipur

- My thoroughly reviewed and evidence-based answer remains…"YES"
- The evidence for the universal blood pressure (BP) goal of <130/80 mmHg is strong.

NOACS IN MITRAL VALVE DISEASE – CURRENT DATA

Dr George Koshy A, Thiruvananthapuram

Non-vitamin K oral anticoagulants (NOACs) are effective and safe in mitral regurgitation and other valvular heart disease with AF. They are safe in mitral bioprosthetic valve with AF, beyond 3 months (may be beyond 48 hours). Mechanical heart valve (MHV) does require vitamin K antagonist (VKA). Newer data suggest that NOACs are more effective than VKA in mitral stenosis (MS) with AF, less bleed. The randomized trial required before NOACs is recommended as "standard of care" in moderate-to-severe MS and AF.

EVOLVING ROLE OF ANTIPLATELETS IN ACS: IS IT TWILIGHT OF ASPIRIN?

Dr Marco Valgimigli, Switzerland

Ticagrelor on top of aspirin at 90 mg b.i.d. in the first year after acute coronary syndrome (ACS) or at 60 mg b.i.d. thereafter is associated with lower rates of fatal and nonfatal ischemic events and similar bleeding risk than aspirin (ASA) plus clopidogrel but higher bleeding rates than ASA alone. Ticagrelor monotherapy after a short-course of dual antiplatelet therapy (DAPT) preserves ischemic protection and lower bleeding risk compared with a DAPT regimen (Conservative statement given the mortality benefit observed in SIDNEY). Given the dramatic difference in bleeding when ticagrelor alone is compared to ticagrelor and aspirin and the absence of ischemic hazard when ASA is early discontinued, ticagrelor monotherapy is emerging as a new standard of care among ACS/PCI patients.

BIOPROSTHETIC VALVE – IS IT THE FUTURE (IN VIEW OF PERCUTANEOUS INTERVENTION)

Dr Bashi V Velayudhan, Chennai

Rheumatic heart disease still remains the commonest valvular heart disease among Indian patients. This includes younger patients with multiple valve involvements. Further, the Indian subset of patients have a peculiar anatomy of aortic root, wherein the aortic root is small, and low origin of coronary arteries. There is a strong evidence that bioprosthetic valves degenerate faster in younger and diabetic patients. The average longevity of tissue valve in my personal experience is 12 years. TAVI as an option for structural valve degeneration is a matter of debate given the small aortic root and low origin of coronary arteries. In view of all the above findings, it is not advisable in India to use a bioprosthetic valve in patients less than 55 years of age. Nevertheless to say, we need to accept the risk of anticoagulation with mechanical valve and wait for an 'ideal valve' in future.

LASER ANGIOPLASTY: NEW FRONTIER

Dr L Sridhar, Bengaluru

Laser angioplasty is an effective debulking strategy, especially in complex coronary lesions and is a simple, safe, promising, novel, user-friendly tool in the armamentarium of Interventional Cardiology.

NEWER DRUGS IN PAH MANAGEMENT

Dr BKS Sastry, Hyderabad

Selexipag, a prostacyclin receptor agonist, which is likely to be introduced in India shortly, would be a very useful drug in the management of pulmonary arterial hypertension (PAH). Its dose has to be titrated from 200 μg twice a day to a maximum of 1600 μg twice a day, depending upon patient's tolerance. New data is emerging that riociguat would be beneficial in patients who do not have adequate response to PDE5 inhibitors.

THROMBOLYSIS IN INTERMEDIATE-RISK PULMONARY EMBOLISM: NO, I WILL NOT LYSE

Dr Dharmendra Jain, Varanasi

Routine use of thrombolysis in the intermediate-risk group is not indicated. Patients in the intermediate high-risk group who have persistent or worsening signs of distress may proceed with rescue thrombolytic therapy since the benefits likely outweigh the risk at that point. As per Class III-B ESC 2019 guidelines, routine use of thrombolysis in the intermediate-risk group is not indicated. While approaching such patients: Anticoagulants during the first 24 hours following the diagnosis. If, during the 24 hours, patients have persistent or worsening signs of distress, they may proceed with rescue thrombolytic therapy since the benefits likely outweigh the risk at this point.

However, owing to the equivocal nature of the clinical data related to systemic thrombolytic therapy in patients with submassive pulmonary embolism, the decision to treat these individuals needs careful consideration of the risks and benefits involved. It should be noted that with regard to patients with intermediate-risk pulmonary embolism, studies have indicated the importance of appropriately stratifying each patient based on his or her comorbidities and mortality risk before administering thrombolytics.

TRICUSPID VALVE DISEASE: THE NEW FRONTIER

Dr Vera H Rigolin, USA

The tricuspid valve (TV) has a complex anatomy that must be appreciated to safely and successfully treat tricuspid regurgitation (TR). Prognosis of severe TR is poor regardless of etiology. Functional TR is more common than primary TR; most commonly due to left heart disease. Quantification is challenging but important. Treatment of TR is dependent on severity, symptoms, etiology, RV function and concomitant left heart surgery. Percutaneous TV repair – the new frontier - is in its infancy but will likely change the landscape of TR treatment in the near future.

ISCHEMIC DISEASE IN WOMEN

Dr Dipti Itchhaporia, USA

The decline in heart disease mortality is due to our better understanding of sex differences and conditions that affect women, which has led to sex-specific approaches and recognition of entities such as MI without apparent epicardial coronary thrombus or stenosis. MINOCA (**M**yocardial **I**nfarction with **N**on-**O**bstructed **C**oronary **A**rteries) patients are more likely to be younger women and they can experience plaque disruption. Takotsubo syndrome, also known as broken heart syndrome, is not the same as an MI and is often seen in elderly postmenopausal women after an emotionally and/or physically traumatic event. MINOCA can be caused by spontaneous coronary artery dissection (SCAD), coronary vasospasm and coronary thrombosis or embolism.

Treatment for MINOCA is based on the underlying cause and involves use of aspirin, statin, β-blockers, clopidogrel, ACE inhibitors, and/or angiotensin receptor blockers (ARBs). Women with ST elevation MI are more likely to develop bleeding complications and less likely to receive guideline-directed medical therapy (GDMT) than their male counterparts. These bleeding complications can be reduced with a radial approach for angiography and PCI. The medical community needs to increase awareness about CVD as the primary cause of mortality in women.

STRATEGIES TO INCREASE AWARENESS OF HYPERTENSION IN INDIA

Dr A Muruganathan, Tirupur

Balance your life when possible, and make time for fun, and help others to achieve well-being.

India has more people with hypertension than any other country. The disease attributable to hypertension is a hemodynamic malignancy. Hypertension prevalence in India is high, but the proportion of adults with hypertension who are aware of their diagnosis, are treated, and achieve control is low.

The recommended public health actions for national hypertension organizations include increasing awareness that hypertension is mostly preventable, largely caused by unhealthy eating, and can be inexpensively and easily detected. National initiatives such as training community health workers to deliver primary care and implementing universal health coverage should be considered to curb the spread of hypertension and consequent CVDs.

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

News and Views

Real-World Data Suggest COVID-19 Vaccine Reduces Asymptomatic Infection Risk

Two studies based on real-world data indicate that mRNA coronavirus disease 2019 (COVID-19) vaccines decreased the risk of developing asymptomatic infection.

While one of the studies, from researchers at the Mayo Clinic, was published in a journal, the other was mentioned in a press release. The first study, published in *Clinical Infectious Diseases*, was a retrospective review of around 48,000 asymptomatic patients in Mayo Clinics in Minnesota, Wisconsin and Arizona. The patients were subjected to COVID-19 testing before undergoing surgical procedures. This included nearly 3,000 who had been given at least one dose of either the Pfizer or Moderna mRNA vaccine.

About 3.2% of the unvaccinated patients tested positive, compared to 1.4% of those who had been administered a vaccine. After adjustment for confounding variables, the relative risk of asymptomatic infection was 0.35 (95% confidence interval [CI] 0.26-0.47) with vaccination.

In a press release issued recently, Pfizer and BioNTech claimed that their vaccine was 94% effective against asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The data came from de-identified aggregate surveillance from the Israeli Ministry of Health between January 17 and March 6… (*Medpage Today*)

More Than 1 in 5 Healthcare Workers Experienced Depression and Anxiety During Pandemic: Study

New research suggests that over 1 in 5 healthcare workers have experienced anxiety, depression or post-traumatic stress disorder (PTSD) during the pandemic.

The systematic review and meta-analysis, published in *PLOS One*, included 65 studies involving more than 97,000 people. On breaking down the numbers by region, healthcare workers in the Middle East were found to have the highest rates of anxiety and depression, with 28.9% and 34.6% experiencing these mental health conditions, respectively. North America, ranking the lowest, had 14.8% of healthcare workers who experienced anxiety and 18.7% who experienced depression. Around 21.5% of healthcare workers across all regions experienced moderate levels of PTSD… (*CNN*)

HIV, High-risk Pregnancy and COVID-19

While developing COVID-19 during a high-risk pregnancy is bad both for the mother and the baby, having HIV (human immunodeficiency virus) infection as well doesn't seem to make it any worse, reports a study from South Africa.

Among 100 women diagnosed with COVID-19 while receiving care at a high-risk obstetric care service, 8 deaths were reported. These included 6 among the 72 women (8%) with COVID-19, and 2 among the 28 women (7%) who had HIV co-infection. Among the women who died during the study, only 2 of the babies they were carrying survived, reported Liesl De Waard, MBChB, of Stellenbosch University in suburban Cape Town during an oral presentation at the virtual Conference on Retroviruses and Opportunistic Infections (CROI)… (*Medpage Today*)

2021 KDIGO Clinical Practice Guideline: Major Update of BP Guidance

The updated 2021 Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guideline for the management of blood pressure in adults with chronic kidney disease (CKD) not on dialysis advises a target systolic blood pressure of <120 mmHg, given that the measurements are standardized and that the blood pressure is measured properly.

The blood pressure target is based on evidence from the Systolic Blood Pressure Intervention Trial (SPRINT). This portrays a major update from the 2012 KDIGO guideline wherein clinicians were advised to treat to a target blood pressure of ≤130/80 mmHg for patients with albuminuria and ≤140/90 mmHg for patients without albuminuria. The new target is also lower than the target of <130/80 mmHg recommended in the 2017 American College of Cardiology/American Heart Association (ACC/AHA) guideline… (*Medscape*)

Novavax Vaccine Shows 96% Efficacy Against Original Coronavirus Strain, 86% Against UK Variant

Novavax COVID-19 vaccine has been found to be 96% effective in preventing COVID-19 cases due to the original version of the coronavirus in a late-stage trial in the United Kingdom, reported the company.

No cases of severe illness or deaths were evident among those given the vaccine. Additionally, the vaccine had an efficacy of 86% in protecting against the more contagious variant first detected in the United Kingdom. The combined effectiveness rate based on data from infections due to both versions of the coronavirus was estimated as 90%. A smaller trial in South Africa, where people were exposed to another new, more contagious variant widely prevalent there, noted that the Novavax vaccine was 55% effective, based on people without HIV. However, the vaccine still completely prevented severe illness… (*Mint*)

COVID-19–related Death in Rheumatic Patients

Evaluation of data from an international registry suggests that patients with rheumatic diseases who developed COVID-19 had greater odds of death, with risk factors similar to those observed in the general population, but also because of factors specific to their underlying disease and treatment.

Out of 3,729 patients enrolled in the COVID-19 Global Rheumatology Alliance from March through July 2020, 10.5% died. Older age was a major factor in mortality - 68.7% of those who died were older than 65 years of age. The odds ratios for death were 3 (95% CI 2.13-4.22) among those 66-75 years of age, and increased to 6.18 (95% CI 4.47-8.53) for those over 75 years, reported researchers online in *Annals of the Rheumatic Diseases*. Higher disease activity at the time of COVID-19 diagnosis was shown to have a significant association with increased mortality… (*Medpage Today*)

Wearing Face Mask During Exercise Safe, Says Study

A new research suggests that wearing a face mask during intense exercise appears to be safe for healthy individuals and could diminish the risk of spread of COVID-19 at indoor gyms.

Investigators conducted detailed testing on breathing, heart activity and exercise performance in 12 people when they were using an exercise bike with and without a mask. There were differences in some measurements between wearing a mask and not wearing a mask, but none of the results pointed to any risk to health. Wearing a mask was found to have a small effect on the participants. An average reduction of around 10% was noted in their ability to perform the aerobic exercise. The findings suggested that masks could be worn safely during intense exercise to reduce COVID-19 transmission among people in an indoor gym… (*HT – ANI*)

Type 2 Diabetes Tied to Increased Risk for Parkinson's Disease

New analyses of observational as well as genetic data have suggested that type 2 diabetes is tied to an increased risk for Parkinson's disease. Two separate analyses were conducted - a meta-analysis of observational studies looking into the association between type 2 diabetes and Parkinson's and a Mendelian randomization analysis of genetic data on these two conditions. Similar results were obtained in both studies. The observational data indicated that type 2 diabetes was associated with a 21% increased risk for Parkinson's disease while the genetic data pointed to an 8% increased risk. The findings also pointed that type 2 diabetes might be linked with faster progression of Parkinson's symptoms. The analyses are reported in a paper published online in *Movement Disorders*… (*Medscape*)

WHO Urges Healthcare Workers to Allow Mother-Baby Contact

The COVID-19 pandemic has been affecting the care of sick or premature newborn babies, as many of them are unnecessarily separated from their mothers and put at risk of death or long-term health problems.

Now, two studies cited by the WHO have shown that thousands of neonatal healthcare workers are not letting mothers with confirmed or suspected COVID-19 infection have skin-to-skin contact with their newborns, and about a quarter of those who were surveyed are not allowing breastfeeding. Keeping mothers and babies together and letting the babies have kangaroo mother care could be able to save over 1,25,000 lives, reported a study published in the *Lancet EclinicalMedicine* journal.

A study published in the *BMJ Global Health* noted that two-thirds of the 1,120 healthcare workers surveyed reported that they would separate mothers and babies with a positive COVID-19 test or if there was no clarity on whether they might have the infection. Anshu Banerjee, a WHO expert in maternal and newborn health, stated that newborn babies have a right to life-saving contact with their parents and should not be denied the same due to COVID-19… (*Reuters*)

COVID-19 Antibodies Present in About 1 in 5 Blood Donations from Unvaccinated People: Data from American Red Cross

In the first week of March, over 20% of blood donations from unvaccinated people were found to have COVID-19 antibodies, report data from the American Red Cross.

From the mid of June 2020 to early March 2021, the American Red Cross assessed over 3.3 million donations from unvaccinated people across 44 states for the presence of COVID-19 antibodies. Nearly 7.5% of the donations tested in that time frame had COVID-19 antibodies, thus suggesting that the donors had likely been infected with COVID-19 at some point. Nearly 1.5% of donations tested in the first week of July were found to be positive, rising to around 4% of donations tested in the first week of October. It increased to around 12% of donations tested in the first week of January and about 21% of donations tested in the first week of March… (*CNN*)

Tobacco Control to Improve Child Health and Development: WHO Report

The WHO has released a new report, titled "Tobacco Control to Improve Child Health and Development" that calls for increasing awareness among practitioners and policymakers about the significance of robust tobacco control measures in order to protect the health and development of children. This includes ban on tobacco advertising, implementation of 100% smoke-free environments and increasing the taxes on tobacco.

Dr Vinayak M Prasad, Unit Head, No Tobacco (TFI) at the WHO Department of Health Promotion, has stated that creating comprehensive smoke-free policies leads to increased benefits, particularly when the policies are enforced appropriately, without any exceptions… (*WHO*)

Coronavirus Strains First Detected in California "Variants of Concern": CDC

Two coronavirus strains that were first detected in California have been officially declared as "variants of concern", as per the US Centers for Disease Control and Prevention (CDC).

The variants may be around 20% more transmissible, according to early research. Certain COVID-19 treatments may also be less effective against these variants, officially called B.1.427 and B.1.429. However, the CDC didn't say that vaccines won't work against them. Laboratory studies have shown that antibodies from vaccinated individuals appear to be less effective at neutralizing the strains. However, lower levels of antibodies may still suffice to protect against COVID-19, particularly severe cases. Health officials are still concerned that some treatments may not work as well against the variants… (*CNN*)

Disruption in Kidney Function Appears to Persist Following AKI in COVID-19

Patients who developed acute kidney injury (AKI) during hospitalization for COVID-19 were found to have significantly faster reduction in kidney function and slower recovery following hospital discharge, in comparison with patients with AKI not related to COVID-19, in a new research published in *JAMA Network Open*.

The greater decline was found to be independent of AKI severity and comorbidities. Investigators assessed 182 patients from five hospitals in Connecticut and Rhode Island who developed AKI after COVID-19 diagnosis between March 10 and August 31, 2020, and who survived after discharge and did not need dialysis within 3 days. They were compared with 1,430 patients who developed AKI not linked with COVID-19. Outpatient creatinine levels in the first 6 months after discharge revealed that among patients with AKI associated with COVID-19, the mean rate of decrease in estimated glomerular filtration rate (eGFR) after discharge was faster compared to the patients who did not have COVID-19, after adjustment for baseline characteristics and comorbidities. A subanalysis evaluated the time to recovery among 319 patients who had not fully recovered from AKI at the time of discharge. Patients with AKI after COVID had lesser odds of having experienced kidney recovery at follow-up… (*Medscape*)

New Clinical and Service Delivery Recommendations for HIV Prevention, Treatment and Care Released by WHO

The WHO has published new guidelines that provide new and updated recommendations on the use of point-of-care testing in children below 18 months of age and point-of-care tests to follow the treatment in people living with HIV; the treatment monitoring algorithm; as well as the timing of antiretroviral therapy (ART) in people living with HIV undergoing treatment for tuberculosis.

The new recommendations delineate pivotal new actions for countries to enhance the delivery of HIV testing, treatment and care services. The new recommendations come as an update to the 2016 WHO Consolidated Guidelines on the use of antiretroviral drugs for the treatment and prevention of HIV… (*WHO*)

COVID-19 Reinfection Rare, But More Common in Older Individuals: Study

Most of the people who have had COVID-19 are protected against getting the infection again for at least

6 months, reported a study published in *The Lancet*; however, older individuals appear to be more vulnerable to reinfection compared to younger people.

The study noted that only 0.65% of the patients tested positive a second time after previously being infected during Denmark's first and second waves of COVID-19 infection. This figure is much lower than the 3.27% who were found to be positive after initially being negative. It was noted that people above 65 years of age had only 47% protection against repeat infection, compared to 80% protection for younger individuals… (*Reuters*)

Baby Born to Partially Vaccinated Mother has COVID Antibodies

A baby girl born 3 weeks after her mother was vaccinated with the first dose of the Moderna COVID-19 vaccine has antibodies against the virus, reports a pre-print paper published on the *medRxiv* server.

The mother is a healthcare worker in Florida who developed COVID-19 antibodies after receiving the vaccine dose. Testing has shown that the antibodies passed through the placenta to the baby. Previous research has shown that mothers who have recovered from COVID-19 can deliver babies with antibodies, but this appears to be the first report showing that vaccination during pregnancy can also provide antibodies… (*Medscape*)

Ageism a Global Challenge, Says UN

Every second person in the world seems to be holding ageist attitudes, which results in poorer physical and mental health as well as deteriorated quality of life for older individuals, suggests a new report on ageism by the United Nations.

The report by WHO, Office of the High Commissioner for Human Rights (OHCHR), United Nations Department of Economic and Social Affairs (UN DESA) and United Nations Population Fund (UNFPA), encourages urgent action to fight ageism and calls for better assessment and reporting to uncover ageism. WHO Director-General, Dr Tedros Adhanom Ghebreyesus stated that while the world tries to recover from the pandemic, age-based stereotypes, bias and discrimination should not be allowed to restrict the opportunities to assure health and well-being of people globally… (*WHO*)

Sleep Survey Findings Highlight New Sleep Challenges Faced by Indians During Pandemic

Findings of the India Sleep Survey Report titled "Philips Global Sleep Survey 2021" have been released that focus on the impact of COVID-19 pandemic on sleep health and the surge in acceptance of digital health technologies owing to the pandemic.

About 60% of Indians stated that they have used or are willing to use telehealth for sleep-related issues. Since the onset of the pandemic, Indian adults experienced new sleep challenges: about 37% had difficulty falling asleep, 27% reported difficulty staying asleep and 39% reported waking up during the night. The survey revealed that 80% of patients with sleep apnea experience daytime drowsiness while 52% of those without sleep apnea experience the same. About 47% of the respondents stated that sleep apnea is affecting their relationships… (*ET Healthworld*)

Aspirin can Decrease Risk of ICU Admission and Death in COVID-19 Patients: Researchers

Low-dose aspirin may have a role in protecting the lungs and decreasing the need for ventilators, suggest researchers. In a report published in the journal *Anesthesia & Analgesia*, researchers stated that aspirin could keep patients out of ICUs and could also decrease the risk of death, possibly by preventing blood clots. Researchers assessed the records of 412 patients admitted to US hospitals from March through July 2020. Nearly 24% of the patients received aspirin within 24 hours of hospital admission, or in the 7 days prior to hospitalization. Aspirin use was found to be associated with a 44% decline in mechanical ventilation, a 43% reduction in ICU admission, and a 47% decrease in in-hospital mortality… (*CNN*)

Women with PCOS have Increased Risk for COVID-19

Women with polycystic ovary syndrome (PCOS) have around 30% increased risk for COVID-19 compared with women without PCOS, even after adjusting for cardiometabolic and other related factors, suggested assessment of UK primary care data.

Investigators obtained data from The Health Improvement Network primary care database. The analysis included 21,292 women with PCOS/PCO and 78,310 controls. The mean age at diagnosis of PCOS was 27 years, while the mean duration of the condition was 12.4 years. The crude incidence of COVID-19 was found to be 18.1 per 1,000 person-years among women with PCOS compared to 11.9 per 1,000 person-years among those without the condition. Cox regression analysis adjusted for age suggested that women with PCOS had a significantly higher risk for COVID-19 compared to those without (HR 1.51)… (*Medscape*)

Indian Drugmaker to Produce 200 Million Doses of Sputnik V

The developer of Russia's Sputnik V COVID-19 vaccine stated that it had entered into a partnership with an Indian drugmaker to produce 200 million doses of the vaccine.

The Russian Direct Investment Fund (RDIF) released a statement that it had partnered with Stelis Biopharma for production and supply of at least 200 million doses of the Russian Sputnik V vaccine. The Indian drugmaker is expected to start supplying the vaccine from the second half of 2021.

RDIF stated that 52 countries have approved the use of Sputnik V vaccine. Moscow registered the vaccine in August before large-scale clinical trials, and the medical journal *The Lancet* has also stated that the jab is safe and more than 90% effective… (*NDTV - Agence France-Presse*)

Cancer Patients' Response Poor to First COVID-19 mRNA Vaccine Dose

Only a quarter of patients with cancer obtained protection against COVID-19 following one dose of the Pfizer/BioNTech COVID-19 vaccine, suggested a prospective study.

The study revealed a considerably low immune efficacy rate of 28% in patients with cancer, including 13% in patients with blood cancers. On the contrary, first-dose seroconversion was noted in 97% of healthy controls, stated investigators in a report posted on the medRxiv preprint server. A second dose, given at Day 21, led to adequate immunity in almost all of the cancer patients. The study thus advocated that cancer patients should be prioritized for an early second dose of the vaccine… (*Medpage Today*)

New Estimate of Ischemic Stroke Rate in COVID-19

Data from the American Heart Association's COVID-19 Cardiovascular Disease Registry, which included over 20,000 US adults hospitalized with COVID-19 between March and November 2020, has revealed an overall rate of ischemic stroke of 0.75%.

While the rate appears to be lower than earlier estimates of risk of ischemic stroke with severe COVID-19, it is higher than that observed in other infections, like influenza or sepsis. Patients with ischemic stroke while hospitalized for COVID-19 had double the odds of death compared to those who did not have a stroke. The data were presented at the virtual International Stroke Conference (ISC) 2021. It was noted that patients who had an ischemic stroke were more likely older than patients who did not have a stroke and were also more likely to be male (63% vs. 54%)… (*Medscape*)

Lockdown due to COVID-19 Negatively Affected Mental Health of Teenagers, Says Study

A new study suggests that the lockdown imposed to check the spread of the novel coronavirus in March 2020 took a toll on mental health of teenagers.

The CS Mott Children's Hospital National Poll on Children's Health at Michigan Medicine noted 46% of parents reported that their teen has shown signs of a new or worsening mental health condition since the pandemic started in March 2020. It was more likely for parents of teen girls to say that the child had a new onset or worsening of depressive symptoms and anxiety compared to parents of teen boys.

Investigators received responses from 977 parents of teens, 13-18 years of age. According to the poll, 36% of parents of teen girls and 19% parents of teen boys reported a surge in anxiety/worry, while 31% parents of teen girls and 18% parents of teen boys reported a rise in depression/sadness… (*HT – ANI*)

COVID-19 Tied to Atypical Thyroid Inflammation

People experiencing inflammation of the thyroid gland during acute COVID-19 disease may continue to have subacute thyroiditis months later even if thyroid function normalizes, reveals new research.

Additionally, the thyroiditis appears to be different from the thyroid inflammation that is caused by other viruses, said Ilaria Muller, while presenting data at the virtual ENDO 2021 meeting. Investigators described patients hospitalized with severe COVID-19 in July last year. About 15% of these had thyrotoxicosis from atypical subacute thyroiditis, compared to just 1% of a comparison group that was admitted to the same ICUs during spring 2019.

The atypical thyroiditis noted in COVID-19 patients was not associated with neck pain and was found to impact more men than women. It was associated with low thyroid-stimulating hormone (TSH) and free-triiodothyronine (T3) levels, as well as normal or raised free thyroxine (T4). An evaluation of 51 patients 3 months following hospitalization for moderate-to-severe COVID-19 revealed normalization of both inflammatory markers and thyroid function; however, on imaging, one-third of patients still had focal hypoechoic areas indicating thyroiditis… (*Medscape*)

1.4 Million Fewer People Received Care for TB in 2020

Preliminary data compiled by the WHO from more than 80 countries suggest that around 1.4 million fewer people received care for TB in the past year compared to 2019, translating to a reduction of 21% from 2019. The countries that demonstrated the biggest relative gaps include Indonesia (42%), South Africa (41%), Philippines (37%) and India (25%). The WHO issued new guidance on World TB Day in order to assist countries identify the needs of communities, the populations that have the highest risk of TB, and the locations that are most affected so that people have access to appropriate prevention and care services. Systematic use of screening tools is vital to achieve this aim… (*WHO*)

Inequity of COVID-19 Vaccines Becoming "More Grotesque Every Day", Says WHO Chief

The increasing gap between the number of vaccines being given in rich countries and those given through COVAX is becoming "more grotesque every day", stated the chief of the WHO.

Director-General of the WHO, Tedros Adhanom Ghebreyesus, had stated in January that the world was on the verge of a disastrous moral failure and there is a need for urgent action to ensure equitable distribution of vaccines. At a recent news briefing, he stated that little has been done to avert this failure, adding that WHO was constantly working to find solutions to enhance the production and equitable distribution of vaccines across the world. He emphasized that some countries are vaccinating their entire populations, while others have no vaccine at all… (*UN*)

Interval Between Doses of Covishield Increased to 4-8 Weeks in India

The Indian Government decided to increase the interval between the two doses of Covishield vaccine to 4-8 weeks, stated the Health Ministry.

According to the Ministry, the protection is increased if the second dose of the vaccine is given between 6-8 weeks, but not later than 8 weeks, considering the existing scientific evidence. The Center has directed states and union territories to increase the interval between two doses of Covishield on the basis of recommendations of National Technical Advisory Group on Immunization (NTAGI) and National Expert Group on Vaccine Administration for Covid-19 (NEGVAC). (*ET Healthworld – IANS*)

Israel, New Zealand Give Interim Approval for Sale of Nitric Oxide Nasal Spray

Israel and New Zealand have provided interim approval for the sale of Nitric Oxide Nasal Spray (NONS) developed by SaNOtize Research and Development. The spray could help prevent the transmission of COVID-19 virus, stated the company.

Manufacturing of NONS has been started in Israel with SaNOtize's partner Nextar Chempharma Solutions Ltd and the product is expected to be on sale this summer. Meanwhile, in New Zealand, the company has registered the spray with the New Zealand Medicines and Medical Devices Safety Authority. The company has been allowed there to distribute and sell the nasal spray over-the-counter immediately. New Zealand's Health Ministry; however, clarified that the spray has not been approved for use as an antiviral nasal spray… (*Reuters*)

UK is Planning COVID-19 Vaccinations for Children from August

Children in the United Kingdom will likely start receiving a COVID-19 vaccine from August under provisional government plans in order to push for maximum immunity nationwide from the coronavirus, reported in *The Telegraph*.

This timeline would be months earlier than anticipated, stated the newspaper. Officials are awaiting the results from a child vaccine trial being conducted by Oxford University on the vaccine that it has developed along with AstraZeneca Plc, before a final decision on the rollout is taken. According to *The Telegraph*, safety data from the study of 300 individuals aged 6-17 years will be available soon, with conclusions expected in June or July… (*Reuters*)

Less Sleep, More Professional Burnout Tied to Higher Risk for COVID-19: Study

A new study, published online in *BMJ Nutrition, Prevention and Health*, has shown that more sleep at night, few or no sleep problems and low levels of work-related burnout among healthcare workers who are considered to have a high risk for exposure to COVID-19 patients, seem to be linked with a reduced risk of developing COVID-19.

For every extra hour of sleep at night, the risk for COVID-19 declined by 12% in the study that included 2,844 frontline healthcare workers. Participants who experienced work-related burnout had 2.6-fold greater likelihood of reporting having COVID-19, having the

illness for a longer duration, and having more severe COVID-19… (*Medscape*)

CDC: Counties with Large Asian, Black or Hispanic Populations had Higher Number of Coronavirus Cases

The US CDC has stated that the counties in the United States that had large Black, Asian and Hispanic populations had a greater number of COVID-19 cases in the initial months of the pandemic. A new study suggests that over a quarter of counties with large Asian or Black populations had a high incidence rate of COVID-19 infections in the first 2 weeks of April 2020. High incidence has been defined by the CDC as over 100 new cases per 1,00,000 people in the population. At the time, around 11.4% of all counties were reported to have a high COVID-19 incidence rate, as opposed to around 29% of counties that had an above-average share of Asian individuals and about 28% of counties with an above-average share of Black individuals… (*CNN*)

COVID-19: Remdesivir Beneficial in Minority Groups

Remdesivir was found to be associated with faster clinical improvement in a largely non-white group of patients admitted to the hospital with COVID-19, reported a new study. A little over 80% of patients receiving remdesivir in the study identified as non-white. A retrospective analysis of nearly 2,300 hospitalized COVID-19 patients in Baltimore and Washington, DC noted that the median time to clinical improvement was shorter among patients who were given remdesivir compared to those who were not given the drug (5 vs. 7 days, adjusted HR 1.47, 95% CI 1.22-1.79). There was no significant difference in 28-day mortality, though the trend favored remdesivir (7.7% vs. 14.0% in controls). The findings were published in *JAMA Network Open*… (*Medpage Today*)

Oral COVID Vaccine to Enter Clinical Trials

A COVID-19 vaccine that could be taken as an oral pill may enter into clinical trials in the second quarter of this year. The oral vaccine is being developed by Oravax Medical, a joint venture of the Israeli-American company Oramed and the Indian company Premas Biotech. An advantage of an oral vaccine is that it can be taken at home instead of having it administered by healthcare personnel at a central location. It would also be easier to distribute an oral vaccine as it could be shipped in a normal refrigerator and stored at room temperature. This yeast-based vaccine targets three structural proteins of the novel coronavirus… (*Medscape*)

Caffeine Prior to Exercise Helps Burn Fat

Intake of caffeine, or drinking strong coffee, half an hour prior to doing aerobic exercise can escalate fat-burning, suggests a new study.

The effects of caffeine appear to be higher if the exercise is done in the afternoon as compared to when it is done in the morning, reported the authors in the *Journal of the International Society of Sports Nutrition*. It was noted that taking caffeine 30 minutes before aerobic exercise increased fat oxidation during exercise, irrespective of the time of day. The rate of fat-burning was found to be higher in the afternoon compared to morning for equal hours of fasting. Additionally, in comparison with placebo, caffeine was found to raise fat oxidation by 10.7% in the morning and 29% in the afternoon. Caffeine also had an impact on exercise intensity, increasing it by 11% in the morning and 13% in the afternoon… (*Medscape*)

COVID-19 Vaccines Provide Protection for Pregnant and Lactating Women and Their Newborns

A new study published in the *American Journal of Obstetrics and Gynecology* has noted that the Pfizer/BioNTech and Moderna COVID-19 vaccines are effective among pregnant and lactating women, and that they can pass protective antibodies to their newborns.

Researchers at Massachusetts General Hospital, Brigham and Women's Hospital and the Ragon Institute of MGH, MIT and Harvard evaluated 131 women who were administered either the Pfizer/BioNTech or Moderna vaccine. Eighty-four of these women were pregnant, 31 were lactating and 16 were not pregnant. Investigators collected samples from the study participants from December 17, 2020 through March 2, 2021. The vaccine-induced antibody levels appeared to be equivalent in pregnant and lactating women, compared to nonpregnant women. The antibody levels were considerably higher than the levels reached after coronavirus infection during pregnancy. It was also noted that these women passed protective antibodies to their newborns, measured in breast milk and placenta… (*CNN*)

Glucocorticoid Use at Presentation Tied to Severe Outcomes of COVID-19 in Patients with Systemic Vasculitis

A study published in *Arthritis & Rheumatology* has noted that among patients with systemic vasculitis, glucocorticoid use at presentation and comorbid respiratory disease are linked with severe outcomes of

COVID-19. The study looked at data from 65 patients with systemic vasculitis who contracted COVID-19 infection and were registered with the UK and Ireland Vasculitis Registry and the Irish Rare Kidney Disease Registry. Around 85% of the study participants had antineutrophil cytoplasm antibody (ANCA)-associated vasculitis (AAV). About 69% of the participants were receiving background glucocorticoids at the time of COVID-19 diagnosis. Background glucocorticoid treatment was found to be associated with severe outcome with an adjusted odds ratio (aOR) of 3.7. Comorbid respiratory disease was also linked to a severe outcome in these patients with an aOR of 7.5… (*DG Alerts*)

Successful Results Prompt Early Closure of Drug-resistant TB Trial

Médecins Sans Frontières (MSF/Doctors without Borders) have announced that the phase II/III trial of a 6-month multidrug regimen for multidrug-resistant tuberculosis (MDR-TB) has been stopped early as it was ascertained by an independent DSMB that the multidrug regimen was superior to current therapy, stated a press release. The TB PRACTECAL trial compared the local standard of care with a 6-month regimen of bedaquiline, pretomanid, linezolid and moxifloxacin. The interim analysis involved 242 patients and the randomized controlled trial was done in Belarus, South Africa and Uzbekistan. The preliminary data will be shared with the WHO and will be submitted to a peer reviewed journal as well… (*Medscape*)

COVID-19 in Pregnancy Tied to Adverse Maternal and Fetal Outcomes

SARS-CoV-2 infection in pregnancy has been found to be associated with increased risks of pre-eclampsia, preterm birth and other adverse pregnancy outcomes in a meta-analysis published in the *Canadian Medical Association Journal*.

The meta-analysis included 42 studies involving 4,38,548 pregnant women. In comparison with no infection, SARS-CoV-2 infection in pregnancy was found to be linked with pre-eclampsia (odds ratio [OR] 1.33), preterm birth (OR 1.82) and stillbirth (OR 2.11). Additionally, having the infection in pregnancy was tied to a heightened risk of ICU admission, neonatal ICU (NICU) admission and lower birth weight, when compared with pregnancy without SARS-CoV-2 infection. Severe COVID-19 during pregnancy had a strong link with pre-eclampsia, preterm birth, gestational diabetes, low birth weight, NICU admission and cesarean delivery, when compared with mild infection… (*DG Alerts*)

Encephalopathy Common, Fatal in Hospitalized COVID-19 Patients

According to new research published in *Neurocritical Care*, toxic metabolic encephalopathy (TME) appears to be common and often fatal in hospitalized COVID-19 patients. A retrospective study of around 4,500 patients with COVID-19 noted that 12% were diagnosed with TME. About 78% of these developed encephalopathy immediately before hospitalization. The most common causes included septic encephalopathy, hypoxic-ischemic encephalopathy (HIE) and uremia; however, multiple causes were identified in nearly 80% of the patients. TME was also found to be tied to a 24% higher risk of death during hospitalization. The researchers noted that around 1 in 8 patients hospitalized with COVID-19 had TME, which was not connected with the effects of sedatives… (*Medscape*)

Harmony Transcatheter Pulmonary Valve Approved by FDA

The first in the world nonsurgical heart valve has been approved by the US FDA for the treatment of children and adult patients with a native or surgically-repaired right ventricular outflow tract (RVOT).

The device is intended for use in patients with severe pulmonary valve regurgitation. The Harmony Transcatheter Pulmonary Valve (TPV) System aims to improve blood flow to the lungs in patients with severe pulmonary valve regurgitation without having to do open-heart surgery. The use of the new device is expected to delay the time before a patient needs additional open-heart surgery. The use of the device may also decrease the total number of open-heart surgeries required over a person's lifetime… (*FDA*)

More Americans Below 30 Report Anxiety, Depression During Pandemic: CDC

More young adults in the US reported having anxiety or depression over the past 6 months of the COVID-19 pandemic, and fewer individuals reported getting the required help, suggests a US government study.

It was noted that the percentage of adults below 30 years of age with recent symptoms of anxiety or depressive disorder increased significantly nearly 5 months after the COVID-19–related lockdowns were imposed. From August 2020 to February 2021, this number rose to 41.5% from 36.4%. According to the study, the surge in anxiety or depressive disorder symptoms corresponded with the weekly figures of reported COVID-19 cases… (*Reuters*)

EU Regulator Supports Pfizer Vaccine Storage at Regular Freezer Temperature

The EU drugs regulator stated that the Pfizer/BioNTech COVID-19 vaccine can be stored at normal freezer temperatures for short periods of time instead of being kept in ultra-cold storage.

The European Medicines Agency stated that this change would facilitate rapid rollout of vaccines across Europe. The EU regulator gave a positive opinion to permit the transportation and storage of vaccine vials at temperatures of -25 to -15°C, for a one-off period of 2 weeks. This is a substitute to the long-term storage at a temperature of -90 to -60°C in special freezers, said the regulator.

The US had also made a similar decision about the Pfizer vaccine on February 25… (*NDTV - Agence France-Presse*)

Infected Saliva could Push COVID Through the Body, Says Study

The sites of SARS-CoV-2 infection are well-known in the airways and other body parts; however, new research suggests that the virus infects mouth cells as well.

The new findings may help explain the loss of taste and smell, dry mouth and blistering seen in some patients with COVID-19. This comes as the first direct evidence that SARS-CoV-2 not only infects and replicates in cells of the mouth but the fluid generated by the mouth is infectious too. The researchers noted that the salivary glands were actually working as a virus production factory. Additionally, the study findings also help validate the importance of wearing masks, appropriate use of personal protective equipment (PPE) and social distancing. The findings are published online in *Nature Medicine*… (*Medscape*)

$29 Billion a Year Required by 2025 to Get Back on Track in the Fight Against AIDS

A new report from UNAIDS, the agency working towards ending HIV and acquired immune deficiency syndrome (AIDS), has revealed that an investment of $29 billion a year to HIV response in low- and middle-income countries by the year 2025 will help us get back on track to eliminate the virus as a public health threat by 2030.

The agency adopted the new Global AIDS Strategy 2021-2026 during a special session held on March 24 and 25, 2021. The new strategy updates the 2016 targets for 2020, which were unmet. The three priorities mentioned in the strategy include maximizing equal access to comprehensive people-centered HIV services; breaking down legal and societal barriers to attaining HIV outcomes; and sustaining HIV responses and incorporating them into systems for health, social protection and humanitarian settings… (*UN*)

Pfizer, Moderna Coronavirus Vaccines Highly Effective After First Dose in Real-World

The Pfizer/BioNTech and Moderna COVID-19 vaccines have been shown to decrease the risk of COVID-19 infection by 80% 2 weeks or more following the first dose in data obtained from a real-world US study.

The study included around 4,000 US healthcare personnel and first responders and revealed that the risk of infection declined by 90% by 2 weeks following the second dose. The real-world data from the use of these mRNA vaccines confirm the efficacy seen in large controlled clinical trials conducted before EUAs were given by the US FDA. The findings endorse previous studies that suggested that the vaccines started working soon after the first dose, and verify that they prevent asymptomatic infections as well… (*Reuters*)

Very Low Chance of COVID-19 Origin from Frozen Food: WHO Report

International health experts have stated that the odds that COVID-19 emerged in Wuhan from imported frozen food are very low, thus questioning one of the key theories China has adopted for the cause of the first COVID-19 outbreak in late 2019.

China has challenged the initial assumption that the virus originated in Wuhan. Scientists from the WHO and China have reported that the chances of a cold-chain contamination with the virus from a reservoir are extremely low, adding that the introduction of the virus into the country through frozen food would have been 'extraordinary' in December 2019, considering the fact that it had not been detected anywhere else at that time. The report stated that the odds were high that the virus first passed to humans from a bat through an intermediary animal… (*NDTV - Agence France-Presse*)

COVID Vaccine Hesitancy could Result in More Deaths, Longer Restrictions

Researchers with Imperial College London (ICL)'s COVID-19 Response Team attempted at modeling what would happen with vaccine hesitancy and noted that despite the availability of highly effective vaccines against the virus, at the current levels of vaccine hesitancy in the United States, the country would need to continue with interventions like closing of workplaces and

schools and wearing masks at least through the end of next year in order to keep the pandemic under control. It is also estimated that thousands of more people, both vaccinated and unvaccinated ones, could die and need hospital admission over the coming months because some people question the vaccines. The model also predicts several surges in COVID-19 cases in the future, particularly over the winter months, which may continue into 2024… (*Medscape*)

Congenital Heart Disease Alone does not Increase COVID-19 Risk

According to new research, adults with congenital heart disease (CHD) do not have an inherently increased risk for COVID-19 mortality or severe infection. However, physiological stage was a key risk factor.

Investigators noted that among patients with confirmed or suspected COVID-19, those across the spectrum of CHD complexity and comorbidity had a case fatality rate of 2.3%, which is comparable with the general population. Presence of a structural CHD was not essentially predictive of an increased risk of mortality or morbidity from COVID-19 infection. In this study of 1,044 infected CHD patients, worse physiological stage (cyanosis, pulmonary hypertension) was found to have a link with mortality, while anatomic complexity and defect group did not. The findings are published in the *Journal of the American College of Cardiology*… (*Medpage Today*)

T cells-induced by COVID-19 Respond to New Variants

A US laboratory study suggests that T cells that respond to fight infection from the original version of the novel coronavirus appear to provide protection against three of the concerning new virus variants as well.

The study by researchers at the NIAID assessed blood samples from 30 individuals who had recovered from COVID-19 prior to the emergence of the new variants. Investigators identified a specific form of T-cell from these samples that was active against the virus, and analyzed how these T cells worked against the new variants from South Africa, the UK and Brazil. The T-cell responses remained intact to a great extent and were able to identify all mutations in the variants that were assessed. The paper was accepted for publication in *Open Forum Infectious Diseases* (*Reuters*)

Depressive Symptoms and Inflammatory Diet Tied to Higher Frailty Risk

Depressive symptoms and a pro-inflammatory diet, including red meat, refined carbohydrates and sweetened beverages, seem to heighten the risk of frailty in adults, according to new research.

New findings from the Framingham Heart Study suggest that adults with depressive symptoms who consumed such a diet had a 28% higher likelihood of developing frailty compared to their counterparts who did not have depression, but consumed a pro-inflammatory diet. Over a 16-year period, 227 participants became frail. The mean dietary inflammatory index (DII) for the study group was –0.17. The mean DII for frail individuals was 0.08 while that for nonfrail individuals was –0.20. A more positive score indicates a more pro-inflammatory diet. The mean Center for Epidemiologic Studies Depression (CES-D) score at baseline was significantly higher in frail individuals compared to nonfrail ones. After the investigators adjusted for baseline age, sex, energy intake, smoking, diabetes treatment, cardiovascular disease and nonmelanoma cancers, an 1-unit higher DII was tied to 13% higher likelihood of developing frailty in those with no depressive symptoms (CES-D <16) and 41% higher odds in those having depressive symptoms (CES-D >16). The study was presented at the virtual Anxiety and Depression Association of America (ADAA) Conference 2021… (*Medscape*)

Abbott's Rapid COVID-19 Test for At-home Testing in those without Symptoms Cleared in US

Abbott Laboratories has stated that US regulators have cleared the company's rapid COVID-19 antigen test for over-the-counter, at-home use among people who do not have symptoms, thus rendering the tests more easily available for regular screening at places like schools and workplaces.

The company will start shipping the test to retailers in the coming weeks. This is an extensively available COVID-19 test in the United States and provides results in about 15 minutes. People will now be able to purchase the tests at stores or online without a prescription and use them at home. It will be sold to retailers for less than $10 each; however, the cost of the test when sold over-the-counter is not clear yet… (*Reuters*)

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

The Seven Dhatus in Ayurveda

KK AGGARWAL

As per Ayurveda physiology, food is Brahman and contains the same consciousness as in every one of us and this consciousness is the essence of any food.

Any food digested is converted into three portions - the gross undigested food is converted into waste (feces); the middle one is converted in one of the Dhatus and the subtlest form is converted into ojas or the immunity.

As per Ayurveda, food once eaten is converted into the first Dhatu - Rasa. Once the formation of Rasa is complete, the remaining is converted into Rakta (blood). The left over essence of food makes Mamsa (muscles), the leftover of which makes Medha (adipose tissue) and so on to form Asthi (Bone), Majja (bone marrow) and Shukra (sperm/ova).

As per this physiology, the second Dhatu will only form once the first Dhatu is of good quality and so on and at any step, if a Dhatu is not formed properly, the subsequent Dhatu will also show defective formation.

For example, a defective Dhatu at the stage of Asthi (bone) will have normal plasma (blood), muscle and adipose tissue but may have an impaired immunity/sperm/bone marrow. Similarly, defective Dhatu at the level of bone marrow may have only impaired immunity with no impairment of other Dhatus. On the other hand, impairment of Dhatus at the level of plasma or blood will involve all other Dhatus in sickness. Isolated disorders of Shukra may have no involvement of other Dhatus at all.

This Ayurveda principle can help us in answering several unanswered questions in modern allopathy, such as – Why are all the organs involved in typhoid fever? Why no other organ is involved in azoospermia?

Upanishads have described the formation of Dhatus in much more detail. According to them, different types of foods make different types of Dhatus. The fiery foods like oil and ghee are responsible for formation of Karamaindriyan (part of Shukra), bone and bone marrow (Dhatu). Earthy foods are responsible for formation of Gnanandriyan, and water in food is responsible for formation of Rasa and Rakta (plasma and blood) and Pran (Shukra).

This means that every different type of food would make different types of Dhatus and balanced food with a combination of fire, water and earth will only be responsible for formation of Shukra, immunity or the essence.

(Disclaimer: The views expressed in this write up are my own).

Group Editor-in-Chief, IJCP Group

■■■■

FDA Revises Moderna COVID-19 Vaccine Emergency Use Authorization to Increase Number of Doses Available

The US FDA has introduced two revisions pertaining to the number of doses per vaccine vial available for the Moderna COVID-19 vaccine.

In its first revision, the agency mentions the number of doses per vial for the vials that are available at present, stating that the maximum number of extractable doses is 11, with a range of 10-11 doses. The second revision mentions about the availability of an additional vial wherein each vial contains a maximum of 15 doses, having a range of 13-15 doses. The revisions are aimed at helping provide more vaccine doses to the people and ramp up vaccinations… (*FDA*)

Family

I ran into a stranger as he passed by, "Oh excuse me please," was my reply. He said, "Please excuse me too; I wasn't watching for you." We were very polite, this stranger and I. We went on our way saying good-bye.

But at home a different story is told, how we treat our loved ones, young and old. Later that day, cooking the evening meal, my son stood beside me very still. As I turned, I nearly knocked him down. "Move out of the way," I said with a frown. He walked away, his little heartbroken. I didn't realize how harshly I'd spoken.

While I lay awake in bed, God's still small voice came to me and said, "While dealing with a stranger, common courtesy you use, but the children you love, you seem to abuse. Go and look on the kitchen floor, you'll find some flowers there by the door. Those are the flowers he brought for you. He picked them himself: pink, yellow and blue. He stood very quietly not to spoil the surprise, and you never saw the tears that filled his little eyes."

By this time, I felt very small, and now my tears began to fall. I quietly went and knelt by his bed, "Wake up, little one, wake up," I said. "Are these the flowers you picked for me?" He smiled, "I found 'them, out by the tree. I picked 'them because they're pretty like you. I knew you'd like 'them, especially the blue."

I said, "Son, I'm very sorry for the way I acted today; I shouldn't have yelled at you that way." He said, "Oh, Mom, that's okay. I love you anyway." I said, "Son, I love you too, and I do like the flowers, especially the blue."

If we died tomorrow, the company that we are working for could easily replace us in a matter of days. But the family we leave behind will feel the loss for the rest of their lives. We pour ourselves more into work than to our own family. Is it wise?

Do you know what the word FAMILY means?

FAMILY = (F) ATHER (A) ND (M) OTHER, (I) (L) OVE (Y) OU!

(Source: 30 Days to Taming Your Tongue Workbook By Deborah Smith Pegues)

■■■■

COVID-19 Led to a Surge in Stillbirths, Maternal Mortality and Depression Globally

The COVID-19 pandemic has had a negative impact on pregnant women and their infants, suggests a global review of studies. According to the review, stillbirths and maternal deaths seem to have increased by nearly one-third, as per pooled data from 40 studies across 17 countries. Additionally, there has been a six-fold surge in ectopic pregnancies from January 2020 through January 2021. The number of women reporting symptoms of depression had also increased, and the rates of maternal anxiety were also found to be high. Researchers from St. George's University of London figured that several of these problems may be associated with a lack of access to healthcare during the COVID-19 pandemic. The findings have been published in *The Lancet*… (*CNN*)

COVID-19 Vaccine Rollout Very Slow in Europe, Cautions WHO

The regional office of the WHO that covers 53 countries and territories has expressed concern that the COVID-19 vaccine rollout in Europe is moving at an unacceptably slow pace, while new cases continue to rise among almost all age groups. Most countries have registered a spike in COVID-19 transmission over the past week, with 1.6 million fresh cases and around 24,000 deaths reported. New cases are increasing in all age groups, except in the 80 and above age bracket, thus pointing to early signs of the impact of vaccination, stated the UN agency. Dr Hans Kluge, the WHO's Regional Director, stated that vaccines seem to be the best way out of the pandemic, and are very effective in preventing infection. According to Dr Kluge, till the time vaccine coverage remains low, public health measures will have to be implemented to compensate for the delays… (*UN*)

IJCP
A Medical Communications Group

Subscription Form

Jan-Dec 2021

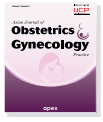
Subscribe to **All Journals** ₹ 10,500/-

SAVE ₹ 500/-

Special Discount on Institutional Packages

Yes, I am interested in subscribing to the *Institutional Combo package for one year (Institutional) ☐

Yes, I am interested in subscribing to the following journal(s) for one year (Institutional) ☐ (individual) ☐

JOURNALS	ISSUES	INSTITUTIONAL (₹ Amount)	INDIVIDUAL (₹ Amount)
Indian Journal of Clinical Practice 	12	5,000/- ☐	1,650/- ☐
Asian Journal of Clinical Cardiology 	4	1,500/- ☐	550/- ☐
Asian Journal of Diabetology 	4	1,500/- ☐	550/- ☐
Asian Journal of Obs & Gynae Practice 	4	1,500/- ☐	550/- ☐
Asian Journal of Paediatric Practice 	4	1,500/- ☐	550/- ☐

Payment Information

Name: .....

Speciality: .....

Address: .....

.....

Country: ..... State: .....

Pincode: .....

Telephone: ..... Mobile: .....

E-mail: .....

Total ₹11,000/- for 1 year

Pay Amount: .....

Dated (dd/mm/yyyy): .....

Cheque or DD No.: .....

Drawn on Bank: .....

Cheques/DD should be drawn in favor of "M/s IJCP Publications Ltd."

IJCP
A Medical Communications Group

Mail this coupon to (HO):

IJCP Publications Ltd.

Head office: E - 219, Greater Kailash Part - 1, New Delhi - 110 048

Telefax: 40587513 Mob.: 9891272006 E-mail: subscribe@ijcp.com

Website: www.ijcpgroup.com

We accept payments by Cheque/DD only, Payable at New Delhi. Do not pay Cash.

Online subscription: http://subscription.ijcpgroup.com/Default.aspx

Indian Journal of Clinical Practice, Vol. 31, No. 11, April 2021

Lighter Side of Medicine

HUMOR

EMBARRASSING TRAFFIC STOP

A police car pulled me over near the high school where I teach. As the officer asked for my license and registration, my students began to drive past. Some honked their horns, others hooted and still others stopped to admonish me for speeding.

Finally, the officer asked me if I was a teacher at the school, and I told him I was. "I think you've paid your debt to society," he said with a smile, and left without giving me a ticket.

FIVE MINUTES LATER

Man calls up the doc at 2 am. "Doc, my wife is having severe abdomen pain. I think it's her appendix."

"What nonsense!" says the doc sleepily.

"I took out your wife's appendix 2 years ago. Go back to sleep."

Five minutes later, the phone rings and it's Santa again.

"Doc, I'm sure it's her appendix."

"Oh God!" the doctor groaned.

"Did you ever hear of anyone having a second appendix?"

"No. But I'm sure you must have heard of someone having a second wife!!!!"

LAW OF THE RESULT

When you try to prove to someone that a machine won't work, it will.

WHAT'S FOR DINNER?

I have changed my system for labeling homemade freezer meals. I used to carefully note in large clear letters, "Meatloaf" or "Pot Roast" or "Steak and Vegetables or "Chicken and Dumplings" or "Beef Pot Pie." However, I used to get frustrated when I asked my husband what he wanted for dinner because he never asked for any of those things. So, I decided to stock the freezer with what he really likes.

If you look in my freezer now you'll see a whole new set of labels. You'll find dinners with neat little tags that say: "Whatever," "Anything," "I Don't Know," "I Don't Care," "Something Good," or "Food." My frustration is now reduced because no matter what my husband replies when I ask him what he wants for dinner, I know that it is there waiting.

NEVER BE RUDE TO ANYONE

An American tourist asked a boat guy in Zanzibar, "Do you know Biology, Psychology, Geography, Geology or Criminology?"

The boat guy said, "No. I don't know any of these."

The tourist then said, "What the hell do you know on the face of this Earth? You will die of illiteracy!"

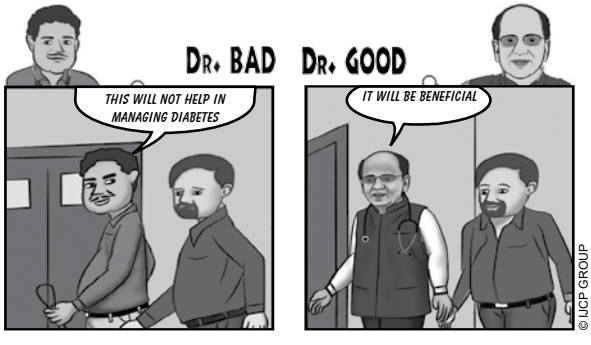
The boat guy said nothing. After a while the boat developed a fault and started sinking. The boatman then asked the tourist, "Do you know Swimology and Escapology from Crocodiology?"

The tourist said, "No!"

The boat guy replied, "Well, today you will Drownology and Crocodiology will eat you. I will not Helpology and you will Dieology because of your Badmouthology."

Dr. Good and Dr. Bad

SITUATION: A man with type 2 diabetes who was on oral hypoglycemic drugs was advised to perform some laughter exercises at home as a part of treatment.



LESSON: It has been reported that laughter therapy is effective in retarding the onset of diabetic complications, enhancing cardiovascular functions and rectifying homeostatic abnormalities associated with type 2 diabetes. Thus, it should be used as an adjunctive therapy.

Diabetes Res Clin Pract. 2017;135:111-9.

Talking Point Communications

-A Unit of the IJCP Group of Medical Communications

IJCP
A Medical Communication Group

Brand
Launches

Start-Up
Profiling

Celebrity
Coordination

Conferences
Events

New product
& Service Launches

Media
Outreach

CEO/Leadership
Profiling

Digital
Marketing

Reputation
Management

HEART CARE FOUNDATION OF INDIA · MTNL Perfect Health Mela Since 1993 · APHRS · DR. REDDY'S · translumina therapeutics · IIC SUMMIT 2014 · afgc

For More Information call: 9582363695, E-mail naina.a@talkingpointcommunications.com
Website: http://talkingpointcommunications.com

Indian
JOURNAL of
CLINICAL PRACTICE

Information for Authors

Manuscripts should be prepared in accordance with the 'Uniform requirements for manuscripts submitted to biomedical journals' compiled by the International Committee of Medical Journal Editors (Ann. Intern. Med. 1992;96: 766-767).

Indian Journal of Clinical Practice strongly disapproves of the submission of the same articles simultaneously to different journals for consideration as well as duplicate publication and will decline to accept fresh manuscripts submitted by authors who have done so.

The boxed checklist will help authors in preparing their manuscript according to our requirements. Improperly prepared manuscripts may be returned to the author without review. The checklist should accompany each manuscript.

Authors may provide on the checklist, the names and addresses of experts from Asia and from other parts of the World who, in the authors' opinion, are best qualified to review the paper.

Covering letter

- The covering letter should explain if there is any deviation from the standard IMRAD format (Introduction, Methods, Results and Discussion) and should outline the importance of the paper.
- Principal/Senior author must sign the covering letter indicating full responsibility for the paper submitted, preferably with signatures of all the authors.
- Articles must be accompanied by a declaration by all authors stating that the article has not been published in any other Journal/Book. Authors should mentioned complete designation and departments, etc. on the manuscript.

Manuscript

- Three complete sets of the manuscript should be submitted and preferably with a CD; typed double spaced throughout (including references, tables and legends to figures).
- The manuscript should be arranged as follow: Covering letter, Checklist, Title page, Abstract, Keywords (for indexing, if required), Introduction, Methods, Results, Discussion, References, Tables, Legends to Figures and Figures.
- All pages should be numbered consecutively beginning with the title page.

Note: Please keep a copy of your manuscript as we are not responsible for its loss in the mail. Manuscripts will not be returned to authors.

Title page

Should contain the title, short title, names of all the authors (without degrees or diplomas), names and full location of the departments and institutions where the work was performed, name of the corresponding authors, acknowledgment of financial support and abbreviations used.

- The title should be of no more than 80 characters and should represent the major theme of the manuscript. A subtitle can be added if necessary.
- A short title of not more than 50 characters (including inter-word spaces) for use as a running head should be included.
- The name, telephone and fax numbers, e-mail and postal addresses of the author to whom communications are to be sent should be typed in the lower right corner of the title page.
- A list of abbreviations used in the paper should be included. In general, the use of abbreviations is discouraged unless they are essential for improving the readability of the text.

Summary

- The summary of not more than 200 words. It must convey the essential features of the paper.
- It should not contain abbreviations, footnotes or references.

Introduction

- The introduction should state why the study was carried out and what were its specific aims/objectives.

Methods

- These should be described in sufficient detail to permit evaluation and duplication of the work by others.
- Ethical guidelines followed by the investigations should be described.

Statistics

The following information should be given:

- The statistical universe i.e., the population from which the sample for the study is selected.
- Method of selecting the sample (cases, subjects, etc. from the statistical universe).
- Method of allocating the subjects into different groups.
- Statistical methods used for presentation and analysis of data i.e., in terms of mean and standard deviation values or percentages and statistical tests such as Student's 't' test, Chi-square test and analysis of variance or non-parametric tests and multivariate techniques.
- Confidence intervals for the measurements should be provided wherever appropriate.

Results

- These should be concise and include only the tables and figures necessary to enhance the understanding of the text.

Discussion

– This should consist of a review of the literature and relate the major findings of the article to other publications on the subject. The particular relevance of the results to healthcare in India should be stressed, e.g., practicality and cost.

References

These should conform to the Vancouver style. References should be numbered in the order in which they appear in the texts and these numbers should be inserted above the lines on each occasion the author is cited (Sinha[12] confirmed other reports[13,14]...). References cited only in tables or in legends to figures should be numbered in the text of the particular table or illustration. Include among the references papers accepted but not yet published; designate the journal and add 'in press' (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as 'unpublished observations' (in parentheses). At the end of the article the full list of references should include the names of all authors if there are fewer than seven or if there are more, the first six followed by et al., the full title of the journal article or book chapters; the title of journals abbreviated according to the style of the Index Medicus and the first and final page numbers of the article or chapter. The authors should check that the references are accurate. If they are not this may result in the rejection of an otherwise adequate contribution.
Examples of common forms of references are:

Articles

Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

Tables

– These should be typed double spaced on separate sheets with the table number (in Roman Arabic numerals) and title above the table and explanatory notes below the table.

Legends

– These should be typed double spaces on a separate sheet and figure numbers (in Arabic numerals) corresponding with the order in which the figures are presented in the text.

– The legend must include enough information to permit interpretation of the figure without reference to the text.

Figures

– Two complete sets of glossy prints of high quality should be submitted. The labelling must be clear and neat.

– All photomicrographs should indicate the magnification of the print.

– Special features should be indicated by arrows or letters which contrast with the background.

– The back of each illustration should bear the first author's last name, figure number and an arrow indicating the top. This should be written lightly in pencil only. Please do not use a hard pencil, ball point or felt pen.

– Color illustrations will be accepted if they make a contribution to the understanding of the article.

– Do not use clips/staples on photographs and artwork.

– Illustrations must be drawn neatly by an artist and photographs must be sent on glossy paper. No captions should be written directly on the photographs or illustration. Legends to all photographs and illustrations should be typed on a separate sheet of paper. All illustrations and figures must be referred to in the text and abbreviated as "Fig.".

Please complete the following checklist and attach to the manuscript:

1. Classification (e.g. original article, review, selected summary, etc.)_____
2. Total number of pages _____
3. Number of tables _____
4. Number of figures _____
5. Special requests _____
6. Suggestions for reviewers (name and postal address)

Indian	Foreign
1. _____	1. _____
2. _____	2. _____
3. _____	3. _____
4. _____	4. _____

7. All authors' signatures_____
8. Corresponding author's name, current postal and e-mail address and telephone and fax numbers _____

Online Submission
Also e-Issue @ www.ijcpgroup.com

For Editorial Correspondence
Dr KK Aggarwal
Group Editor-in-Chief
Indian Journal of Clinical Practice
E-219, Greater Kailash Part-1
New Delhi - 110 048. Tel: 40587513
E-mail: editorial@ijcp.com Website: www.ijcpgroup.com

Indian
JOURNAL of
CLINICAL PRACTICE

Indian Citation Index (ICI),

IndMed (http://indmed.nic.in/)

MedIND (http://medind.nic.in/)

University Grants Commission (20737/15554).

ISSN number 0971-0876

RNI number 50798/1990.

The Medical Council of India (UGC, ICI)

Indian Journal of Clinical Practice is published by the IJCP Group. A multispecialty journal, it provides clinicians with evidence-based updated information about a diverse range of common medical topics, including those frequently encountered by the Indian physician to make informed clinical decisions. The journal has been published regularly every month since it was first launched in June 1990 as a monthly medical journal. It now has a circulation of more than 3 lakh doctors.

IJCP is a peer-reviewed journal that publishes original research, reviews, case reports, expert viewpoints, clinical practice changing guidelines, Medilaw, Medifinance, Lighter side of medicine and latest news and updates in medicine. The journal is available online (http://ebook.ijcpgroup.com/Indian-Journal-of-Clinical-Practice-January-2018.aspx) and also in print. IJCP can now also be accessed on a mobile phone via App on Play Store (android phones) and App Store (iphone). Sign up after you download the IJCP App and browse through the journal.

IJCP is indexed with Indian Citation Index (ICI), **IndMed** (http://indmed.nic.in/) and is also listed with **MedIND** (http://medind.nic.in/), the online database of Indian biomedical journals. The journal is recognized by the University Grants Commission (20737/15554). The Medical Council of India (MCI) approves journals recognized by UGC and ICI. Our content is often quoted by newspapers.

The journal **ISSN number** is 0971-0876 and the **RNI number** is 50798/1990.

If you have any Views, Breaking news/article/research or a rare and interesting case report that you would like to share with more than 3 lakh doctors send us your article for publication in IJCP at editorial@ijcp.com.

Dr KK Aggarwal
Padma Shri Awardee
Group Editor-in-Chief, IJCP Group

Quista® DN

Researched Nutritional Supplement for Diabetics

- **Provides 26 g of good quality proteins* per day** – Meets 43% of the Recommended Dietary Allowance (RDA)#
- **Low GI with sustained energy release** – Contains low GI carbohydrates, slow (casein) and medium digesting (pea) proteins, and soluble and insoluble fiber which help optimize glycemic response
- **Fortified with powerful ACCTI♦ nutrients** – For beneficial effects in diabetics
- **Fortified with key nutrients** including B complex vitamins, chromium, and zinc – Help in modulating glucose metabolism
- Free from trans fatty acids
- No added sucrose

ACCTI ADVANTAGE
For Diabetic Care

*Twice daily in 200 mL of toned milk. #Nutrient Requirement and RDA for Indians. ICMR 2010.
♦Alpha-Lipoic acid, Coenzyme Q10, L-Carnitine, Taurine, and Inositol

Indications

Prediabetes and diabetes.

Directions for use:
2 scoops (approx. 25 g) of Quista DN powder to be added into 200 mL of lukewarm/chilled toned milk or water and stirred briskly until well mixed.

Recommended servings:
Twice daily in between meals or at bedtime, or as directed by your healthcare professional. One serving of Quista DN in 200 mL of toned milk provides 212 kcal.

Delicious
Milk Masala and Vanilla Flavors

FOOD FOR SPECIAL DIETARY USE – For diabetic and prediabetic individuals.
NOT FOR MEDICINAL USE
Store this pack out of reach of children. Not for parenteral use.
Contains milk and soy ingredients. Manufactured in a facility handling nuts and soy ingredients. Not for individuals with lactose intolerance.
To be used under the advice of a healthcare professional as part of diabetes management regimen for adults, which includes physical activity and diet.

The Himalaya Drug Company
Makali, Bengaluru 562 162, India
www.himalayawellness.com
E-mail: write.to.us@himalayawellness.com

R.N.I. No. 50798/1990
Date of Publication 13th of Same Month
Date of Posting 13-14 Same Month

POSTAL REGISTRATION NO. DL(S)-01/3200/2021-2023
POSTED AT LPC DELHI RMS DELHI-110006