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In this issue

- Observational Study
- Clinical Study
- Case Report
- Expert Opinion
- Medicolegal
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EDITORIAL

- 5 Minutes of an International Weekly Meeting on COVID-19
Held by the HCFI Dr KK Aggarwal Research Fund

OBSERVATIONAL STUDY

- 8 Laboratory Profile of Adult Hemoglobinopathies Picked Up During Routine Health Check in a Tertiary Care Hospital from South India
Vijai Kumar Chinnaswami, Udhaya Balasubramanian, Aishwarya K Marimuthu

CLINICAL STUDY

- 14 Predictors of Mucormycosis in COVID-19
Gaurav Sharma, Hemant Mahur, DP Singh, Shreya Binaykiya, Kartikeya Mathur, Raghavendra G
- 18 Correlation of Vitamin D Levels with COVID-19 Severity and Outcome
Gurdeep Kaur, Gaurav Sharma, Jainendra Sharma, Shweta Biyani, Ranjna Veerwal

CASE REPORT

- 24 Post-COVID-19 Disease Associated with Mucormycosis and Guillain-Barré Syndrome: A Causal Association or Just a Coincidence?
Sahil Kharbada, Baldev Kumar Meena, Abhishek Nyati, Gurdeep Kaur, DP Singh
- 28 Modified Tinea – A Mithering Problem
Raj Kirit EP, AS Kumar

EXPERT OPINION

- 32 Topical Eberconazole for the Treatment of Recalcitrant Tinea Cruris Morphologically Modified
AS Kumar, Rajyalaxmi Konathan

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MEDICOLEGAL**34 Wrong Site Surgery: An Act of Gross Medical Negligence****MEDICAL VOICE FOR POLICY CHANGE****37 HCFI Dr KK Aggarwal Research Fund****CONFERENCE PROCEEDINGS****43 79th AIOC 2021: All India Ophthalmological Society****AROUND THE GLOBE****46 News and Views****SPIRITUAL UPDATE****51 The Five Interior Powers****INSPIRATIONAL STORY****52 Hitting Unseen Target****LIGHTER READING****54 Lighter Side of Medicine****IJCP's EDITORIAL & BUSINESS OFFICES**

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5th September 1958 - 17th May 2021

Minutes of an International Weekly Meeting on COVID-19 Held by the HCFI Dr KK Aggarwal Research Fund

TRANSTHYRETIN CARDIAC AMYLOIDOSIS: MYTHS, CHALLENGES AND SOLUTIONS

Speaker: Dr Saurabh Malhotra, *Director of Advanced Cardiac Imaging and Director of Clinical Research, Division of Cardiology, Cook County Health, Associate Professor of Medicine, Rush Medical College, USA*

23rd October, 2021 (Saturday, 9.30 am-11 am)

- There are two major types of amyloidosis: light chain amyloidosis and transthyretin amyloidosis (ATTR).
- Transthyretin is a tetrameric protein and appears like a four-leaf clover. Genetic mutations lead to tetramers changing to dimers, which are unstable and result in the formation of amyloid fibrils, which are resistant to proteolysis. They are deposited in the heart and various systems of the body.
- Amyloidosis is a systemic disease similar to diabetes.
- The prevalence of senile systemic amyloidosis, also called the wild type amyloidosis, is reportedly 25% in patients ≥85 years of age. Wild type ATTR is more often seen in elderly men. The variant amyloidosis is population specific. V122I is seen in the US, Caribbean, Africa; V30M is seen in Portugal, Sweden, Japan; while T60A is seen the UK and Ireland.
- In early onset disease, neurological complications are more likely, while in late onset disease, cardiac manifestations are more likely.
- There is a diverse clinical presentation, such as carpal tunnel syndrome, lumbar stenosis, gait disturbances, peripheral neuropathy, autonomic neuropathy, gastrointestinal (GI) disturbances, orthostatic hypotension, syncope, valvular heart disease, heart blocks, arrhythmias.
- Patients carrying the V142I mutation have worse heart failure (HF) outcomes (Atherosclerosis Risk in Communities [ARIC] study).
- The type of mutation also decides the disease penetrance.
- Patients with Leu111Met mutation have an early onset of disease, whereas in ATTRwt gene mutation, the disease presents late.

- Till about a decade back, the prevalence of amyloidosis was at the threshold for rare disease. This was possibly an underestimation as the sample included only hospitalized patients.
- AL amyloidosis is a rare disease; there are ~2,500 cases in the US and only 50% have cardiac involvement. Hereditary forms of amyloidosis are seen in 4% of African American (carriers). There are several thousand cases. There are about 1 million cases of the wild type amyloidosis.
- Disease starts with carpal tunnel syndrome; patients develop peripheral neuropathy and it takes several years before the disease is diagnosed.
- In patients who have cardiac amyloidosis, the conventional HF therapy is poorly tolerated. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) can worsen orthostatic hypotension. Digoxin binds to amyloid fibrils resulting in increased toxicity.
- Just because a patient has hypertension and aortic stenosis (AS) does not mean that the patient cannot have amyloidosis. TTR amyloidosis is a disease of the elderly, who often have hypertension. Left ventricular hypertrophy (LVH) and AS are common.
- Studies have shown that a large number of patients with cardiac amyloidosis have comorbid conditions such as hypertension, coronary artery disease (CAD), diabetes mellitus (DM), atrial fibrillation and chronic kidney disease (CKD).
- Presence of low ejection fraction does not rule out cardiac amyloidosis.
- Most of these patients do not present with HF; heart blocks are present in a minority of patients. Low-voltage electrocardiogram (ECG) is supposed to be the hallmark, but it is present in only about 27% of cases.
- Another challenge is the complicated diagnostic evaluation of suspected cardiac amyloidosis. Tissue biopsy is the gold standard.
- Red flags must be identified. If the patients have HF, thick ventricles along with the presence of certain features like carpal tunnel syndrome, low-voltage EKG, cherry on top Echo pattern.
- Imaging of hypertrophy, amyloid fibrils, extracellular volume in the heart can now be done.
- Echocardiography is usually the first step showing LVH, right ventricular hypertrophy (RVH) and hypertrophy of the interatrial septum. Restrictive physiology is classically seen in patients with amyloidosis.
- Strain imaging improves diagnostic accuracy.
- Echo is a very sensitive test, but is not very specific.
- Cardiac magnetic resonance imaging (MRI) has high accuracy for cardiac amyloidosis with sensitivity of 85% and specificity of 92%. Although it is very specific, it does not differentiate between the types of amyloidosis. MRI is very useful to follow the treatment response.
- There were sporadic case reports on cardiac uptake on bone scans in elderly men who underwent bone scans for prostate cancer. These are the patients who have wild type amyloidosis. Bone scintigraphy is now being used to diagnose cardiac amyloidosis. It is widely available, easy to perform and has very high accuracy for transthyretin amyloidosis (ATTR). If AL amyloidosis has been ruled out by monoclonal antibodies, the specificity is as high as 100%.
- The focus is based on imaging-based diagnosis.
- Now targeted therapies are available: TTR suppressors/silencers (inotersen, patisiran), which cleave the mRNA that makes the protein within the cells. The other class of drugs is TTR stabilizers and fibril disrupters (tafamidis/diflunisal or Doxy/taurodesoxycholic acid [TUDCA]). Only preclinical studies with Doxy/TUDCA.
- *In vivo* gene editing for transthyretin amyloidosis using CRISPR-Cas9 is a new exciting therapeutic approach to treat ATTR amyloidosis (*NEJM*. Aug. 5, 2021).
- T119M is benevolent rescue mutation, which is present in some patients that causes stabilization of this protein. Acoramidis (AG 10) acts in a similar manner to T119M and is being studied in phase III clinical trials.
- Treatment not only involves targeted therapy towards the disease but also nontargeted symptomatic management helps the patient to feel better in the short-term – reduction/discontinuation of β -blockers, ACEI/ARBs, avoid digoxin, treatment of orthostatic hypotension, prokinetic agents for gastroparesis, management of arrhythmias (Afib) and pacemakers for heart blocks. Diuretic therapy with loop diuretics is the mainstay. Treatment of HF in patients with amyloid must be less aggressive.

- One of the myths about transthyretin amyloidosis is that it is a rare disease. It is not so. In Chicago, there is V142I mutation; about 60k patients in Chicago are carriers of this mutation. V30M mutation is found in UK and Japan. The Thr60Ala mutation is found in Ireland.
 - Amyloidosis is not a death sentence; palliation and supportive care are not the only options. The elderly patients are being treated with transcatheter valves and clips.
 - Heart failure with preserved ejection fraction (HFpEF) is not the classic presentation; many patients have reduced ejection fraction.
 - Aggressive treatment of HF may be detrimental in these patients.
 - The challenges in TTR cardiac amyloidosis include long delay in diagnosis, overlapping clinical features, lack of awareness on prevalence, diagnosis and therapy, diagnostic challenges and coexistence with other cardiac conditions, hesitation in reducing or stopping conventional therapy.
 - The solutions include understanding disease prevalence and distribution in communities; it's a disease without any barriers especially the wild type amyloidosis.
 - Diagnosis is important not only for the patient, but also for the family members as it runs in families.
 - Targeted therapy is now available; nontargeted therapy is also a therapy. Reduction or removal of medications also forms part of the treatment.
 - Wild type amyloidosis has been noted to be more prevalent in men. The male-to-female ratio is 50:1.
 - For hereditary amyloidosis the prevalence is more equal – 1:1 or 2:1 for men and women. In US, the prevalent mutation is V142I and the ratio is 1:1 or 2:1 between men and women. The age of onset is late, around 65 years.
 - The V30M mutation occurs in younger people in their 40s.
 - It is a generational disease and knowledge about parents carrying the mutation is important as it is an autosomal heterozygous dominant mutation.
 - Amyloidosis is a debilitating disease. It starts with neuropathy; patients lose their fine and gross motor skills.
 - Many patients have diabetes and hypertension, both of which can mimic symptoms of amyloid. Carpal tunnel syndrome is not a neuropathy. Diabetes does not give bilateral carpal tunnel syndrome.
 - The disease has a relation with age. Certain mutations express the disease at a certain age. The type of mutation also decides the types of symptoms. If detected early, there is no cardiomyopathy. Once cardiomyopathy develops, the life span is limited. With the wild type, the life span is longer; but with mutation type, the life span is shorter.
 - Patients of amyloidosis must be vaccinated against COVID-19.
- Participants – Member National Medical Associations:**
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- Moderator:** Mr Saurabh Aggarwal

■ ■ ■ ■

Laboratory Profile of Adult Hemoglobinopathies Picked Up During Routine Health Check in a Tertiary Care Hospital from South India

VIJAI KUMAR CHINNASWAMI*, UDHAYA BALASUBRAMANIAN†, AISHWARYA K MARIMUTHU‡

ABSTRACT

Background and aim: Hemoglobin (Hb) variants can clinically range from being completely asymptomatic to frequent requirement of transfusions. Some individuals may become aware of a variant only when a complete blood count (CBC), hemoglobin analysis or genetic testing is done for a different reason. These individuals are typically heterozygous for an autosomal recessive variant. A study was conducted to find out the different types of hemoglobinopathies in adults presenting to a tertiary care hospital for routine health check and its geographic distribution. **Objective:** 1) To find out the severity of anemia associated with different hemoglobinopathies. 2) To find the relevance of glycated hemoglobin (HbA1c) in the presence of various hemoglobinopathies. **Methods:** A retrospective cross-sectional observational study was done in 111 consecutive patients who were found to have hemoglobinopathies during routine health checks in a tertiary care hospital in South India from 2013 to 2021. **Results:** One hundred eleven patients were found to have abnormality in Hb electrophoresis and there was a male predominance (69 patients, 62.2%). Majority of patients with beta-thalassemia (28 patients, 63.6%) were from West Bengal. Both HbE trait (17 patients, 65.4%) and homozygous HbE (23 patients, 62.2%) were from Assam. There was statistically significant distribution (p value 0.0001). HbA1c detected Hb variant in those with HbE disease. **Conclusion:** Hemoglobinopathies constitute a huge hereditary burden and a serious healthcare concern in India. Hence, it is the need of the hour to pick up such asymptomatic cases and provide appropriate premarital and prenatal counseling. Also, it is essential to devise strategies other than routine HbA1c testing to guide blood sugar control.

Keywords: Hemoglobinopathy, HbE, HbS, beta-thalassemia, high performance liquid chromatography, HbA1c

The normal hemoglobins (Hbs) are produced during embryonic, fetal and postnatal life. Adult Hb is produced starting in the first year of life. The predominant form found is HbA (95-98%), consisting of two alpha chains and two beta chains. Red blood cells (RBCs) also contain a small portion of HbA2 (2-3%), which contains two alpha chains and two delta chains, and HbF (<2%). There are over 1,000 different variants (genetic changes) that have been described in the genes that encode the different globin chains. Hemoglobin variants can be classified based on their

clinical phenotype (asymptomatic to severe anemia), by the type of hematologic changes they produce (hemolysis, reduced expression, altered oxygen affinity), by which globin chain is affected (alpha, beta or gamma), and by the type of mutation (base change, insertion and deletion). Some individuals may become aware of a variant only when a complete blood count (CBC), hemoglobin analysis or genetic testing is done for a different reason. These individuals are typically heterozygous for an autosomal recessive variant.

The present study highlights the detection of the hemoglobinopathies in adult population picked up during routine health up by high performance liquid chromatography (HPLC). This study was undertaken as there are limited studies available on the adult population hemoglobinopathies.

AIM

To find out the different types of hemoglobinopathies in adults presenting to a tertiary care hospital and its geographic distribution.

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OBJECTIVE

- To find out the severity of anemia associated with different hemoglobinopathies.
- To find the relevance of glycated hemoglobin (HbA1c) in the presence of various hemoglobinopathies.

STUDY DESIGN

A retrospective cross-sectional observational study was done in 111 consecutive patients who were found to have hemoglobinopathies during routine health checks in a tertiary care hospital in South India from 2013 to 2021. The privacy and confidentiality of patients were maintained as per norms.

DATA COLLECTION

We retrospectively collected the clinical and laboratory data of patients diagnosed with hemoglobinopathy by HPLC on their routine Master Health checks. This included epidemiological data, comorbidities of patients, laboratory parameters, like hemoglobin, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), ferritin and HbA1c. After collection of all required data and careful medical chart review, the clinical data was compiled and tabulated.

Inclusion Criteria

Age more than 18 years.

Exclusion Criteria

Patients with a recent history of transfusion (3 months prior to sample collection) were excluded from the study.

STATISTICAL ANALYSIS PLAN

All continuous variables are expressed as mean \pm standard deviation, if they are normally distributed. Not normally distributed continuous variables are expressed as median (interquartile range). Comparisons of categorical variables are done by Chi-square test. Comparisons of normally distributed continuous variables between more than two groups are done

by analysis of variance (ANOVA). Data entry has been done in Microsoft Excel 2007 spreadsheet. Data analysis has been carried out by IBM SPSS statistics for windows version 25.0, Armonk, NY: IBM CORP. All p values <0.05 are considered as statistically significant.

RESULTS

Gender Distribution

One hundred eleven patients were found to have abnormality in Hb electrophoresis. There was a male predominance (69 patients, 62.2%; Fig. 1).

Table 1 depicts gender distribution of various hemoglobinopathies present in our study.

Though there was a male predominance, there was no statistically significant gender distribution (p value 0.897).

Age Distribution

Mean age of the patients was 42 years (Range – 18–69 years). Table 2 depicts the frequency of hemoglobinopathy in different age groups of study participants.

Geographic Distribution

Majority of patients were from Assam (47 patients, 42.3%), followed by West Bengal (40 patients, 36%),

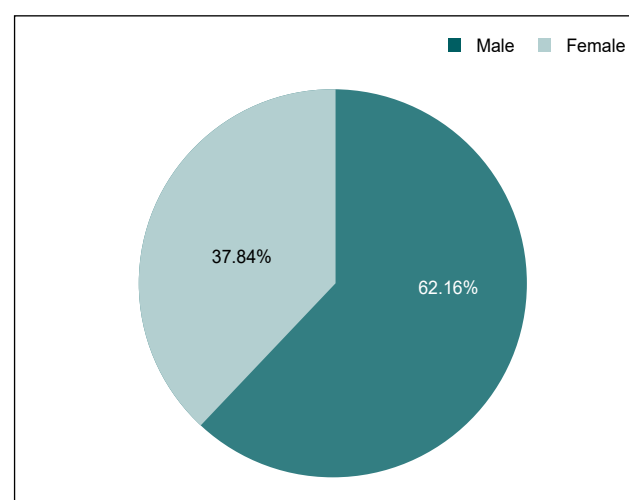


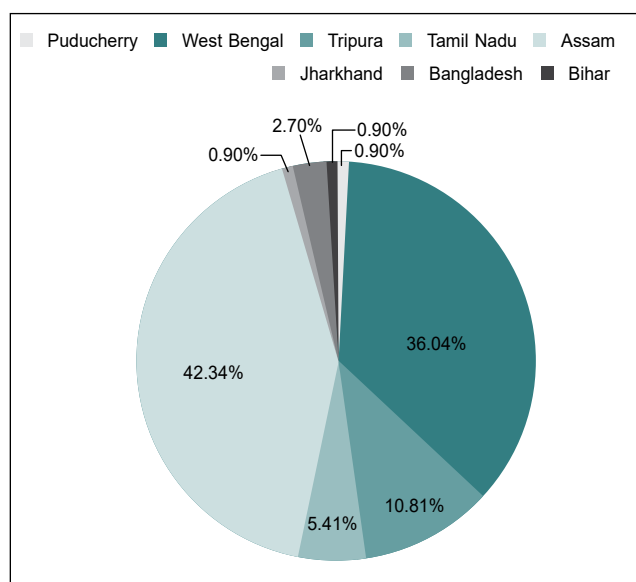
Figure 1. Gender distribution of study participants with abnormality in Hb electrophoresis.

Table 1. Gender Distribution of Various Hemoglobinopathies

Gender	Beta-thalassemia trait	HbE trait	Homozygous HbE	HbE+Beta-thalassemia	HbS disorder	HbD trait
Male	26 (37.7%)	17 (24.6%)	23 (33.3%)	1 (1.4%)	1 (1.4%)	1 (1.4%)
Female	18 (42.9%)	9 (21.4%)	14 (33.3%)	1 (2.4%)	0	0

Table 2. Frequency of Hemoglobinopathy in Different Age Groups

Age group (years)	Frequency of hemoglobinopathy	Percentage of hemoglobinopathy
<30	23	20.7
31-40	21	18.9
41-50	43	38.7
51-60	18	16.2
>60	6	5.4

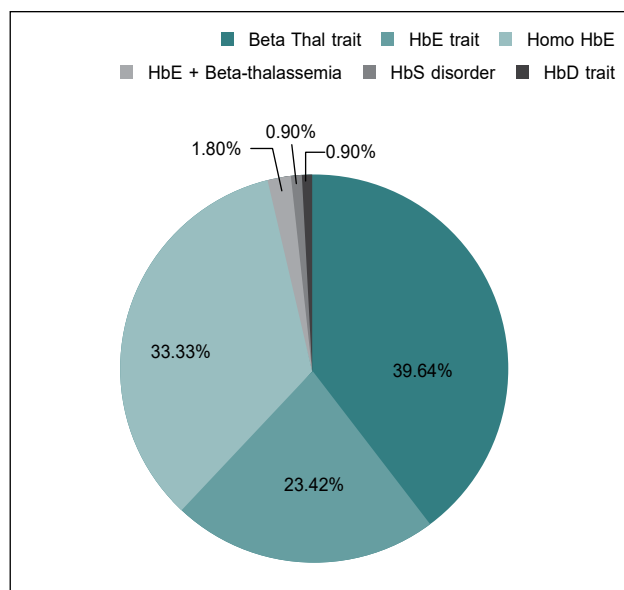
**Figure 2.** Geographic distribution of study participants.

Tripura (12 patients, 10.8%), Tamil Nadu (6 patients, 5.4%) and 1 patient (0.9%) each from Puducherry, Jharkhand and Bihar (Fig. 2). There were 3 patients (2.7%) from Bangladesh.

Majority of patients with beta-thalassemia (28 patients, 63.6%) were from West Bengal. Both HbE trait (17 patients, 65.4%) and homozygous HbE (23 patients, 62.2%) were from Assam. There was statistically significant distribution (p value 0.0001).

Different Types of Hemoglobinopathies

In our study group, beta-thalassemia trait (44 patients, 39.6%) was the most common hemoglobinopathy, followed by homozygous HbE (37 patients, 33.3%) and HbE trait (26 patients, 23.4%). Smaller proportion of patients also had HbE with beta-thalassemia (2 patients, 1.8%), HbS disorder (1 patient, 0.9%) and HbD trait (1 patient, 0.9%) (Fig. 3).

**Figure 3.** Presentation of different hemoglobinopathies in study participants.

Comorbidities

Various associated comorbidities in the study group were diabetes mellitus (8 patients, 7.2%), hypertension (4 patients, 3.6%), hypothyroidism (2 patients, 1.8%), asthma (2 patients, 1.8%), ankylosing spondylitis (2 patients, 1.8%) and rheumatoid arthritis, dyslipidemia, Ca stomach and benign prostatic hyperplasia in 1 patient each (0.9%).

Hemoglobin Indices

Table 3 depicts the mean value of Hb, MCV, MCH, MCHC and RBC among various hemoglobinopathies found in our study population.

HbA2

HbA2 couldn't be detected in HbE disease. Table 4 shows mean HbA2 value in different hemoglobinopathies.

HbA1c Detection in Hemoglobinopathy

HbA1c testing was done in 61 patients. Among these, mean HbA1c was 5.7% (Range: 4.1-8%). Hb variant was detected in those with HbE disease (Homozygous HbE, HbE trait and HbE with beta-thalassemia).

DISCUSSION

India is well-known for its cultural diversity. This makes it an ideal place for studying heritable disorders, like hemoglobinopathy. The understanding and

Table 3. Hemoglobin Indices among Different Hemoglobinopathies in Study Group

Hemoglobinopathy	No. of cases	Mean Hb	Mean MCV	Mean MCH	Mean MCHC	Mean RBC
Beta-thalassemia trait	44	11.15	65.20	20.61	30.93	5.59
HbE trait	26	11.45	75.04	23.85	31.85	4.79
Homozygous HbE	37	10.6	62.11	20.11	32.32	5.28
HbE + Beta-thalassemia	2	10.85	69	23	32.50	4.81
HbS disorder	1	13.2	71	21	30	6.33
HbD trait	1	14	74	24	32	5.94

Table 4. Mean HbA2 in Different Hemoglobinopathies

Hemoglobinopathies	Number of cases	Mean HbA2
Beta-thalassemia trait	41	4.85
HbS disorder	1	2.80
HbD trait	1	2.60

analysis of pooling up of hemoglobinopathies in certain geographic areas is very essential for premarital and prenatal counseling. A study by Iyer et al has reported around 40 Hb variants.¹

In South-East Asia and the Indian subcontinent, hemoglobinopathies represent the most common monogenic blood illnesses, which represent a severe genetic and public health burden.^{2,3} There are three types of Hb variants which are commonly present in India, namely sickle cell (HbS), hemoglobin E (HbE) and hemoglobin D (HbD). These structural variants of hemoglobin have geographical variations; the total allele frequency for these variants has been determined to be 5.35% in different parts of India.⁴

In India, the average allele frequency of sickle cell and HbD was found to be 4.3% and 0.86%, respectively, with HbE accounting for 10.9% gene frequency in the North-East India.⁴ Sickle cell disease is prevalent in both tribal and nontribal people, particularly in Central-East India. The carrier frequency of hemoglobinopathy ranges from 3% to 17% in India.⁵ Hemoglobinopathies, as a result, constitute a huge hereditary burden and a serious healthcare concern in India.

The sickle cell hemoglobin (HbS) is a structurally abnormal variant where valine replaces glutamic acid residue at 6th position of beta-globin polypeptide chain of the molecule. HbE is caused by point mutation of beta-globin, which results in substitution of lysine for glutamic acid in position 26. HbD is a result

of substitution of glutamine for glutamic acid in codon 121 of beta-globin gene.

HPLC is very helpful in the accurate diagnosis of hemoglobinopathies and thalassemias. It has exceptional resolution, reproducibility and quantification of normal and abnormal hemoglobins, thus helping with accurate diagnosis.⁶

Our study included 111 adult patients diagnosed with abnormal Hb by HPLC during routine health check. There was a male predominance (62.2%). Our study included adult patients with age ranging from 18 to 69 years. Majority of the patients belonged to the 41 to 50 years age group. Beta-thalassemia trait, HbE trait, homozygous HbE disease, HbS disorder and HbD trait were the hemoglobin abnormalities detected in our study population. Beta-thalassemia trait was the most common abnormality found in 44 patients (39.6%). Similar findings have been reported in other Indian studies as well.⁷ This was followed by homozygous HbE (37 patients, 33.3%) and HbE trait (26 patients, 23.4%).

Majority of patients with beta-thalassemia (63.6%) were from West Bengal. Both HbE trait (65.4%) and homozygous HbE (62.2%) were from Assam. This geographic distribution was statistically significant with significant p value. Other studies also show clustering of such Hb variants in specific parts of India.¹

The mean Hb was 11.15 g% in beta-thalassemia trait, 11.45 g% in HbE trait and 10.6 g% in homozygous HbE disease.

OBSERVATIONAL STUDY

Hb variant was detected in those with structural abnormalities like homozygous HbE, HbE trait and HbE with beta-thalassemia. Antibodies that identify the N-terminal glycated amino acids in the first 4 to 10 amino acids of the beta-globin chain of hemoglobin are used in immunoassay-based HbA1c assays.⁸ As a result, Hb variations with mutations in this particular area will impact HbA1c immunoassay measurements. To avoid errors in the management of diabetes patients, it is critical to understand and be aware of Hb variations that alter HbA1c values, particularly in regions with a high frequency of hemoglobinopathy. In patients with hemoglobin variations, other techniques of evaluating glycemic control, such as fructosamine, glycated serum albumin or self-monitoring of blood glucose may be better options compared to HbA1c.

LIMITATIONS

The major limitation of our study is its retrospective design and small sample size.

CONCLUSION

Hemoglobinopathies constitute a huge hereditary burden and a serious healthcare concern in India. Hence, it is the need of the hour to pick up such asymptomatic cases and provide appropriate premarital and prenatal counseling. Also, it is essential to devise strategies other than the routine HbA1c testing to guide blood sugar control.

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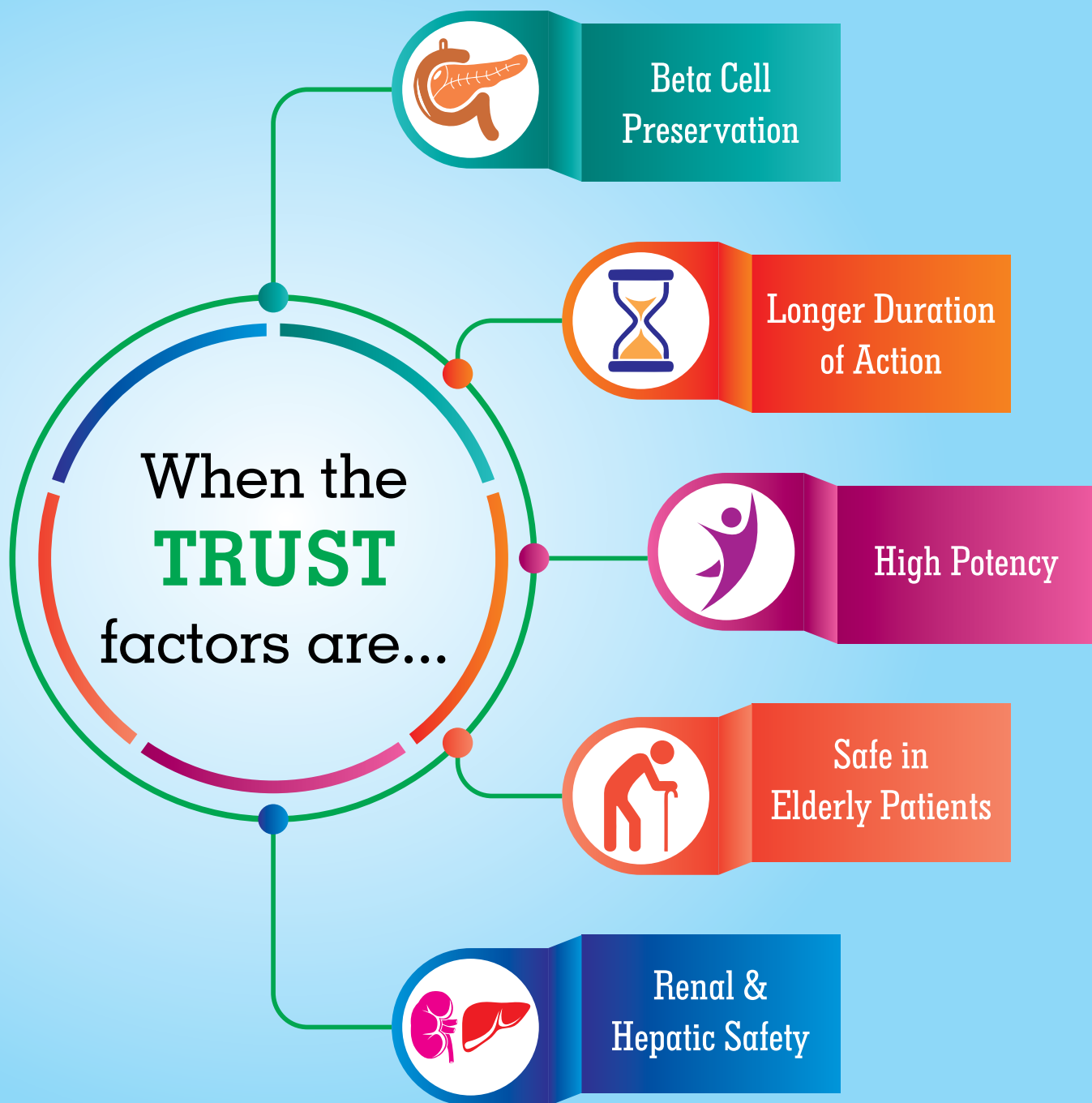
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Melatonin Improves Sleep in Patients with MS

A pilot study, presented at the annual meeting of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), suggested that melatonin could improve sleep time and sleep efficiency in patients with multiple sclerosis (MS) who were also having sleep disturbance.

Though the study had only 30 patients, the results suggest that melatonin could help MS patients with sleep issues, stated Wan-Yu Hsu, PhD, who presented the study. The double-blind, placebo-controlled, crossover study included participants with a Pittsburgh Sleep Quality Index (PSQI) score of 5 or more, or an Insomnia Severity Index (ISI) score more than 14 at baseline. Other assessments done at baseline included patient-reported outcomes for sleep disturbances, sleep quality, daytime sleepiness, walking ability, fatigue and mood. Half of the study subjects were given melatonin for the first 2 weeks and were then switched to placebo. The other half initially received placebo and switched to melatonin at the beginning of the third week. During weeks 2 and 4, the subjects wore an actigraph watch, and the patient-reported outcome measures were repeated at the end of weeks 2 and 4. Melatonin led to an improvement in average sleep time (6.96 vs. 6.67 hours). Sleep efficiency was also slightly improved (84.7% vs. 83.2%); however, it was not statistically significant ($p = 0.07$). Improvements in ISI (-3.5 vs. -2.4; $p = 0.07$), change in PSQI component 1 (-0.03 vs. 0.0; $p = 0.07$), and change in the NeuroQoL-Fatigue score (-4.7 vs. -2.4; $p = 0.06$) were the other trends toward statistical significance... (Source: Medscape)



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Predictors of Mucormycosis in COVID-19

GAURAV SHARMA*, HEMANT MAHUR†, DP SINGH‡, SHREYA BINAYKIYA‡, KARTIKEYA MATHUR‡, RAGHAVENDRA G‡

ABSTRACT

Background and Aims: Mucormycosis, a serious angioinvasive infection caused by common filamentous fungi, that is, mucormycetes, constitutes the third most common invasive fungal infection, following aspergillosis and candidiasis. Although a rare infection, in recent times we witnessed a sudden surge of mucormycosis cases post-COVID-19 (coronavirus disease 2019). The present study was carried out to understand its relation to COVID-19, inflammatory markers, steroid use during COVID-19 treatment, clinical course and outcome of the disease. **Material and methods:** The present study was conducted at RNT Medical College, Udaipur over a period of 1 month. Written and informed consent from patients were taken. In this study, 15 patients admitted in COVID wards, medical wards, mucormycosis ward and ICU were included if fungal hyphae were found on potassium hydroxide (KOH) mount and there was a history of COVID-19 illness; negative KOH mount patients were excluded. **Results:** In the present study, on admission, out of 15 patients, 7 (46.7%) were admitted with mean neutrophil-to-lymphocyte ratio (NLR) >5.5, mean C-reactive protein (CRP) 126, mean interleukin (IL)-6 82.4, mean lactate dehydrogenase (LDH) 528, mean ferritin 662, mean D-dimer 1760; 5 (33.3%) patients were admitted with mean NLR 3.5-5.5, mean CRP 68, mean IL-6 39.6, mean LDH 336, mean ferritin 448, mean D-dimer 780; and 3 (20%) patients were admitted with mean NLR <3.5, mean CRP 16, mean IL-6 12.8, mean LDH 172, mean ferritin 226, mean D-dimer 430. Out of the 7 patients who were admitted with NLR >5.5, 3 (42.8%) were admitted with orbital cellulitis and 4 (57.2%) with invasive sinusitis. Out of 5 patients admitted with NLR 3.5-5.5, 3 (60%) were admitted with orbital cellulitis and 2 (40%) with invasive sinusitis. Out of 3 patients admitted with NLR <3.5, 1 (33.3%) patient had orbital cellulitis and 2 (66.7%) had invasive sinusitis. Out of total 7 patients who were admitted with orbital cellulitis, in 71.4% patients, steroid was used during COVID-19 treatment and out of 8 patients who were admitted with invasive sinusitis, in 62.5% patients, steroid was used during COVID-19 treatment. In the present study, 68% patients were male and 32% were female. Around 78% patients were from rural area and 22% patients were from urban area. Overall, 74% cases were treated with amphotericin B. Among these, 36% cases were diagnosed with orbital cellulitis and 38% cases were diagnosed with invasive sinusitis. Around 26% cases were treated with posaconazole, and among these 9% were orbital cellulitis cases and 17% were invasive sinusitis cases. About 85.72% cases of orbital cellulitis and 75% cases of invasive sinusitis improved. Nearly 42.86% cases who were admitted with NLR >5.5 did not improve with treatment. **Conclusion:** As per present study, inflammatory markers of COVID-19, NLR and history of steroid use during treatment can be considered as predictors of mucormycosis occurrence and their outcome.

Keywords: COVID-19, NLR, CRP, LDH, IL-6, mucormycosis

Mucormycosis is an angioinvasive infection caused by filamentous fungi mucormycetes. It is the third most common invasive fungal infection after aspergillosis and candidiasis.¹ The pathogens can result in infections with high mortality in immunocompromised individuals, particularly in

diabetes patients and people taking steroids.² Although a rare infection, in recent times we witnessed a sudden surge of mucormycosis cases post-COVID-19 (coronavirus disease 2019). Mucorales includes different species associated with rhinocerebral, pulmonary, skin and gastrointestinal infections and some other less frequently encountered infections in immunocompetent and immunocompromised people. Members of the genus *Rhizopus* are the most commonly isolated pathogens in a clinical setting, with *Rhizopus arrhizus* being the most common. Irrespective of the route of infection, whether inhalation of spores, ingestion or direct skin inoculation, the mucor hyphae eventually invade blood vessels, causing tissue infarction and necrosis.³ Risk factors for the infection include long-term neutropenia, use of steroid therapy, hematological

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malignancies, aplastic anemia, myelodysplastic syndromes, solid organ or hematopoietic stem-cell transplantation, human immunodeficiency virus (HIV) infection, diabetic and/or metabolic acidosis, intravenous substance abuse, prematurity and older age.^{4,6} The rhinocerebral type is the most commonly reported form of the infection, others being cutaneous, gastrointestinal, pulmonary and disseminated infections.⁷

MATERIAL AND METHODS

The present study was conducted at RNT Medical College, Udaipur, Rajasthan. This study was done over a period of 1 month after getting approval from Institutional Ethics Committee. Written and informed consent from patients were taken. In this study, 15 patients admitted in COVID wards, medical wards, mucormycosis ward and ICU were included if fungal hyphae were found on potassium hydroxide (KOH) mount and there was a history of COVID-19 illness; negative KOH mount patients were excluded.

RESULTS

In the present study, 68% patients were male and 32% patients were female. Around 78% patients were from rural area and 22% patients were from urban area.

On admission, out of 15 patients, 7 (46.7%) were admitted with mean neutrophil-to-lymphocyte ratio (NLR) >5.5, mean C-reactive protein (CRP) 126, mean interleukin (IL)-6 82.4, mean lactate dehydrogenase (LDH) 528, mean ferritin 662, mean D-dimer 1760; 5 (33.3%) patients were admitted with mean NLR 3.5-5.5, mean CRP 68, mean IL-6 39.6, mean LDH 336, mean ferritin 448, mean

D-dimer 780; and 3 (20%) patients were admitted with mean NLR <3.5, mean CRP 16, mean IL-6 12.8, mean LDH 172, mean ferritin 226, mean D-dimer 430.

Table 1 summarizes the distribution of patients as per mean NLR, CRP, IL-6, LDH, ferritin and D-dimer level on admission.

Out of the total 7 patients who were admitted with NLR >5.5, 3 (42.8%) were admitted with orbital cellulitis and 4 (57.2%) with invasive sinusitis. Out of 5 patients who were admitted with NLR 3.5-5.5, 3 (60%) were admitted with orbital cellulitis and 2 (40%) with invasive sinusitis. Out of 3 patients who were admitted with NLR <3.5, 1 (33.3%) patient was admitted with orbital cellulitis and 2 (66.7%) with invasive sinusitis (Table 2).

Out of total 7 patients who were admitted with orbital cellulitis, in 71.4% patients, steroid was used during COVID-19 treatment and out of 8 patients who were admitted with invasive sinusitis, in 62.5% patients, steroid was used during COVID-19 treatment (Table 3).

Around 74% cases were treated with amphotericin B, and among these, 36% were diagnosed with orbital cellulitis and 38% were diagnosed with invasive sinusitis. About 26% cases were treated with posaconazole, and among these 9% were orbital cellulitis cases and 17% were invasive sinusitis cases.

Nearly 85.72% cases of orbital cellulitis improved and 75% cases of invasive sinusitis improved (Table 4).

Additionally, around 42.86% cases who were admitted with NLR >5.5 did not improve with treatment (Table 5).

Table 1. Distribution of Patients as per Mean NLR, CRP, IL-6, LDH, Ferritin and D-dimer Levels on Admission

Mean NLR	N	Mean CRP	Mean IL-6	Mean LDH	Mean ferritin	Mean D-dimer
<3.5	3	16	12.8	172	226	430
3.5-5.5	5	68	39.6	336	448	780
>5.5	7	126	82.4	528	662	1760

Table 2. Prevalence of Orbital Cellulitis and Invasive Sinusitis in Patients Based on NLR Value on Admission

NLR	Orbital cellulitis (N) (%)	Invasive sinusitis (N) (%)	Total (N) (%)
<3.5	1 (33.3)	2 (66.7)	3 (100)
3.5-5.5	3 (60)	2 (40)	5 (100)
>5.5	3 (42.8)	4 (57.2)	7 (100)

CLINICAL STUDY

Table 3. Steroid Use in Patients with Orbital Cellulitis and Invasive Sinusitis

Steroid	Orbital cellulitis (N) (%)	Invasive sinusitis (N) (%)
Used	5 (71.4)	5 (62.5)
Not used	2 (28.6)	3 (37.5)
Total	7 (46.7)	8 (53.3)

Table 4. Outcome in Patients with Orbital Cellulitis and Invasive Sinusitis

Improved	Orbital cellulitis (%)	Invasive sinusitis (%)	Total (%)
Yes	85.72	75	80
No	14.28	25	20

Table 5. Outcome in Patients with Treatment Based on NLR on Admission

NLR	Orbital cellulitis (N) (%)	Invasive sinusitis (N) (%)	Improved with treatment (%)	Did not improve with treatment (%)
<3.5	1 (33.3)	2 (66.7)	100	-
3.5-5.5	3 (60)	2 (40)	100	-
>5.5	3 (42.8)	4 (57.2)	57.14	42.86

DISCUSSION

In the present study, more patients were male and from rural background, and more number of patients were admitted with severe COVID-19 disease with NLR >5.5, mean CRP >50, mean IL-6 >50, mean LDH >300, mean ferritin >400 and mean D-dimer >1000. More number of cases were diagnosed with invasive sinusitis than orbital cellulitis and in these cases more number of patients were admitted with severe COVID-19 disease. Mucormycosis developed more commonly in patients

who were admitted with severe form of COVID-19 illness with cytokine storm and were treated with steroid during their COVID illness. Amphotericin B was used more commonly than posaconazole in mucormycosis treatment. Around 80% patients improved with treatment and they were of mild and moderate severity, while 20% patients did not improve, who were admitted with severe form of COVID-19 illness with cytokine storm.

CONCLUSION

As per present study, inflammatory markers of COVID-19, NLR and history of steroid use during treatment can be considered as predictors of mucormycosis occurrence and their outcome.

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ECTRIMS and EAN Issue Statement on COVID Vaccination in MS Patients

The ECTRIMS and the European Academy of Neurology (EAN) have released a joint position statement on COVID-19 vaccination among patients with MS. It states that the COVID-19 vaccines currently available are safe for patients with MS. It also mentions that the vaccines provide the same protection to patients with MS as to the general population. However, there may be exceptions, such as patients taking the S1P modulator fingolimod and anti-CD20 drugs. Antibody responses have been found to be reduced in these patients. Presenting the statement at the 37th Congress of ECTRIMS 2021, held online, Mauricio Farez said that no specific contraindications for any COVID-19 vaccines in MS patients have been reported thus far... (Source: Medscape)

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Correlation of Vitamin D Levels with COVID-19 Severity and Outcome

GURDEEP KAUR*, GAURAV SHARMA†, JAINENDRA SHARMA‡, SHWETA BIYANI‡, RANJNA VEERWAL†

ABSTRACT

Background and aims: Low vitamin D levels have been associated with an increase in inflammatory cytokines and a significantly increased risk of pneumonia and viral upper respiratory tract infections. Vitamin D deficiency is associated with an increase in thrombotic episodes, which are frequently observed in coronavirus disease 2019 (COVID-19). These conditions are reported to carry a higher mortality in COVID-19. So, we conducted a study to prove the correlation of vitamin D levels with COVID-19 infection and severity. **Material and methods:** The present study was conducted at RNT Medical College, Udaipur, Rajasthan. This study was done over a period of 2 months after getting approval from Institutional Ethics Committee. Written and informed consent was obtained from patients. In this study, 81 patients admitted in COVID wards and ICU, with COVID reverse transcriptase-polymerase chain reaction (RT-PCR) positive reports were included. **Results:** Out of a total 81 patients, 37 (45.7%) were in the 41-60 years age group, 29 (35.8%) were more than 60 years of age and 15 (18.5%) were less than 40 years of age. Seventeen patients had severe vitamin D deficiency, 27 patients had moderate vitamin D deficiency, 20 patients had mild vitamin D deficiency and 17 patients had normal vitamin D level. Out of 17 patients who had severe vitamin D deficiency, 11 (64.7%) patients required invasive mechanical ventilation and out of these 17 patients, 13 (76.47%) patients died. Out of 17 patients who had normal level of vitamin D, 16 (94.1%) maintained SpO₂ at room air and only 1 patient required invasive mechanical ventilation. As the level of vitamin D increased from severely low to normal level, requirement of high oxygen support decreased and SpO₂ at room air increased. Mean of vitamin D among the patients who died was 10.4963 while mean of vitamin D level among patients who survived and were discharged was 27.2362. All 17 patients who had normal level of vitamin D were discharged from the hospital. Mean of serum ferritin and mean of interleukin (IL)-6 was high in patients who died and low in patients who were discharged. **Conclusions:** Vitamin D level plays an important role in COVID-19 disease. Vitamin D have significant role in protection from severe form of disease.

Keywords: COVID-19, vitamin D, T regulatory lymphocytes, acute respiratory distress syndrome, IL-6, serum ferritin

The severity of coronavirus disease 2019 (COVID-19) is influenced by several factors, including the evidence of pneumonia, severe acute respiratory distress, myocarditis, microvascular thrombosis and/or cytokine storm. All these conditions have underlying inflammation. A major defense against inflammation, and viral infection in general, is the T regulatory lymphocytes (Tregs). It has been reported that Treg levels can be low in COVID-19 patients and can be

increased with vitamin D supplementation.¹ Treg levels can be particularly lower in severe COVID-19 infection.² Low vitamin D level has been tied to an increase in inflammatory cytokines as well as a significant increase in the risk of pneumonia and viral respiratory tract infections. Additionally, vitamin D deficiency has also been tied to an escalation in thrombotic episodes, often seen in patients with COVID-19.¹

Deficiency of vitamin D is common in patients with obesity and diabetes. Moreover, these are among the conditions known to be associated with a higher mortality in COVID-19.¹

MECHANISMS THAT LINK COVID-19 WITH VITAMIN D

The COVID-specific CD8 T cells and the specific antibodies produced by B cells are vital to eliminate the virus. However, unchecked non-specific inflammation and production of cytokines can result in injury to the lungs and other vital organs. Thus, limiting the early

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non-specific inflammation during COVID-19 illness may give time to the specific acquired immunity to develop.

As mentioned earlier, Treg levels have been reported to be low in some COVID-19 patients, and are markedly reduced in severe cases.² In a study by Johnstone et al conducted among older nursing home patients, high Treg blood levels were found to be tied to decreased risk of respiratory viral disease.³ This implies that if Treg levels are increased, it may prove to be beneficial for decreasing the severity of viral disease and possibly of COVID-19 as well.

Vitamin D supplementation can increase Treg levels in both healthy individuals as well as those with autoimmune disorders.^{4,5} Low levels of vitamin D are associated with a significantly increased risk of pneumonia and viral respiratory tract infections.^{6,7}

Low vitamin D levels are tied to an increase in inflammatory cytokines. In healthy individuals, researchers have noted a significant inverse relationship between the serum 25-hydroxyvitamin D [25(OH)D] and tumor necrosis factor (TNF)- α .⁸ The levels of interleukin (IL)-6 have been found to be increased in those who were vitamin D deficient.⁹ Several animal studies and *in vitro* cell models have shown vitamin D3 to down-regulate the production of inflammatory cytokines, such as TNF- α and IL-6, while increasing inhibitory cytokines.¹⁰ All these observations suggest that adequate levels of vitamin D can potentially decrease the incidence of cytokine storm, which is seen in COVID-19.

Thrombotic complications are also frequently encountered in COVID-19 patients.¹¹ A large number of patients with COVID-19 have been found to have elevated D-dimer levels. Vitamin D is known to regulate thrombotic pathways, and the deficiency of this vitamin is associated with an increase in thrombotic episodes.¹² Vitamin D deficiency has also been found to occur more frequently in patients with obesity and diabetes.¹³ These conditions are associated with higher mortality in COVID-19 patients.

MATERIAL AND METHODS

The present study was conducted at RNT Medical College, Udaipur, Rajasthan. This study was done over a period of 2 months after getting approval from Institutional Ethics Committee. Written and informed consent was obtained from patients. In this study, 81 patients admitted in COVID wards and intensive care unit (ICU), with COVID reverse transcriptase-

polymerase chain reaction (RT-PCR) positive report, were included.

Patients admitted in COVID ICU and wards were tested for vitamin D level. Patient were grouped into: severe deficiency of vitamin D <10 ng/mL, moderate deficiency of vitamin D 10-20 ng/mL, mild deficiency of vitamin D 20-30 ng/mL and normal level >30 ng/mL. Association of vitamin D level was tested with outcome of patient in the form of discharge and death and maintenance of SpO₂ level.

RESULTS

In the present study, out of total 81 patients 37 (45.7%) were in the 41-60 years age group, 29 (35.8%) were more than 60 years of age and 15 (18.5%) were less than 40 years of age. Most of patients were male (n = 59), 72.8% and 27.2% (n = 22) were female (Table 1).

Table 2 depicts the association of vitamin D level and SpO₂ maintained by patients. Among the patients who had severe vitamin D deficiency, all patients (100%) required mechanical ventilation. Out of 17 patients who had normal level of vitamin D, 16 (94.1%) maintained SpO₂ at room air. As the level of vitamin D increased from severely low to normal level, requirement of mechanical ventilation decreased. This association of vitamin D level and SpO₂ maintained by patients was found to be statistically significant, with Chi-square 88.163 and p value <0.0001.

Table 3 depicts means of vitamin D level as per the outcome of death and discharge. The mean of vitamin D level among the patients who died was 10.4963, while mean of vitamin D level among patients who survived and were discharged was 27.2362. As depicted in the table, patients who survived and were discharged had high mean level of vitamin D and patients who died had low mean level of vitamin D. The difference in mean of vitamin D level with outcome was statistically significant with p value 0.0015.

Table 1. Distribution of Study Participants According to Age and Gender (n = 81)

Age Group	Frequency	Percentage (%)
Age Group (Years)		
<40	15	18.5
41-60	37	45.7
>60	29	35.8
Gender		
Male	59	72.8
Female	22	27.2

Table 2. Association Between Vitamin D Level and Peak Requirement of Oxygen Support in COVID RT-PCR Positive Patients (n = 81)

	Peak requirement of oxygen support				Total	Chi-square and p value
	Room air	Nasal prong/mask	NIV	Invasive mechanical ventilation		
Vitamin D level (ng/mL)						
0-10	0 (0.0%)	0 (0.0%)	6 (35.29%)	11 (64.7%)	17 (100.0%)	88.163,
11-20	5 (18.5%)	6 (22.2%)	14 (51.9%)	2 (7.4%)	27 (100.0%)	<0.0001
21-30	12 (60.0%)	2 (10.0%)	5 (25.0%)	1 (5.0%)	20 (100.0%)	
>30	16 (94.1%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	17 (100.0%)	
Total	33 (40.7%)	8 (9.9%)	25 (30.9%)	15 (18.5%)	81 (100.0%)	

Table 3. Association Between Mean of Vitamin D Level and Outcome of Death and Discharge (n = 81)

Outcome	Mean	N	SD	P value
Death	10.4963	18	5.76154	t = 3.3002
Discharge	27.2362	63	20.00015	0.0015
Total	23.9295	81	19.26664	

Table 4. Association Between Different Vitamin D Levels and Outcome of Death and Discharge (n = 81)

	Outcome		Total	Chi-square and p value
	Death	Discharge		
Vitamin D level (ng/mL)				
0-10	13 (76.47%)	4 (23.53%)	17 (100.0%)	29.018,
11-20	4 (14.8%)	23 (85.2%)	27 (100.0%)	<0.0001
21-30	1 (5.0%)	19 (95.0%)	20 (100.0%)	
>30	0 (0.0%)	17 (100.0%)	17 (100.0%)	
Total	18 (22.2%)	63 (77.8%)	81 (100.0%)	

Table 4 depicts the association of vitamin D levels and outcome of patients in form of death and discharge of patients. Out of 17 patients who had severely low vitamin D level, 13 (76.47%) patients died. All 17 patients who had normal level of vitamin D were discharged from hospital. As the level of vitamin D increased from severely low to normal level, chance of survival and discharge increased. This association of vitamin D level and outcome of patients in form of death and discharge of patients was found statistically significant, with Chi-square 29.018 and p value <0.0001.

Table 5 depicts that the mean of inflammatory marker IL-6 among the patients who died was 58.3231, while mean of IL-6 among patients who survived and were discharged was 40.7815. As depicted from the table,

patients who survived and were discharged had low mean level of IL-6 and patients who died had high mean level of IL-6. However, the difference in mean of IL-6 level with outcome was statistically insignificant with p value 0.440.

Table 5 also depicts that the mean of inflammatory marker serum ferritin among the patients who died was 1050.7375, while mean of serum ferritin among patients who survived and were discharged was 459.0000. As depicted in the table, patients who survived and were discharged had low mean level of serum ferritin and patients who died had high mean level of serum ferritin. The difference in mean of serum ferritin level with outcome was found statistically significant with p value 0.001.

Table 5. Association Between Inflammatory Markers (IL-6 and Serum Ferritin) and Outcome of COVID RT-PCR Positive Patients (n = 81)

	Outcome		't' value and p value
	Death	Discharge	
IL-6			
Mean	58.3231	40.7815	t = 0.7752
N	16	65	p = 0.440
SD	60.3941	85.2127	
Serum ferritin			
Mean	1050.7375	459.0000	t = 4.4711
N	16	65	p = 0.001
SD	644.5592	425.5343	

DISCUSSION

The present study was conducted at RNT Medical College, Udaipur, Rajasthan. In the present study, out of total 81 patients, 37 (45.7%) were in the 41-60 years age group, 29 (35.8%) were more than 60 years of age and 15 (18.5%) were less than 40 years of age. In our study, the association of vitamin D level and SpO₂ of patients was found to be statistically significant. It was observed that if patients had normal level of vitamin D, they maintained SpO₂ with room air/nasal prong/mask (low oxygen support) and they did not get severe form of disease. As depicted in our study, patients who survived and were discharged had high mean level of vitamin D and low mean level of serum ferritin and IL-6 and patients who died had low mean level of vitamin D and high mean level of serum ferritin and IL-6.

The difference in mean of vitamin D level with outcome and serum ferritin level with outcome was statistically significant. It was interpreted that if the patients had high mean level of vitamin D and low mean level of serum ferritin and IL-6, they had less severe disease, or in other words, patients who had low level of vitamin D and high level of serum ferritin and IL-6 had more severe disease and higher death rate.

In the present study, it was found that as the level of vitamin D increased from severely low to normal level, chance of survival and discharge increased. This association of vitamin D level and outcome of patient in the form of death and discharge of patients was found statistically significant. It was interpreted that patients who had severe vitamin D deficiency had more chance of severe disease and death.

CONCLUSIONS

In the present study, it was interpreted that vitamin D levels play an important role in COVID-19 disease. Vitamin D has a significant role in protection from severe form of the disease. Patients who have severe vitamin D deficiency have more chance of severe disease, more chance of requiring high oxygen support to maintain SpO₂ and have more chance of mortality from COVID-19.

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Oral Contraceptive Pills may Check PCOS-related Diabetes Risk

A retrospective, population-based study has found that some of the oral contraceptives are tied to a lower risk for type 2 diabetes and prediabetes among women with polycystic ovary syndrome (PCOS). An analysis of 64,051 women with PCOS revealed that they had around two-times greater risk for developing type 2 diabetes (adjusted hazard ratio [aHR] 2.04) and dysglycemia (aHR 1.87) compared to the general population, reported researchers online in *Diabetes Care*.

However, combined oral contraceptive pills (COCs) were found to counter this risk over a median follow-up of 3.5 years. Women who were prescribed COCs had a 16% to 17% reduced risk for type 2 diabetes. The risk reduction appeared to be similar for contraceptives with an antiandrogenic progestin component (aHR 0.84) and without it (aHR 0.83)... (Source: *Medpage Today*)

Nurse Survey Highlights Mental Health Difficulties During COVID-19 Pandemic

A COVID-19 survey on mental health and wellness by the American Nurses Foundation has shown that over half of the nurses working in critical care reported that they were not emotionally healthy.

Out of 9,572 nurses surveyed in the third of a series of pandemic-related polls, around 75% nurses across all roles stated that they were stressed, while 10% reported feeling worthless. Around 51% of nurses, 25 to 34 years of age, reported feeling 'not emotionally healthy'.

Among critical care nurses, 80% reported that they felt stressed or exhausted in the last 14 days, and nearly half reported feeling depressed. About 39% reported feeling numb, and 15% felt worthless. Regarding behavior, 71% of the nurses reported increased difficulty in sleeping in the previous 14 days, 45% reported that they were overeating, 29% reported an increase in alcohol consumption, 6% reported that they had increased suicidal thoughts and 2% reported increase in self-harm behavior... (Source: *Medpage Today*)

Excessive Screen Time Leads to Developmental Delays: Study

Excessive exposure to television or mobile phone screens for children less than 5 years old could have adverse effects on their development, suggested a study by Chennai-based researchers, published in *PLOS One*.

The researchers evaluated the performance of children and their understanding of commands from their mothers. It was found that children exposed to several hours of television or mobile phone screens were not able to comprehend what they were being told.

A total of 718 children, aged 6 months to 5 years, were included in the study. Around 70% of them had been exposed to excessive screen time, noted the researchers. Though the study was done in 2019, lead study author, Samya Varadarajan said that it could also apply to the current scenario, as children are forced to study through online classes during the pandemic... (Source: *The Hindu*)

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Post-COVID-19 Disease Associated with Mucormycosis and Guillain-Barré Syndrome: A Causal Association or Just a Coincidence?

SAHIL KHARBANDA*, BALDEV KUMAR MEENA†, ABHISHEK NYATI*, GURDEEP KAUR‡, DP SINGH#

ABSTRACT

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Originating from Wuhan, China, COVID-19 has rapidly spread worldwide. COVID-19 is primarily considered to be a respiratory illness, but with time there is enough evidence about the extrapulmonary manifestations of the disease. One of the neurological manifestations is Guillain-Barré syndrome (GBS). It may be associated with mucormycosis, with majority of cases occurring in India. Here, we report a case of a 40-year-old male patient, a known case of hypertension and diabetes mellitus who presented with the complaints of fever, cough and shortness of breath since May 10, 2021. He was found to be RT-PCR positive for COVID-19 on May 12, 2021. While recovering from COVID-19, on May 25, he was suspected to have rhino-orbital mucormycosis, which was confirmed on tissue specimen. While recovering from rhino-orbital mucormycosis, on July 26, the patient complained of weakness in bilateral lower limbs, followed by weakness in both upper limbs after 2 days. GBS was confirmed on nerve conduction study (NCS) and cerebrospinal fluid (CSF) examination. Patient was treated with intravenous immunoglobulin (IVIG), and while on treatment, the patient showed no significant improvement. Invasive ventilation was started in view of respiratory muscle involvement. The patient also developed autonomic dysfunction. He went into cardiac arrest and despite best efforts, couldn't be revived. Currently, to the best of our knowledge, there is no data to tell that both mucormycosis and GBS can occur in association with COVID-19. This case aims to raise awareness among the healthcare providers for this type of association. COVID-19 may be a cause or it may just be a mere coincidence, needs further study.

Keywords: COVID-19, mucormycosis, Guillain-Barré syndrome

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Originating from Wuhan, China, COVID-19 has rapidly spread worldwide. COVID-19 is primarily considered to be a respiratory illness, but with time there is enough evidence about the extrapulmonary manifestations of the disease, reports of which are increasing even today and is now considered to be a multisystem disorder. Extrapulmonary manifestations

are as follows: neurological- headache, encephalopathy, Guillain-Barré syndrome (GBS), ageusia, anosmia, stroke; hematological- deep vein thrombosis, pulmonary embolism; cardiovascular- cardiomyopathy, myocardial ischemia, acute cor pulmonale; endocrinological- hyperglycemia, diabetic ketoacidosis (DKA); dermatological- livedo reticularis, urticaria; gastrointestinal- anorexia, nausea and/or vomiting, diarrhea and abdominal pain; renal- acute kidney injury, proteinuria, hematuria; hepatic manifestation- elevated aminotransferases, elevated bilirubin.¹

As India continues to achieve stability over COVID-19, another imminent threat has emerged as a challenge to the country in the form of coronavirus disease-associated mucormycosis. Mucormycosis, caused by a group of molds called mucormycetes, is a rare but potentially fatal infection if inadequately treated. Commonly known as black fungus, the incidence of mucormycosis increased more rapidly during the second COVID wave compared to the first one in India.

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The most common causes reported to be accountable for the surge of mucormycosis in COVID-19 patients are likely to be uncontrolled diabetes, the rampant use of corticosteroids and longer stays in the intensive care unit (ICU). India contributed to more than two-thirds of the global cases of mucormycosis in patients with COVID-19.²

We report a case suffering from both GBS and mucormycosis associated with post-COVID-19. This case aims to raise awareness among healthcare providers for this type of association. To the best of our knowledge, this is one of the first cases of this association. COVID-19 may be a cause or it may be just an incidental finding.

CASE REPORT

A 40-year-old male patient, a known case of hypertension and diabetes mellitus, was admitted in some peripheral hospital with the complaints of fever, cough and shortness of breath since May 10, 2021. He was found to be reverse transcription-polymerase chain reaction (RT-PCR) positive for COVID-19 on May 12, 2021. The patient was suffering from moderate COVID-19 illness and DKA. He was given injection remdesivir and corticosteroids in that hospital. While recovering from COVID-19, on May 25, he complained of pain in teeth, facial swelling and headache. Contrast-enhanced computed tomography (CECT) paranasal sinuses (PNS)/orbit and brain was suggestive of left maxillary sinusitis with soft tissue thickening in the region of right lower buccal mucosa, likely due to fungal infection. Potassium hydroxide (KOH) mount from nasal secretions was negative for fungal hyphae. Punch biopsy was done from right lower buccal mucosa which was positive for fungal hyphae, suggestive of mucormycosis.

On June 8, the patient was brought to MBGH Hospital, Udaipur for further treatment of mucormycosis. Then, the patient was treated with injection liposomal amphotericin B. Magnetic resonance imaging (MRI) was done on June 10, which revealed invasive fungal sinusitis extending into right cheek, orbit and neck space (Figs. 1 and 2).

While recovering from rhino-orbital mucormycosis, on July 26, the patient complained of weakness in bilateral lower limbs, followed by both upper limbs after 2 days. Weakness was ascending and symmetrical in nature, not associated with bowel and bladder complaints.

On examination, deep tendon reflexes of both upper and lower limbs were absent and power was noted as 3/5 in all four limbs. Proprioception was abnormal; no cranial nerve involvement was seen at that time. Next day,

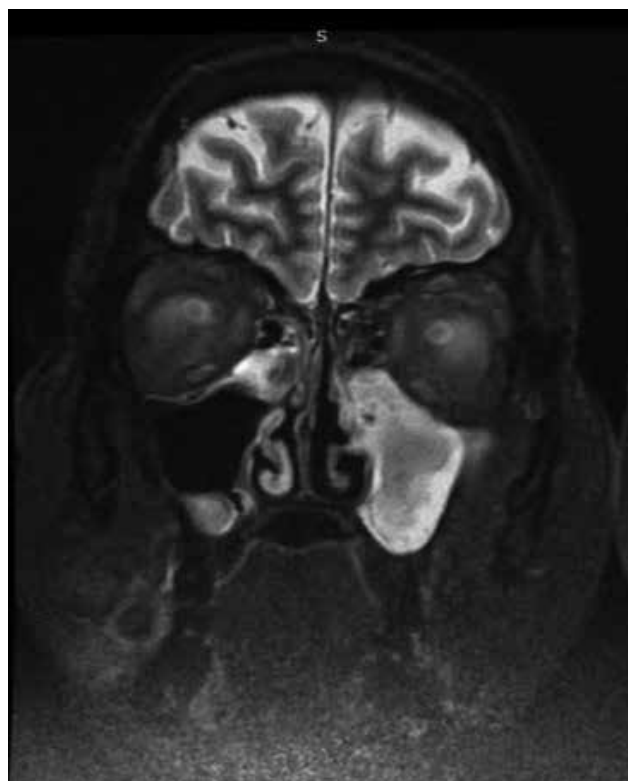


Figure 1. STIR-weighted coronal MRI image shows poly-poidal mucosal thickening in bilateral maxillary sinuses.

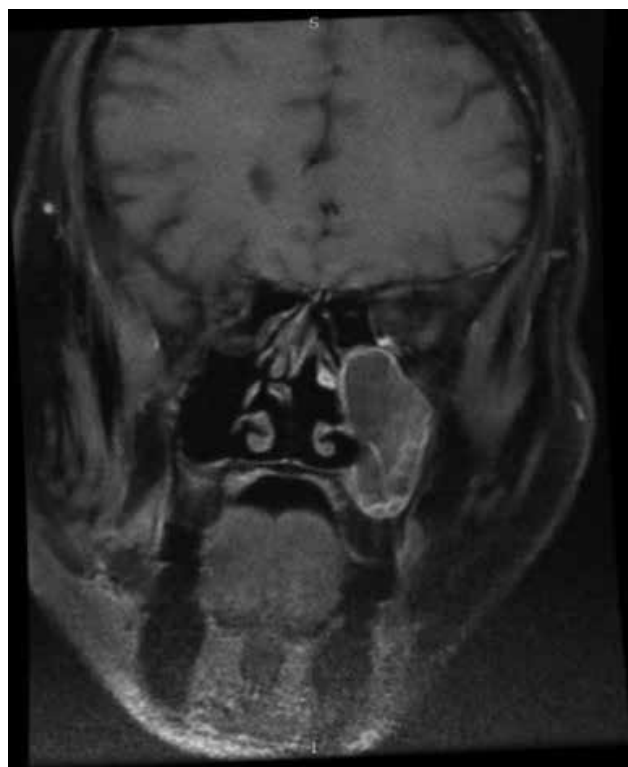


Figure 2. Post-contrast T1-weighted coronal MRI image shows heterogeneous post-contrast enhancement in the mucosa of bilateral maxillary sinuses.

CASE REPORT

the patient developed dysarthria and dysphagia and difficulty in opening mouth. On examination, bilateral facial nerve and right-sided 9th and 10th cranial nerve palsy was found. Electrolytes were within normal range. Clinically suspected to be a case of GBS, the patient was shifted to ICU. Nerve conduction study (NCS) revealed sensory motor severe axonal polyradiculoneuropathy. The patient was started on intravenous immunoglobulin (IVIG).

On investigation, serum electrolytes were: Na - 132 mEq/L, K - 3.8 mEq/L, Cl - 100 mEq/L. Other findings included: ESR - 53 mm/hr, Hb - 13.1 g/dL, TLC - 12.7 K/ μ L, platelets - 3.23 lakh/ μ L, N/L ratio - 12, D-dimer - 1026 ng/mL, ferritin - 1237 ng/mL, LDH - 447 units/L, urea - 42 mg/dL, creatinine - 2.0 mg/dL, CRP - 143 mg/L, HbA1c - 12.4%. Cerebrospinal fluid (CSF) examination was done on Day 6 of illness which showed albuminocytological dissociation with protein - 128 mg/dL, glucose - 85 mg/dL and no nucleated cells. Patient was human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), hepatitis C virus (HCV) negative. Thus, the diagnosis of acute motor sensory axonal neuropathy (AMSAN) variant of GBS was confirmed. IVIG was continued for 5 days with dose of 2 g/kg. While on treatment, patient showed no significant improvement. He developed respiratory muscle involvement, and was put on invasive mechanical ventilation. He also developed autonomic dysfunction. He went into cardiac arrest and couldn't be revived and was declared dead on August 1, 2021.

DISCUSSION

COVID-19 is predominantly a respiratory illness, but extrapulmonary manifestations are also seen in this disease. It may be associated with mucormycosis. Our patient first developed rhino-orbital mucormycosis and then developed extrapulmonary manifestation in the form of GBS.

In a study conducted by Singh et al,³ 101 cases of mucormycosis in COVID-19 patients were reported. Of these, 82 cases were from India and the remaining 19 from other parts of the world. Mucormycosis was more commonly seen in males (78.9%), both in individuals who were active (59.4%) or had recovered (40.6%) from COVID-19. Pre-existing diabetes was reported in 80% of cases, and concomitant DKA was evident in 14.9% cases. Corticosteroid intake for COVID-19 treatment was reported in 76.3% of cases. Mucormycosis involving nose and sinuses (88.9%) was most frequently seen, followed by rhino-orbital mucormycosis (56.7%). Mortality was noted in 30.7%. We also reported a male

Table 1. Brighton Criteria for Diagnosis of Guillain-Barré Syndrome

Level 1 of diagnostic certainty	Bilateral, flaccid limb weakness
	<i>plus</i>
	Reduced or absent deep tendon reflexes in weak limbs
	<i>plus</i>
	Monophasic illness with interval between onset and nadir of weakness of 12 hours to 28 days; subsequent clinical plateau
Level 2 of diagnostic certainty	<i>plus</i>
	Electrophysiological findings conforming with GBS
	<i>plus</i>
	Cytoalbuminologic dissociation (Raised CSF protein above laboratory normal value with CSF total white cell count <50 cells/ μ L)
	<i>plus</i>
Level 3 of diagnostic certainty	No detectable alternative diagnosis for weakness
	Bilateral, flaccid limb weakness
	<i>plus</i>
	Reduced or absent deep tendon reflexes in weak limbs
	<i>plus</i>
Level 3 of diagnostic certainty	Monophasic illness with interval between onset and nadir of weakness of 12 hours to 28 days; subsequent clinical plateau
	<i>plus</i>
	CSF total white cell count <50 cells/ μ L (with or without raised CSF protein above laboratory normal value)
	OR
	Electrophysiological studies conforming with GBS (If CSF not collected or results not available)
Level 3 of diagnostic certainty	<i>plus</i>
	No detectable alternative diagnosis for weakness
	Bilateral, flaccid limb weakness
	<i>plus</i>
	Reduced or absent deep tendon reflexes in weak limbs
Level 3 of diagnostic certainty	<i>plus</i>
	Monophasic illness with interval between onset and nadir of weakness of 12 hours to 28 days; subsequent clinical plateau
	<i>plus</i>
	No detectable alternative diagnosis for weakness

patient who was a known case of diabetes mellitus, and presented with DKA along with COVID-19 for which

corticosteroid treatment was given. He developed rhino-orbital mucormycosis while having active COVID-19.

The first case of COVID-19-associated GBS was reported from Wuhan, as a suspected parainfectious disease, where the patient developed symptoms of COVID-19 seven days after the onset of GBS symptoms.⁴ But, this was not seen in our patient as our patient presented with GBS as post-COVID complication, 2 months after COVID-19.

Diagnosis of GBS is based on Brighton criteria which was developed by Brighton collaboration in 2011 (Table 1).⁵ Our patient fulfilled Brighton's criteria with level 1 of diagnostic certainty.

GBS can be treated with IVIG (2 g/kg body weight divided in 5 daily doses) or plasmapheresis.

Mortality rate is <5% in optimal settings, prognosis is poor with advanced age, a fulminant or severe attack, delay in onset of treatment and if patient presents with AMSAN variant.⁶

Our patient was middle-aged, and was started on IVIG on Day 3 of onset of weakness and there was no undue delay in treatment. As the outcome of patient was death, severe attack of AMSAN variety with respiratory involvement and dysautonomia may be the cause of poor prognosis in the patient.

CONCLUSION

GBS and mucormycosis are likely to be complications of post-COVID-19. They should always be considered if a COVID-19 patient, during the infection or in recovery phase, develops progressive areflexic paralysis.

The patient should be diagnosed and treated as early as possible to reduce morbidity and mortality. Thus, our case report aims to raise awareness among healthcare providers for this type of association, i.e., possibility of GBS and mucormycosis both in association with COVID-19. In our knowledge, this is one of the first cases with this association. COVID-19 may be a cause or a mere coincidence, needs further study.

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Male Sex, Older Age Linked with Risk of Antibiotic Failure in Pneumonia

According to a secondary analysis of a randomized trial, two factors have been found to be associated with a greater risk for antibiotic failure in clinically stable patients hospitalized with community-acquired pneumonia (CAP). These factors include age and sex.

In around 300 CAP patients who were stable after 3 days of beta-lactam treatment, the rate of treatment failure was 26.8% at 15 days. Multivariable analysis after adjustment for Pneumonia Severity Index (PSI) scoring and baseline urea level revealed that male sex (odds ratio [OR] 1.92, 95% confidence interval [CI] 1.08-3.49) and age (OR 1.02 per year, 95% CI 1.00-1.05) were predictors of treatment failure, and were independent of duration of antibiotic therapy or biomarkers, such as CRP and procalcitonin. The results were published in *JAMA Network Open...* (Source: *Medpage Today*)

Modified Tinea – A Mithering Problem

RAJ KIRIT EP*, AS KUMAR†

ABSTRACT

Eberconazole has an anti-inflammatory effect and in our experience, also has a better role in managing steroid-modified and facial lesions. Eberconazole has a better role in clearance of the lesions. In these 5 cases of tinea infections, treatment with eberconazole helped in attaining favorable outcomes.

Keywords: Tinea, steroids, eberconazole

Tinea barbae and tinea incognito are increasingly becoming common due to the rampant misuse of steroid combinations. We herewith present 5 cases with history of using steroids on the affected areas.

CASE 1

A 45-year-old male patient presented with multiple follicular papules to pustules over the beard region (Fig. 1) and had been treated as folliculitis by a general practitioner and he had approached us after failure of therapy. The lesion was itchy. As the patient was a sales executive and had to meet people, he had to shave daily which became very difficult for him.

He was diagnosed as tinea barbae and was started on capsule itraconazole 100 mg twice daily for 1 week and also on topical eberconazole. He responded after 3 weeks of therapy and got excellent response. His lesions disappeared by the end of 1 month, had no relapse after stopping the therapy.

CASE 2

A 52-year-old male presented with boggy swelling on his moustache area (Fig. 2). He was prescribed a steroid combination of clobetasol, gentamicin and clotrimazole preparation by a general practitioner and had remissions on using these creams.

Scrapings for potassium hydroxide (KOH) mount demonstrated hyphae and we started him on

eberconazole. He responded at the end of 5th week. He had no relapse on follow-up until 4th month.

CASE 3

A 35-year-old male had come to the Dermatology Department with complaints of itching, and papules on the back since 5 months. He had been going to many general practitioners who have been prescribing steroid combinations.

On examination, he had papules with crusts and at the edges, had ill-defined margins and few areas of central clearing were visible (Fig. 3).



Figure 1. Multiple follicular papules to pustules over the beard region.

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A KOH mount was done which revealed hyphae. The patient was diagnosed with tinea corporis and prescribed tablet terbinafine 250 mg a day for 10 days and topical eberconazole.

He responded in 2 weeks and was asked to continue the topical therapy for 2 months for morphological clearance.

We did a repeat KOH mount and found no hyphae. Patient had no relapse after 6 months.



Figure 2. Boggy swelling over the moustache area.



Figure 3. Papules on the back.

CASE 4

A 19-year-old male, working in hotel industry, presented with itchy papules on the forearm. On initial examination, we presumed it to be polymorphous light eruption. But on closer inspection, we could elicit an ill-defined border over the wrist (Fig. 4).

On examination and probing the history, we found he had lesions all over the body for which he was applying “sapat malam”, a local quack preparation, and did not get any results.

He was started on tablet griseofulvin (as the patient could not afford) 250 mg every day for 2 months and eberconazole topically. He responded by the end of 3 months and had no relapse after 5 months.

CASE 5

A 27-year-old male working as a driver had presented with itchy, scaly and diffuse patches over the face. He was treated as allergic contact dermatitis with systemic steroids.

On examination, he had a well-defined erythematous border on the face extending to the ears and back of the ears. KOH revealed fungal hyphae.



Figure 4. Ill-defined border over the wrist.

CASE REPORT

He was started on tablet terbinafine and eberconazole topically which led to significant improvement in the lesions.

DISCUSSION

In all these 5 cases, we had started eberconazole topically. Though we had prescribed various oral antifungal therapies, we found local applications to augment the results for clinical clearance.

Eberconazole is a topical imidazole with a mode of action similar to that of other azole antifungals, which is, inhibition of fungal lanosterol 14 α -demethylase.^{1,2}

This drug is effective and has a good safety profile. The duration of therapy depends on the area involved.

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Valneva COVID-19 Vaccine Found Effective in Trial

The Valneva COVID-19 vaccine was found to work well at stimulating the immune system to fight the SARS-CoV-2 virus in a phase 3 trial.

Volunteers who received the vaccine were found to have high levels of neutralizing antibodies against the virus. The vaccine outperformed the AstraZeneca shot on this parameter in head-to-head studies. This is an inactivated whole virus vaccine.

Valneva stated that its vaccine had a neutralizing antibody seroconversion rate of over 95% and there were no severe cases of COVID-19 seen in the trial, in spite of variants like Delta being in circulation... (Source: BBC)

New Migraine Drugs Tied to Less Risk for Adverse Events

According to a new systematic review and meta-analysis, new classes of antimigraine drugs appear to be effective and have improved tolerability among patients with chronic migraine.

Investigators compared the outcomes for acute migraine management using lasmiditan (a 5-hydroxytryptamine [5HT]_{1F}-receptor agonist), and gepants - rimegepant and ubrogepant (calcitonin gene-related peptide [CGRP] antagonists) - with standard triptan (selective 5-HT_{1B/1D}-receptor agonist) treatment. The analysis included 64 double-blind randomized clinical trials with 46,442 patients.

Virtually all medications with extensive clinical use were linked with higher ORs for freedom from pain when compared with placebo. In comparison with ditan and gepants, triptans were linked with significantly higher ORs for pain freedom, with the OR ranges being 1.72-3.40 for lasmiditan, 1.58-3.13 for rimegepant and 1.54-3.05 for ubrogepant. In terms of pain relief at 2 hours, triptans were found to be tied to higher ORs in comparison with other drug classes. The paper is published online in *JAMA Network Open*... (Source: Medscape)

Dupilumab Linked to Improved Lung Function in Children with Asthma

Findings from a randomized study, presented at the CHEST conference, the annual meeting of the American College of Chest Physicians, revealed that children with uncontrolled, moderate-to-severe asthma had better lung function over the long-term when they received treatment with dupilumab.

In the study, use of add-on dupilumab in children ages 6 to 11 years appeared to improve forced expiratory volume in 1 second (FEV1) by a prebronchodilator average of 0.06 liters at week 2, compared to placebo ($p = 0.025$), and by an average of 0.17 liters at week 52 ($p < 0.0001$), noted researchers. There were similar benefits in post-bronchodilator FEV1 (mean difference of 0.09 liters at week 52, compared to placebo; $p = 0.015$).

Investigators, therefore, noted that dupilumab was associated with significant, rapid and persistent improvements in several aspects of lung function in kids 6 to 11 years of age... (Source: Medpage Today)



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Topical Eberconazole for the Treatment of Recalcitrant Tinea Cruris Morphologically Modified

AS KUMAR, RAJYALAXMI KONATHAN

Dermatophytosis is one of the commonest infections in India, with tinea corporis and tinea cruris accounting for a significant proportion of individuals.¹

Moreover, tinea imbricata, also known as Tokelau, is also a dermatophytic infection caused by *Trichophyton concentricum*.² Another clinical entity that falls under this category is tinea pseudoimbricata, having “ring-within-a-ring” appearance. It is named so for its resemblance with tinea imbricata.¹

This review highlights the case of a patient with tinea cruris along with tinea imbricata treated effectively with topical eberconazole cream and oral terbinafine.

CASE PRESENTATION

A middle-aged male presented with scaly lesions in the groin area associated with severe itching since the past 1 year.

History

He had consulted a general practitioner who advised a topical steroid with antifungal combination (beclo-methasone and clotrimazole) on and off along with oral fluconazole 150 mg weekly for 6 weeks.

As there was some improvement in the lesions, the patient discontinued the medicine for few months.

However, similar lesions reappeared in the groin area since the past 4 months and he was again started on combination of the above-mentioned medicines along with clotrimazole powder and oral terbinafine, but there was no response.

Examination

On examination, the lesions in the groin were scaly, annular with raised borders and had one more concentric raised erythematous lesion within the first one (Figs. 1 and 2).

Moreover, the patient had ichthyotic skin in other parts of the body. At some places, lesions were slightly ill-defined.

Sensation over the lesion was intact. General physical examination, vitals and systemic examination were normal.



Figure 1. Erythematous annular patch over inguinal region and thigh.



Figure 2. Lesion showing concentric circles one within the other.

Investigations

- Routine investigations were within normal limits.
- Scraping for potassium hydroxide (KOH) mount was positive for fungus.

Diagnosis

- The patient was diagnosed with tinea cruris along with tinea imbricata.

Management

After confirming the diagnosis, the patient was prescribed topical eberconazole cream 1% to be applied twice daily and oral terbinafine 500 mg/day for 2 weeks.

On follow-up visit after 2 weeks, significant clinical improvement was noticed and the therapy was well-tolerated.

Topical eberconazole was then continued for another 2 weeks, which led to complete resolution of the lesions.

DISCUSSION

Eberconazole, an imidazole derivative is a broad-spectrum antifungal agent. It causes structural and functional changes by preventing fungal growth via inhibition of ergosterol (a key component of the fungal cytoplasmic membrane) synthesis.

It acts by inhibiting lanosterol 14 α -demethylase enzyme which plays an important role in the formation of 14 α -methyl sterols, precursor of ergosterols.³

Evidence-based observations are available to suggest the efficacy of this agent against dermatophytic infections.

According to a phase II pilot study, use of eberconazole cream 1% in patients who had mycologically proven tinea corporis and tinea cruris was found to be effective in 87% patients who applied it once daily and in 93% patients who applied it twice daily.⁴

In addition, eberconazole possesses anti-inflammatory property that makes it different from other imidazoles and a drug of choice for treating inflamed dermatophytic infections.³

Furthermore, many studies have also shown promising outcomes of oral terbinafine in the treatment of dermatophytic infections such as tinea cruris.⁵

CONCLUSION

Fungal resistance because of topical steroid needs special measures like increase of dosage, combination of systemic antifungals or prolonged therapy. Resistance is dealt with topical and systemic therapy.

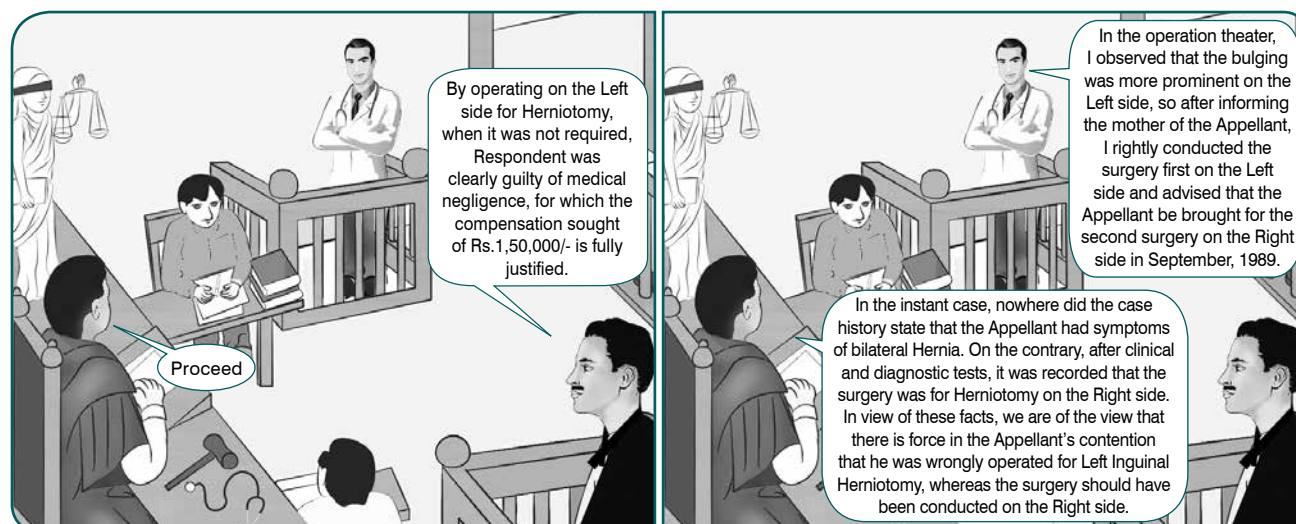
Two systemic antifungals with one topical fungistatic and fungicidal preparations are ideal for the present day of treating recalcitrant/resistant fungal infection. It has been observed that eberconazole displays high potential in the treatment of dermatophytosis. In this case, use of topical eberconazole was associated with favorable outcomes and successful management of the patient with tinea cruris along with tinea imbricata.

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Wrong Site Surgery: An Act of Gross Medical Negligence



Lesson: In the Case No. 494 of 2007, the National Consumer Disputes Redressal Commission (NCDRC), the Commission ruled in the favor of the Appellant holding the Respondent guilty of medical negligence since he had wrongly operated for Left Inguinal Herniotomy, whereas the surgery should have been conducted on the Right side and directed him to pay the Appellant Rs. 1,00,000/- as compensation for the unnecessary suffering and agony caused to him and to his family.

COURSE OF EVENTS

- Appellant, a 6-year-old boy was admitted to Respondent Hospital with complaint of temporary Inguinal Hernia (R) and after diagnostic tests, it was confirmed that he was suffering from Inguinal Hernia (R), and was thus advised surgery. He was taken up for surgery. However, instead of operating on the Right side, Appellant was operated for Left Inguinal Hernia and Herniotomy. This mistake was noted by the main doctor of the hospital.
- **26.08.1989:** The Appellant was discharged with advice to come back in September, 1989.
- **07.09.1989:** Appellant's father got him back to Respondent Hospital, when he was informed that an operation, Right Inguinal Herniotomy, is required.
- Appellant's father refused to get another surgery done and he was taken to Hospital B, where after a medical check-up he was informed by Dr A that Respondent had made a mistake in conducting the first surgery on the Left Inguinal Hernia.
- Being aggrieved by the medical negligence on the part of Respondent, Appellant filed a complaint before the State Commission and requested that Respondent be directed to pay him Rs. 1,50,000/- as compensation.
- Respondent on being served denied these allegations and stated that Hernia in children are often bilateral, as is in the instant case. Since, it is well-established that surgery cannot be done on both sides at the same time, Appellant's parents were informed that both sides would have to be operated through two separate surgeries, which they had agreed.
- At the operation theater, RW-2, the doctor conducting the surgery noted that the Left side scrotum was bulging more and, therefore, it was necessary to conduct an operation on the Left side first, about which the Appellant's mother, who was waiting outside the operation theater, was duly informed. The surgery was successfully conducted and after the wound was sutured on 26.08.1989. Appellant was discharged and was asked to

come back for the second surgery in September, 1989 during school vacations. In the meantime, Appellant was administered medicine and injection for the second surgery.

- However, when the Appellant was readmitted for repair of the Right side Herniotomy, his father for reasons best known to him got him discharged without waiting for the surgery. It was specifically denied that the Appellant's parents were informed that surgery was required only on the Right side. Thus, there was no medical negligence on the part of the Respondent.
- The State Commission after hearing the parties dismissed the complaint filed by the Appellant against the Respondent by stating as follows: *"The fact remained that the mother of the Complainant was aware of the operation of the Left side hernia as she had given consent for herniotomy which meant operation of both sides as explained by RW-2. Further, right through the treatment and surgery of the Complainant, only the mother of the Complainant was present and only on 08.09.1989, the father had as suggested in the cross-examination, had compulsorily asked for the discharge of the Complainant. This was with an intention to extort money from the opposite party. He had projected a false stand as if he was present throughout from the beginning till the complainant was discharged. RW-2 had also in her evidence clearly stated that in children, the swelling would appear and disappear and that was the reason why while operating a child for hernia, the consent was got only for herniotomy, which related to both sides of the scrotum. The opposite party had taken due care in the discharge of their duties and there was no negligence whatsoever in operating the complainant. As a competent surgeon, RW-2 had taken the necessary care and caution so that the child's life could be saved. The Complainant's father had also stated that he had consulted one Dr A. But, no evidence was produced to show that any other doctor had been consulted. There was also no proof produced by the Complainant with regard to the expenses incurred."*
- The State Commission also cited medical literature entitled "The Surgical Clinics of North America" [Vol. 65/Number 5, October 1985], confirming that Hernias in children are often bilateral but both may not always be diagnosed during a medical examination and further that Inguinal Herniotomy also has a silent side, which may not always be apparent on sight.
- Being aggrieved by the dismissal of his complaint, Appellant has filed the present first appeal.

ALLEGATION OF THE APPELLANT

- Learned Counsel for the Appellant stated that the State Commission erred in not taking cognizance of the medical records pertaining to the Appellant's case history in Respondent Hospital, which was in evidence before it.
- As per these records, a clear diagnosis of obstructed Inguinal Hernia on the Right side was made, which was also recorded. This diagnosis was again confirmed in the detailed case history recorded on 13.08.1989.
- On 25.08.1989 when the Appellant was admitted for surgery, it was again clearly noted that he was "Posted for (R) Herniotomy on 25.08.1989". However, it was only on 26.08.1989 i.e., just prior to the surgery that it was noted in the case sheet that Appellant had Left Inguinal Hernia, which required to be operated.
- Counsel for the Appellant stated that Respondent's contention that the Hernia was bilateral and that before the surgery, the Appellant's mother was informed that the surgery would be first done on the Left side, is not factually correct because nowhere does the diagnosis in the case history indicate that the Appellant was suffering from bilateral Inguinal Hernia.
- By operating on the Left side for Herniotomy, when it was not required, Respondent was clearly guilty of medical negligence, for which the compensation sought of Rs. 1,50,000/- is fully justified.

REJOINDER OF THE RESPONDENT

- Learned Counsel for Respondent stated that the State Commission had rightly relied upon the medical literature as also the evidence on record to conclude that there was no medical negligence. It was clear from the record that the Appellant was suffering from bilateral Herniotomy, i.e., both on the Right and Left sides, which is a common phenomenon in children, and in the operation theater when a well-qualified pediatric doctor observed that the bulging was more prominent on the Left side, after informing the mother of the Appellant, she rightly conducted the surgery first on the Left side and advised that the Appellant be brought for the second surgery on the Right side in September, 1989. This is evident from the consent letter signed by Appellant's parents as also the case history recorded on 07.09.1989.

OBSERVATIONS OF THE NCDRC

- It was noted from the recorded case history of the Appellant, that right from the time when he was brought to the hospital, i.e., on 12.08.1989, he was subjected to a number of diagnostic and clinical tests and on the basis of these tests, a clear cut diagnosis of obstructed Inguinal Herniotomy (R) was made. These findings were confirmed on 13.08.1989 following a physical examination when it was specifically noted that the Appellant was a known case of Inguinal Hernia (R) and there was no other complaint. This diagnosis was confirmed at the time of his admission for the required surgery on 24.08.1989 and again on 25.08.1989, when it was stated that the Appellant was posted for (R) Herniotomy.
- It was only on 26.08.1989 at the time of the operation that for the first time it was stated that this was a case of Left Inguinal Herniotomy. The consent letter signed by the Appellant's parents (since he was a minor) only states that the Appellant's mother had given permission for operation of Herniotomy. No mention is made about bilateral Herniotomy.
- Respondent has not been able to produce any evidence that Appellant's parents were informed that Appellant was suffering with bilateral Herniotomy or that just prior to the surgery they were informed that the surgery would be conducted on the Left side and not on the Right side.
- The letter dated 07.09.1989 only states that the Appellant is posted tentatively for Right Herniotomy, which does not help the Respondent and only proves the Appellant's contention that a surgery on the wrong side was carried out on 26.08.1989.
- In view of the overwhelming documentary evidence from Respondent's own hospital discussed in the foregoing paras, we are unable to agree with the finding of the State Commission that as per the evidence on record there was no medical negligence in the treatment of the Appellant. Clearly, Appellant was diagnosed for conducting a surgery for Right Inguinal Hernia, whereas without any evidence that it was the Left side which required the surgery, this surgery was conducted. Had the Respondent advised the Appellant's parents during their visit

to the hospital that the Appellant had bilateral Hernia, then perhaps there would be some case for the Respondent to explain how the surgery was conducted on the Left side. In the instant case, nowhere did the case history state that the Appellant had symptoms of bilateral Hernia. On the contrary, as stated above, after clinical and diagnostic tests, it was recorded that the surgery was for Herniotomy on the Right side. In view of these facts, we are of the view that there is force in the Appellant's contention that he was wrongly operated for Left Inguinal Hernia, whereas the surgery should have been conducted on the Right side.

- What constitutes medical negligence is now well-settled through a number of judgments of this Commission as also of the Hon'ble Supreme Court of India. One of the principles to test medical negligence is whether a doctor exercised a reasonable degree of care and caution in treating a patient [Supreme Court Case Indian Medical Association v. V.P. Shantha (1995) 6 SCC 651 and this Commission case Tarun Thakore v. Dr Noshir M. Shroff (OP No. 215 of 2000)].

ORDER OF NCDRC

- In the instant case, the facts clearly indicate that the required reasonable degree of care and caution was not taken by Respondent in the treatment of the Appellant and, thus, Respondent was guilty of medical negligence, for which the Appellant should justifiably be compensated.
- In view of these facts and respectfully following the judgment of the Hon'ble Supreme Court cited above, we are unable to uphold the order of the State Commission and set aside the same. Respondent being guilty of medical negligence is directed to pay the Appellant Rs. 1,00,000/- as compensation for the unnecessary suffering and agony caused to him and to his family within 2 months from the date of this order.
- The present appeal stands disposed of on the above terms. No costs.

REFERENCE

1. NCDRC First Appeal No. 494 of 2007; Order dated 31.01.2013.

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HCFI Dr KK Aggarwal Research Fund

HCFI Dr KK Aggarwal Research Fund Expert Round Table Meeting on “Health Effects of Environmental Noise Pollution”

2nd October, 2021 (11 am-12 noon)

Key points

- Noise pollution is considered to be any unwanted or disturbing sound that affects the health and well-being of humans and other organisms.
- Exposure to prolonged and excessive noise has been shown to cause a range of health problems such as stress, poor concentration, hearing problem, fatigue, etc.
- We do not know the level at which we should listen to music on our phones.
- Noise is a slow poison going into our body through the auditory route.
- We are surrounded by work environment noise. Some households may be noisy.
- Noise stimulating inner ear has auditory and nonauditory effects.
- Chronic auditory trauma is due to long-term exposure to noise; the upper limit in India is 90 dB. Globally, this has been reduced to 85 and also 80 in some countries.
- Noise-induced hearing loss is a proven fact, which is seen as typical dip at 4000 Hz on audiometry.
- Noise trauma affects every system of the body. It can precipitate hypertension, myocardial infarction, bronchial asthma, hyperacidity, tinnitus, increases anxiety, which directly or indirectly affects the body system. Noise pollution has even been reported to cause premature delivery. It affects the development of children. Noise leads to fatigue and industrial accidents.
- Presbycusis is aging deafness; in India, this is occurring at an earlier age (55 years vs. 70 years globally) due to cumulative effects of continuous exposure to noise and the freedom to take any medicine at any time, even without doctor's prescription, such as aspirin, antimalarials, antibiotics, especially aminoglycosides, which may be ototoxic.
- More than 100 years ago, Nobel Prize winner Bacteriologist Robert Koch had predicted that “one day mankind will have to fight the burden of noise as fiercely as plague and cholera.”
- October is noise pollution month. World Hearing Day is observed every year on 3rd March.
- Four different sources of noise: industries, traffic noise, construction noise and community noise.
- About 20% of industrial workers exposed to high noise levels develop hearing loss.
- The permissible occupational noise exposure limit is 90 dB for all workers for 8 hours.
- One can listen to 150 dB of noise for 15 minutes daily for 6 to 7 years.
- Noise pollution is also affecting the behaviors of birds and animals. They have started communicating in non-peak hours.
- Auditory toughening - when exposed to noise, the temporary threshold shift reduces; it may recover.
- Temporary threshold shift occurs after 2 minutes during hearing tests. In susceptible persons, this shift is more, while in persons with normal hearing, this shift is less.
- For hearing conservation, pre-placement audiogram should be made compulsory in all noisy industries; noisy machinery gadgets should be identified. Gadgets should come with a statutory warning and must be accompanied with head phones, ear muffs. For crackers, upper limit should be 150 dB.
- Noisy areas should have plenty of trees.
- Cattle have a different sensitivity level.
- Many bus drivers have hearing loss. Rear engine buses may protect the drivers from heat and the noise.
- According to the World Health Organization (WHO), 1.1 billion young adults are likely to be exposed to dangerous levels of noise.
- Orthopedic surgeons and plastic surgeons can also face effects of vibrations in instruments, which leads to Dupuytren's contracture. These vibrations can also be transmitted to the ears.
- Diesel vehicles produce more vibrations than petrol vehicles.

- Citizens should be educated about the hazards of noise pollution and its harmful effects on health. Doctors should carry this message to their patients. Hearing is health.
- Noise dose meters are available in India, which give the average noise levels the person is exposed to. There are apps (NIDCD website) to measure noise.
- <https://ngms.delhi.gov.in/> is the noise pollution grievance redressal and monitoring website of Delhi government. A complaint can be lodged here. The Helpline Number is 155271.
- A complete ban on crackers has been imposed in Delhi since 28th September, which will remain in effect up to 1st January, 2022.
- The dangers of recreational noise should be imparted as part of curricula at the school level itself.
- Hearing aids should be made available at a lower cost.
- The 7 Rs of circular economy are Rethink, Reduce, Reuse, Repair, Refurbish, Recover and Recycle. These are the backbone to minimize waste and get wealth from waste. Waste is a misnomer. It is wealth and is full of recoverable resources. This fact is not recognized much. Waste is not waste for the ecosystem.
- There are several different types of waste: e-waste, biomedical waste, solid waste, household waste, etc. Waste can lead to air and water pollution.
- Most of the waste is handled by the unorganized sector, so its exact amount/quantity, including the quantum of people involved, is not known. Waste circular economy has been recognized in the last decade to bring waste into the mainstream economy.
- Resource exploitation increases pollution and waste generation. Optimum levels need to be judged carefully and cautious and conscious decision needs to be taken.

Speakers: Prof AK Aggarwal and Prof Rangasayee R

Participants: Dr AK Agarwal, Dr Rangasayee R, Dr Arun Jamkar, Dr Ashok Gupta, Prof Bejon Misra, Dr DR Rai, Dr KK Kalra, Dr Anil Kumar, Ms Balbir Verma, Mrs Upasana Arora, Ms Ira Gupta, Mr Saurabh Aggarwal, Dr S Sharma

Prof AK Aggarwal, President - Sound Hearing 2030, Medical Advisor - Innovation, Education and Clinical Excellence, Apollo Hospitals, Ex-Dean, Professor of Excellence Department of ENT, MAMC, Ex-President - DMC, Ex-Additional DGHS

Prof Rangasayee R, Chairman of the Audiology Committee of International Association of Communication Sciences and Disorders (Malta), Technical Director and Professor at Dr S R Chandrasekhar Institute of Speech and Hearing, Bangalore, Ex-Director and Prof Ali Yavar Jung National Institute for the Hearing Handicapped (AYJNIHH)

Round Table - Expert Group on Environment Meeting on "Circular Economy – Its Importance and Actions Needed in Present Scenario-General"

29th August and 5th September, 2021 (12 noon-1 pm)

Key points

- Circular economy is emerging as an economic model for its environment and economic benefits.
- Benefits of circular economy include reducing pressure on the environment, improving security of supply of raw material, increasing competitiveness, stimulating innovation, boosting economic growth and job creation.
- Careful integrated planning can result in resource recovery, conservation of resources and can lead to sustainable development, which is the need of the hour.
- Circular economy is more focused towards five Sustainable Development Goals (SDGs): SDG 6 (Clean water and sanitation for all), SDG 8 (Promote inclusive and sustainable economic growth, employment and decent work for all), SDG 11 (Make cities and human settlements inclusive, safe, resilient and sustainable), SDG 12 (Responsible consumption and production), and SDG 13 (Take urgent action to combat climate change and its impacts).
- Half a trillion dollar worth of economic value can be unlocked through circular economy business models in India by 2030 (FICCI).
- Examples of circular economy include use of sugar industry waste in paper industry, conversion of biodegradable wastes into manure/biogas, etc. Valuable resource and material can be recovered from all waste products if approached in a scientific manner.
- Four processes are very important for circular economy: Circular supply chain (provide renewable energy or fully recyclable input materials in place of single life-cycle inputs), recovery and recycling, product life extension (by repairing, upgrading and reselling) and sharing platform.

- In linear economy, a product reaches end of life and ultimately becomes waste. Whereas, a circular value chain operates by employing reuse, sharing, repair, refurbishment, remanufacturing and recycling to create a closed-loop system and minimizing waste generation and pollution.
- There is no consensus yet on a set of central circular economy performance indicators applicable to organizations and individual products.
- More than 8 million tonnes of steel can be extracted from different categories of end-of-life vehicles in 2025, which represents a 2.7-billion dollar opportunity.
- Household gadgets also have a huge potential for extraction of metals. Gold can be extracted from electronic waste. This is called urban mining from e-waste. There is ~\$1 billion of value that can be realized from the extraction of gold from e-waste in India.
- There is significant value realization potential from plastic dumped in landfills. Around 40% of plastic waste in India remains uncollected for recycling. If properly managed, this can create around 14 lakhs jobs and could potentially represent a \$2 billion opportunity.
- Three sectors have been identified: National initiative to set up a conducive ecosystem, material level and sector level action plan and proof of concepts, pilots and scale up. Many more sectoral action plans will come up for different sectors, including state level action plans.
- A vehicle scrapping policy was launched by the Hon'ble Prime Minister of India in August this year to phase out unfit and polluting vehicles in an environment-friendly manner.
- Implementation is the problem; it requires collective effort from all stakeholders and not just from the governments or the regulatory authorities.
- The way forward is optimization in thinking, planning and policy as 5Ps play a major role: People, Policy, Planning, Population and Politics.
- There should be mechanisms in place to account for environmental damage, control of emissions and sustainable management of waste in imports and exports. International cooperation is required for transfer for low-cost technology.
- NITI Aayog has 11 focus areas on circular economy and committees have been formed for these areas.

- A simple lifestyle itself caters to circular economy as we do not have a use and throw culture in India. There is a need to create public awareness and motivate them.

Participants: Dr Anil Kumar, Mr Vivek Kumar, Dr SK Gupta, Dr Dipankar Saha, Mr Pradeep Khandelwal, Dr Dwaraka Nath, Mr Neeraj Tyagi, Mr Ankit Sethi, Mr Ashish Jain, Dr Ravindra Kumar, Mr Vikas Singhal, Mr Virendar Gupta, Mr Varun Singhal, Ms Ira Gupta, Dr S Sharma

HCFI Expert Round Table Meeting on “Hematological Changes in Prevalent Viral Fevers”

9th October, 2021 (11 am-12 noon)

Key points

- Platelets are vital from diagnosis, prognosis and monitoring point of view.
- Hematological changes are good navigational tools to diagnose viral infections.
- Hematology is now restricted to cell counters and flow cytometers. Cell counters are 3-part differential cell counters, 5-part differential cell counters and 7-part differential cell counters. The latest 7-part differential cell counters use laser technology.
- Electronic cell counters are rapid and shorten the time of tests and complete a large number of tests quickly. They also reduce the cost of test, and maintain and improve the accuracy of tests.
- About 33 parameters of complete blood count or CBC (red blood cell [RBC], white blood cell [WBC] and platelet parameters) can be generated with the most sophisticated counters.
- CBC is the most frequently done, easily available, and the most informative investigation.
- Accurate interpretation of CBC can avoid costly and invasive investigations.
- Daily monitoring of automated data must be manually validated. A peripheral smear crosscheck is always warranted when reporting.
- Transfusions of all blood products warrant rational use with the help of newer parameters.
- The immature platelet fraction (IPF) or reticulated platelets is a newer platelet parameter. It contains RNA and can be detected using nucleic acid dyes like new methylene blue. They are the larger strong-staining subset and are typically expressed as a percent of total platelets.

- IPF differentiates between consumptive versus productive reasons for thrombocytopenia. IPF increases in consumptive reasons but not in the latter. This parameter is increased in the setting of platelet destruction or consumption and decreased with bone marrow failure. IPF decides the status of the marrow, whether it is functioning/responding or not. High IPF means that the marrow is responding and in such a situation, one need not panic even if there is thrombocytopenia. In dengue, platelet transfusion is not needed even if platelet count is 10,000. If IPF is low, this means that the bone marrow is not working.
- IPF can better differentiate between the causes of thrombocytopenia. It is a reliable parameter even with very low platelet counts and is valuable for effective risk assessment and therapy monitoring of coronary artery disease (CAD).
- Another new parameter is the platelet-large cell ratio (P-LCR) is indicator of larger (>12 fL) circulating platelets (mega platelets, which have very good hemostatic activity). The normal size of platelets is 7.2-11.7 fL. Their normal percentage range is 15% to 35%. It increases in destructive thrombocytopenia in severe sepsis. P-LCR is inversely related to platelet count and directly related to platelet volume distribution width (PDW) and mean platelet volume (MPV).
- An old but ignored parameter is MPV. The normal MPV ranges from 7.2 to 11.7 fL. When platelet production is increased, young platelets become bigger and more active and MPV levels increase. Increase in MPV during platelet activation is due to change in shape of platelets from biconcave discs to spherical and formation of a pseudopod.
- IPF, P-LCR and MPV must be considered along with platelet count in the clinical condition of the patient to decide if platelet transfusion should be given or not.
- In viral diseases, there will be changes in the WBCs, platelets, RBCs and coagulation and fibrinolytic systems. COVID patients have local or systemic coagulation, as was revealed in few autopsies. Changes in the procoagulant and anticoagulant mechanisms may be caused by the virus.
- RBCs are destroyed by the direct attack of the virus on the heme and similarity of spike protein of the virus and hepcidin which dysregulates the iron metabolism leading to reduction of hemoglobin or hemoglobinopathy.
- WBCs are destroyed due to the direct effect on bone marrow, sepsis, direct effect of the virus on angiotensin-converting enzyme 2 (ACE2) of lymphocytes, virus attack on lymph organs, metabolic products such as lactic acid. These mechanisms cause reduction in total leukocyte count (TLC), apoptosis of lymphocytes.
- Several mechanisms have been postulated for altered coagulation: antiviral anti-inflammatory response, injury due to neutrophil extracellular traps (NETs) and activation of different complement pathways. D-dimer is elevated, as is the prothrombin time.
- There is a definite impact of viruses on thrombocytes.
- Platelets are now regarded as part of the immune system in addition to being capable of forming blood clots.
- Except for viral hemorrhagic fevers and rarely, severe disseminated viral infections, virus-induced thrombocytopenia does not lead to significant bleeding and requires judicious platelet transfusions.
- In viral infections, platelets are reduced because of the direct effect on the bone marrow, immune damage (cytokine storm) and thrombosis (endothelium damage), resulting in decrease in platelet production and increase in platelet consumption (consumptive coagulopathy), leading to low circulating platelets.
- The early nonspecific immune responses limit multiplication of the virus during the acute phase of the infection. The later specific humoral immune responses help eliminate the virus at the end of the acute phase and subsequently to maintain specific resistance to reinfection.
- Platelets influence the innate immune response through regulation of both the maturation and activation of such innate immune cells as macrophages, neutrophils and dendritic cells.
- Almost every viral disease causes thrombocytopenia. The most frequently associated with thrombocytopenia are dengue, measles, chicken pox, Epstein-Barr virus, mumps and rubella. Herpes simplex, hepatitis B, human T-lymphotropic virus type III (HTLV III), and COVID-19 may also cause thrombocytopenia.
- Platelets play a major role in fighting against pathogens, including viruses, in addition to their hemostatic function. The interaction between the virus and platelets through their receptors activates the platelets.

- Viruses cause a decrease in platelet production by infection of megakaryocytes leading to their apoptosis, decreased maturation and ploidy of megakaryocytes or decreased expression of thrombopoietin receptor. The systemic inflammatory response due to viral infection leads to platelet activation. Also, platelets bind to neutrophils forming platelet-neutrophil aggregates, which in turn trigger the phagocytosis of platelets.
- Various mechanisms that contribute to thrombocytopenia in viral infections include aggregation, impaired hemostasis, sequestration and intravascular destruction, platelet expression of pattern recognition receptors (PRR), platelets can induce inflammation and secrete antimicrobial proteins and act as antigen presenting cells.
- Sequestration and intravascular destruction are the primary mechanisms, which leads to correction of thrombocytopenia with the use of low-dose steroids in post viral cases.
- Platelet expression of PRRs is the mechanism which justifies the use of steroids in low platelet counts following viral infection as autoimmunity is suppressed.
- It is important to know the technical points as proper management can only be defined when one knows the why of it. Knowing the how and why of thrombocytopenia helps to draft a proper management plan.
- Isolated platelet transfusions do help in acute crisis management but correcting the underlying cause helps in the long-term management of the situation.
- Hematological analysis is the most easily accessible and helpful tool in assisting the diagnosis of COVID-19. Computed tomography (CT) scan and molecular diagnosis are expensive.
- In COVID-19, CBC is the primary method to screen suspected COVID-19. TLC can be normal or decreased in the early stages of infection; lymphocytopenia and eosinopenia are often seen; increased C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR); D-dimer is increased in severely ill patients; alteration of T-cell subpopulation can also be observed with CD4+ reduction.
- CRP increases within 4 to 6 hours of inflammation; the level doubles every 8 hours and peaks at 36 to 50 hours, which is 100% to 1000% higher than the normal value.
- CRP level and duration is proportional to the severity of infection. Most studies have shown that CRP was markedly raised in all patients, especially in the severe and critically ill patients.
- There are morphological changes in neutrophils; apoptotic and immature granulocytes are seen in PS. Cytokine storm and hyperinflammation are implicated as the possible factors causing these changes.
- Neutrophil-to-lymphocyte ratio (NLR) is a new prognostic indicator. It is an easy-to-use parameter. The cut-off value of NLR is 3.13 (sensitivity 0.875 and specificity 0.717). If NLR is >3.13 and age is >50 years, the patient should be transferred to intensive care unit (ICU).
- NLR is a useful parameter for prognostic evaluation and risk stratification of COVID-19 patients. It predicts severe illness in COVID-19 patients in the early stage.
- An elevated platelet-to-lymphocyte ratio (PLR) may be a prognostic marker in COVID-19. The cut-off value is 180. It is elevated in severe compared to nonsevere COVID-19 patients.
- Presence of widespread microvascular thrombi in both pulmonary and extrapulmonary vessels indicates a systemic prothrombotic state.
- A low to low-normal platelet count is present during peak symptomatic illness, with increased MPV and PDW.
- Desensitization of bone marrow is also a mechanism for thrombocytopenia in COVID-19.
- Platelet-monocyte complexes are formed in severe COVID-19.
- Hematology analysis is helpful in guiding COVID-19 treatment. Along with NLR and CRP, it is of significant clinical value in evaluating disease outcome.
- The requirement of transfusions is low in COVID-19 patients, including in severe cases.
- The hematological parameter of utmost importance in dengue is platelet count. Decrease in platelet count and rise in hematocrit are predictive and recovery parameters of dengue hemorrhagic fever/dengue shock syndrome (DHF/DSS).
- CBC in dengue shows high hemoglobin and hematocrit from D3-D10 (highest on D7) due to plasma leakage, lower WBC on D2-D10 (lowest on D4) and lower platelet count D3-D10 (lowest on D6).

High monocytes on D1-4 (highest on D2), which can be used to predict severity of dengue infection.

- High atypical lymphocytes between D5 and D9 (highest on D7); predict severity of dengue infection – high in DHF than in dengue fever.
- High eosinophils on D9-D10 (highest on D9).
- NLR is >1 during the first 5 days of the infection and then is reversed on D6-D9.
- Thrombocytopenia and platelet dysfunction go hand in hand during dengue infection.
- Leukopenia in dengue may be due to virus-induced destruction or inhibition of myeloid progenitor cells.
- Thrombocytopenia results from destruction of peripheral platelets and bone marrow megakaryocytes by viruses, which consequently reduce the platelet production.
- Influenza infection is associated with thrombocytopenia which depends on severity of infection. In adults, severe influenza is accompanied by an increased risk of pulmonary thromboembolism and cardiovascular events suggesting that platelet activation occurs during infection.

Excerpts from a presentation “Hematological Changes in prevalent viral fevers” by Prof Dr DP Lokwani, Founder Vice Chancellor - MP Medical Sciences University, Consultant Pathologist - Jabalpur Hospital & Research Center, Ex-Prof and Head - NSCB Medical College Jabalpur, MP

Participants: Dr Ashok Gupta, Dr DP Lokwani, Dr KK Kalra, Dr Suneela Garg, Dr Arun Jamkar, Dr B Kapoor, Ms Ira Gupta, Mr Saurabh Aggarwal, Dr S Sharma

Coronavirus Updates

WHO clinical case definition of post-COVID-19 condition

The WHO has developed the first version of a clinical case definition of post-COVID-19 condition as follows: “Post-COVID-19 condition occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others which generally have an impact on everyday functioning. Symptoms may be

new onset, following initial recovery from an acute COVID-19 episode, or persist from the initial illness. Symptoms may also fluctuate or relapse over time. A separate definition may be applicable for children.” This definition may change as new evidence emerges, says the WHO... (Source: WHO)

Increase in antithyroid antibody titers with interferon treatment for COVID-19

A new study from Hong Kong presented at the virtual 90th Annual Meeting of the American Thyroid Association (ATA) has suggested that even short-term treatment of COVID-19 patients (no known history of previous thyroid disorders) with interferon beta-1b is associated with potentially important adverse effects on thyroid function. A significant rise in antithyroid antibodies including antithyroglobulin (anti-Tg) and antithyroid peroxidase (anti-TPO) was seen at 3 months compared to patients not treated with interferon ... (Source: Medscape)

Orphaned children, the hidden US COVID-19 pandemic

One US child loses a parent or caregiver for every four COVID-19-associated deaths, a new modeling study published in *Pediatrics* reveals. The findings illustrate orphanhood as a hidden and ongoing secondary tragedy caused by the COVID-19 pandemic and emphasize that identifying and caring for these children throughout their development is a necessary and urgent part of the pandemic response – both for as long as the pandemic continues, as well as in the post-pandemic era. From April 1, 2020 through June 30, 2021, data suggest that more than 1,40,000 children under age 18 in the United States lost a parent, custodial grandparent, or grandparent caregiver who provided the child’s home and basic needs, which include love, security, and daily care... (CDC)

Myocarditis and mRNA COVID-19 vaccines

In a large study from Israel of patients in an Israeli healthcare system who had received at least one dose of the BNT162b2 mRNA vaccine, the estimated incidence of myocarditis was 2.13 cases per 1,00,000 persons; the highest incidence was among male patients between the ages of 16 and 29 years. Most cases of myocarditis were of mild or moderate severity... (Source: NEJM)

With inputs from Dr Monica Vasudev

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79th AIOC 2021: All India Ophthalmological Society

APPLANATION TONOMETRY – TIPS & PEARLS

Dr Manav Deep Singh, New Delhi

- Be aware of sources of error and limitations of each device.
- Goldmann applanation tonometry (GAT) is the gold standard for intraocular pressure (IOP) measurement; however, central corneal thickness (CCT) measurement with necessary estimation of corrected IOP forms the standard care.
- Even this gold standard equipment has sources of error which needs to be addressed in individual cases and so is the case with other tonometers.
- Tonopen gives higher than GAT readings at <10 mmHg and lower readings at IOP >21. It is useful for screening and is not recommended for glaucoma evaluation.
- Noncontact tonometer readings correspond to GAT measurements only in normal range of CCT – reads lower in low IOP and higher in high IOP. Pachymetry is must for accurate assessment.
- Dynamic contour tonometer is useful after keratorefractive surgery and is more accurate than GAT in thin corneas.
- Factors affecting IOP measurement: Inter-/intraobserver factors, adequacy of tear film fluorescence, width of mires, CCT, corneal curvature and effect of biomechanical properties.

RCOPHTH EXAMINATIONS

Fiona Spencer, Chair of Training RCOPhtH

- During COVID, examination venues were closed or restricted with lockdowns affecting both examiners and candidates. Use of masks may possibly lead to communication issues; F2F was considered as potentially unsafe exposure; social distancing was enforced; and real patients were not able to be used.
- RCOPhtH redeveloped exams to run during COVID-19.
- The Part 1 and 2 FRCOPhtH written exams (MCQs) were moved to online proctored delivery in October 2020 with one proctor to 6 candidates. Candidates take exams at home and are watched live by a proctor through a webcam. Part 1 exam has been

conducted thrice with very successful online delivery. There has been an exponential increase in the number of global candidates since the move to online exams.

- For the refraction certificate, retinoscopy Objective Structured Clinical Examination (OSCE) simulators are used, no real patients used; the exam is heavily retinoscopy based. Changes are approved by the General Medical Council (GMC). More candidates can be examined at each exam. This new format has run successfully in December 2020 and May 2021.
- For Part 2 Oral, clinical OSCEs are replaced by clinical videos prepared, filmed and edited from host center patients; the structured viva and communications OSCE components remain unchanged. Temporary GMC approved.
- Strict COVID-19 protocols in place (distancing, sanitization, temperature checks, etc.).
- The benefits of simulation are significant but not total.
- Take the best of both worlds to create a hybrid combination.

REMOTE ASSESSMENTS AND EXAMINATIONS

Fiona Spencer, Chair of Training RCOPhtH

- For training with COVID, think about how we supervise, make the most of opportunities, develop new ways of trainees to learn and consider making remote assessments meaningful.
- The objectives of good supervision are normative (provides high quality care), formative (good supervision, excellent timely feedback) and restorative (enhances well-being of the supervisee).
- Consultations during COVID-19 are different: Remote consultations, video (attend anywhere), telephone, remote review of tests.
- Virtual assessments to review understanding and interpretation of results, decision-making, follow-up and future planning and communication to the patient.
- Educational supervisors must adapt to remote appraisal on Zoom/Teams, undertake regular contact and updates on mutually agreed times,

be supportive, discuss well-being, review generic professional capabilities, encourage training to plan how to take advantage of opportunities.

DISC EVALUATION – THE KEY SIGNS TO LOOK FOR

Dr Chandrima Paul, West Bengal

- Glaucoma is largely undiagnosed (90%).
- Missed diagnosis is common (50%).
- Pay attention to individuals at high-risk.
- The five R's for assessment of the optic disc in glaucoma: Observe the sclera **R**ing to identify the limits of the optic disc and its size, identify the size of the **R**im, examine the **R**etinal nerve fiber layers, examine the **R**egion of parapapillary atrophy, look for **R**etinal and optic disc hemorrhages.
- Errors that underestimate glaucoma: Not delineating the sclera ring correctly, ignoring the small size of the disc, missing a rim notch, missing a hemorrhage and missing retinal nerve fiber layer (RNFL) defect.
- Adopt good clinical practices. Optic nerve head (ONH) examination is the key skill, which one must learn.
- Be aware of the pitfalls in diagnosis.

THERAPEUTIC VITRECTOMY IN UVEITIS

Dr Simar Rajan Singh, Chandigarh

- Vitrectomy has come up as an effective therapeutic option for both active uveitis as well as sequelae of uveitis.
- Unlike other surgeries in uveitis eyes, a period of quiescence may not be required for vitrectomy.
- Control of inflammation and reducing requirement of immunosuppressive therapy is one of the major roles of therapeutic vitrectomy.
- The added diagnostic value of the sample obtained from the source is a boon.
- Advent of micro-incision vitrectomy surgery (MIVS) has made it safer and reduced the chances of postoperative complications.

GLAUCOMA PROCEDURES IN UVEITIS GLAUCOMA

Dr SS Pandav, Chandigarh

- Glaucoma in eyes with uveitis is challenging.
- The incidence of glaucoma in uveitis is 9.6-18.3%. The goal of therapy is to control inflammation and reduce IOP to protect optic nerve.

- Medical therapy is the first-line of treatment; avoid prostaglandins, pilocarpine. About 25% of intractable cases may need surgery.
- Surgery in uveitic eyes is challenging due to inflammation-induced fibrosis scarring.
- Trabeculectomy or glaucoma-drainage-device (GDD) are viable options. Careful selection of the procedure is important.
- Trabeculectomy had an overall higher cumulative failure rate, higher rate of complications and postoperative surgical interventions.

PEARLS OF PERIMETRY: ANALYZING THE FIELD

Dr Pranav Ranjan, Patna

- Checklist: Refraction with near vision correction; pupil size 3.5 mm; astigmatism >3D cause temporal artifacts; CL for high refractive errors (over 6D); full aperture lens in all cases; cataracts cause generalized loss of sensitivity; consider neurological, vascular and degenerative conditions; repeat fields (2-3 times) to establish baseline; reset baseline after surgical procedures.
- There are two components in field testing: Point pattern and strategy (central 30-2 full threshold means point pattern of 30-2 and strategy of full threshold).
- In perimetry, threshold is particular intensity of light seen in 50% times, suprathreshold seen 90% and infrathreshold seen 15%.
- Light intensity is expressed as decibel (dB) or apostilbs (asb); dB (retinal sensitivity) is inversely proportional to asb (light intensity).
- Statpac analysis simplifies visual field interpretation; it differentiates between normal and abnormal and identifies changes in a series of visual fields.

PCR AND ANTERIOR VITRECTOMY

Dr Nikunj Tank, Indore

- Don't panic. Assess the situation and call for help, if needed.
- Understand the basics of anterior vitrectomy.
- Always look for capsular support before sulcus intraocular lens (IOL) implantation.
- Steps at which posterior capsule rupture (PCR) can happen: Hydrodissection (blowout pupillary snap), during lens manipulation (particularly hard cataracts), during phaco (trenching, phaco/last piece

phaco/surge), during I/A, during IOL implantation or pre-existing (true posterior polar cataracts).

- Automated anterior vitrectomy tips and tricks: Suture/have tight incisions, AFR 10, vacuum 200, cut rate max, split infusion and aspiration, cut I/A mode and I/A mode.

NON-HIV CMV RETINITIS

Dr Mousumi Banerjee, New Delhi

- These cases should be identified early.
- Widespread involvement, vitritis, occlusive vasculopathy are features seen in non-HIV cases. It is important to differentiate cytomegalovirus (CMV) retinitis and leukemic retinopathy, especially in the early stages.
- Regular ophthalmological screening is important during the maintenance phase of chemotherapy.

SUTURED SCLERAL FIXATION OF IOLs

Dr Diva Kant Misra, Lucknow

The first published description of sutured scleral-fixated intraocular lenses (SFIOLs) was in the 1980s.

In 1991, Lewis popularized the concept of ab externo suture passes and made use of scleral flaps to cover the suture knots. Complications include suture breakage, lens dislocation/tilt, knot erosion, suprachoroidal or vitreous hemorrhage, retinal detachment, endophthalmitis, hypotony, ocular hypertension and cystoid macular edema.

THERAPEUTIC KERATOPLASTY

Dr Namrata Sharma, New Delhi

Therapeutic keratoplasty is a high-risk procedure demanding high surgical and medical skills. It has a definite role in the management of microbial keratitis refractory to medical therapy. Intraoperative difficulties are encountered such as spontaneous lens extrusion, expulsive suprachoroidal bleed, graft host junction time over-riding, loose sutures. Advances in microsurgical technique, newer generation antibiotics and control of inflammation improve prognosis. There have been recent advances in therapeutic keratoplasty such as femtosecond laser-assisted penetrating keratoplasty (PKP) for treating infective keratitis and collagen cross-linked therapeutic grafts in fungal keratitis.

Some of the early onset complications of the procedure include glaucoma, suture-related complications, hemorrhage/hyphema, persistent epithelial defect,

recurrence of infection (fungal keratitis, bacterial keratitis, acanthamoeba keratitis, herpetic keratitis); the late onset complications are glaucoma, cataract, graft failure, phthisis bulbi. The Rule of Half in repeat full thickness grafts mentions that Half of the patients after therapeutic PKP require visual rehabilitation, Half (50-60%) of the graft survives at the end of 1 year and Half (40-50%) of the patients after the repeat graft get corrected distance visual acuity (CDVA) >6/60.

Regular follow-up is essential to know the course of disease; but, the COVID-19 pandemic and the nation-wide lockdown hampered regular follow-up of patients – use of U tool might help to monitor disease progression and avoid delayed presentation.

The principles of postoperative management are to prevent recurrence of infection, control of IOP, control of inflammation and epithelial healing. Corticosteroids are a double-edged sword in postoperative management. They are safe in keratoplasty for noninfective indications, viral and proven bacterial keratitis. However, extreme caution must be exercised for fungal and acanthamoeba keratitis; use only after being sure of eradication of infection and histopathology report of no rim involvement.

INTRAOPERATIVE OCT AND THREE-DIMENSIONAL VIEWING SYSTEMS

Dr Katherine E Talcott, USA

Intraoperative optical coherence tomography (iOCT) is a valuable surgical adjunct to ophthalmic surgery. It can provide surgeons with additional information about the subtle changes in the retina in response to surgical maneuvers. It provides real time feedback to the surgeon leading to safer and more efficient surgery with improved outcomes. The 3-year results of the DISCOVER study showed a strong surgeon preference for visualizing the OCT data on a 2D screen that required looking away from the surgical field compared to using the OCT data injected into microscope oculars.

The 3D Heads-up display provides a digital stereoscopic view of the surgical field on a high definition monitor freeing the surgeon from the confines of the microscope. Integration of iOCT with 3D digital surgical visualization is feasible. The large screen based visualization of the OCT DataStream minimized the need for accessory screen utilization. Digitally-enabled iOCT may provide superior ergonomics and increased attention on the surgical field during OCT review. There is a need for additional studies to better assess patient outcomes, surgeon experience, and overall value of integrative technologies to enhance the surgical theater experience.

News and Views

Advise Both Exercise and Calcium and Vitamin D Supplements to Postmenopausal Women with Osteopenia

Postmenopausal women with low bone mass should be advised adequate calcium and vitamin D as well as bone-loading exercises, according to preliminary findings from the Heartland Osteoporosis Prevention Study (HOPS) published in the journal *Osteoporosis International*. These findings were also presented at the American Society of Bone and Mineral Research (ASBMR) 2021 Annual Meeting.

The study included 276 postmenopausal women and had osteopenia. Women who had osteoporosis; had an increased risk of a major fracture or hip fracture; had been on bisphosphonates within the last 6 months; were currently on estrogen, tamoxifen or aromatase inhibitors; had a serum vitamin D level <10 mg/mL or >100 mg/mL were excluded from the study.

In the study, women who had entered menopause within the previous 6 months and had osteopenia (low bone mass, T score -1.0 to -2.49) were randomized to two treatment groups for 12 months. One group received bone-loading and resistance exercise + calcium (1200 mg/day) and vitamin D (1000-3000 IU/day) supplements, while the second group was given risedronate (150 mg) along with calcium and vitamin D supplements. The control group was treated with only calcium and vitamin D supplements. The participants in the exercise group were required to visit the fitness centers three times in a week for the bone-loading exercises (jogging using a weighted vest and resistance exercises) under supervision.

The study outcome measures were bone mineral density (BMD) at the total hip, femoral neck and spine, serum biomarkers of bone turnover - NtX (resorption) and Alkphase B (formation), peripheral quantitative computed tomography (pQCT) at the tibia and Hip Structural Analysis (HAS) and adherence (to exercise) rates.

After 12 months, a significant increase in BMD at the spine was observed with risedronate treatment compared to women in the exercise group or the control group (+1.9%, +0.9% and -0.4%, respectively). The risedronate group also showed greater decreases in rates of bone formation and resorption, as evident by decline in serum levels of NtX and Alkphase B.

Exercise was associated with positive changes in intertrochanter hip structural analysis measures suggesting that exercise improved strength at the hip joint through changes in structure and not BMD. These results will be announced in a forthcoming study, according to the authors.

These findings suggest that prescription for osteopenic postmenopausal women should include both calcium and vitamin D and bone loading exercises. Bisphosphonates such as risedronate may be prescribed in addition for its beneficial effect in increasing BMD.

Laura D Bilek, from the College of Allied Health Professionals, University of Nebraska Medical Center and study coauthor said, "The key takeaway for clinicians is that bone health is about more than just density! In postmenopausal women, exercise appears to improve strength at the hip through changes in structure, not BMD."

Sources: Waltman N, et al. Bone-loading exercises versus risedronate for the prevention of osteoporosis in postmenopausal women with low bone mass: a randomized controlled trial. *Osteoporos Int*. 2021 Sep 14. [Epub ahead of print]; Exercise appears to improve bone structure, not density. *Medscape*. Oct 06, 2021.

WHO Issues Clinical Case Definition of Post-COVID Condition

To make sure that affected patients receive the required care, the World Health Organization (WHO) has issued a clinical case definition of 'post-COVID condition'. The global health body states that the condition occurs in people with a history of possible or confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, often 3 months from its onset with symptoms, persists for at least 2 months, and cannot be explained by another diagnosis.

According to the definition, the symptoms of post-COVID condition include fatigue, shortness of breath, cognitive dysfunction, besides other symptoms and tend to impact everyday functioning. The symptoms may be new onset after initial recovery from acute coronavirus disease 2019 (COVID-19) or may persist from the initial illness. Additionally, the symptoms may fluctuate or relapse over time.

The agency stated that a different definition may apply to kids... (Source: *ET Healthworld*)

COVID Led to Ninefold More Deaths in People with Learning Difficulties: Study

A study published in the *Lancet Regional Health – Europe* has shown that COVID-19 caused nine times more deaths in people with learning difficulties compared to the general population during the first wave of the pandemic in the United Kingdom.

Investigators looked into over 1,60,000 deaths in the UK between March and June 2020. They noted that deaths from COVID-19 among people having eating disorders were about fivefold higher in comparison with the general population, and fourfold higher among people with personality disorders as well as those with dementia. Moreover, deaths due to COVID were threefold higher in people suffering from schizophrenia.

Individuals with nine different mental health conditions and intellectual disabilities had higher mortality from the viral disease during the period, noted investigators... (Source: CNN).

Longer Exposure to Raised LDL Associated with Greater CHD Risk

A new study published in *JAMA Cardiology* suggests that greater exposure to low-density lipoprotein cholesterol (LDL-C) during young adulthood and middle age is tied to a significant increase in the risk of coronary heart disease (CHD), irrespective of lipid levels in midlife.

Pooled data from four prospective studies, which included more than 18,000 participants, having an average age of 56 years, was assessed. Researchers evaluated the potential link between cumulative LDL-C exposure, time-weighted average (TWA)-LDL-C and change in LDL-C slope from young adulthood to middle age and incident cardiovascular disease (CVD). Following adjustment for covariates, people with the greatest cumulative exposure and highest TWA-LDL-C levels had 1.6 times and 1.7 times higher risk of CHD, respectively, in comparison with people with the lowest cumulative exposure and lowest TWA-LDL levels... (Source: Medscape)

COVID Led to Sharp Increase in Depression, Anxiety, Says Study

According to a new study published in *The Lancet*, cases of depression and anxiety increased by over a quarter across the globe during the first year of the COVID-19 pandemic, in particular among women and young adults.

According to the first estimate of the impact of the pandemic on mental health globally, it was estimated that there were an additional 53 million individuals

who had major depressive disorder in 2020, besides an additional 76 million people who suffered from anxiety. This translates to a 28% and 26% rise, respectively, in the two conditions.

Researchers analyzed the data accumulated from North America, Europe and East Asia and modelled the expected prevalence of depression and anxiety. In the absence of the pandemic, 193 million cases of depression would have been expected, while the number of cases actually observed was 246 million during 2020. Additionally, 298 million cases of anxiety would have occurred in the absence of COVID-19, while the actual number was 374 million in 2020... (Source: NDTV-AFP & Reuters)

Study: HEPA Filters may Remove COVID-19 Virus from Air

High-efficiency particulate air (HEPA) filters and ultraviolet (UV) sterilization can be effective in removing SARS-CoV-2 particles from the air, suggest real-world evidence, reported in the preprint server medRxiv.

A study indicates that the filters may have a role in reducing the risk of hospital-acquired SARS-CoV-2, reported the journal *Nature*. HEPA filters were installed in two COVID-19 wards, including a general ward and an ICU. Air samples were collected from the wards during a week when the air filters were operational and 2 weeks when they were off, and the results were then compared. Airborne virus was found in the ward on all 5 days prior to activation of air/UV filtration, while it was not detected on any of the 5 days when the air/UV filter was working. SARS-CoV-2 was detected again on 4 of the 5 days when the filter was nonoperational.

Airborne virus was not frequently found in the ICU, even when the filters were not working... (Source: Medscape)

Delta Variant of Coronavirus does not Seem to Cause More Severe Diseases in Children

According to a study conducted in the UK, Delta variant of coronavirus does not seem to result in more severe disease among children compared to earlier versions of the virus.

Investigators assessed two groups of school-age children with COVID-19. Of these, 694 were infected with the Alpha variant from late December 2020 through early May 2021, while 706 had an infection with Delta between late May and early July. Posted on medRxiv, the study showed that children infected with Delta variant had slightly more symptoms. However, very few children needed hospitalization in both the groups, and long

periods of illness were infrequent. Additionally, in both the groups, about half of the children were ill for not more than 5 days. (Source: Reuters)

Data from Israel Favor Higher Rates of Post-vaccine Myocarditis

According to two reports from Israel, the incidence of myocarditis following the administration of the Pfizer-BioNTech COVID vaccine appeared to be several-fold higher in comparison with some estimates; however, it continued to be low over late spring this year.

Among patients in Clalit Health Services, the country's largest healthcare system, the estimate of myocarditis was 2.13 cases per 1,00,000 vaccinated individuals, with as high as 10.69 cases per 1,00,000 among men and boys in the 16 to 29 years age bracket.

In another study that used Israel's government database, the findings supported a higher risk in young men. The estimate of myocarditis for males of all ages was 0.64 cases per 1,00,000 individuals following the first dose and 3.83 cases per 1,00,000 following the second shot. The incidence increased to 1.34 and 15.07 per 1,00,000 individuals following the first and second shot, respectively, for boys aged between 16 and 19 years. The studies were published online in the *New England Journal of Medicine*... (Source: Medpage Today)

Adolescents Exercising after a Concussion Recover Faster: Study

A randomized controlled trial has suggested that following a concussion, young athletes who resume aerobic exercise relatively early, with an intensity that does not aggravate the symptoms, may recover faster, in comparison with stretching.

Researchers suggested that clinicians must prescribe exercise to promote recovery in patients with a concussion. The study included 118 adolescent athletes, 13 to 18 years of age, who had a sport-related concussion in the previous 10 days. A total of 61 participants were randomized to individualized subsymptom-threshold aerobic exercise, while 57 were assigned to stretching exercise, for a duration of at least 20 minutes a day for up to 4 weeks.

A larger proportion of participants randomized to stretching failed to recover by 4 weeks, compared to those assigned to aerobic exercise (32% vs. 21%). Additionally, the median time to full recovery was 19 days for the stretching group compared to 14 days for the aerobic exercise group... (Source: Medscape)

Salty Foods Just before Bedtime Might Disrupt Sleep

A study conducted in mice suggests that salty foods might have a direct impact on sleep, rather than indirectly contributing to sleep problems by increasing the blood pressure.

Mice were found to have similar physical activity levels whether their diets were high in salt or not. However, mice on a high-salt diet appeared to have more neuronal excitability in the suprachiasmatic nucleus at night compared to the ones on a regular diet. The authors stated that neuronal excitability during the night could disrupt the biological clock, making sleep more difficult.

The findings from the study, presented at the virtual 17th International Conference on Endothelin, put forward a reason for people to look at the amount of salt they consume... (Source: Medscape)

Children Exposed to Harmful Plastics During Cardiac Surgery

According to a preliminary research, the tubing and other bendable equipment used in cardiopulmonary bypass (CPB) exposed young children to phthalates at levels that might have a clinical significance.

At a hospital, children who received blood products during cardiac surgery were noted to have immediate post-procedural rise in serum levels of diethylhexyl phthalate or DEHP (a median of about 3 μ M preoperative to about 5 μ M afterward, $p < 0.0001$) and monoethylhexyl phthalate or MEHP (from about 0 μ M to about 7 μ M, $p < 0.0001$), taking up the total phthalate level from about 4 μ M to about 13 μ M ($p < 0.0001$). The youngest kids appeared to have more phthalate increases, as postoperative phthalate levels had a correlation with more blood products used, longer bypass time and use of methylprednisolone. The findings were presented at the American Academy of Pediatrics (AAP) virtual meeting... (Source: Medpage Today)

AstraZeneca Antibody Cocktail Effective in COVID-19: Study

An experimental COVID-19 antibody drug cocktail developed by AstraZeneca could reduce severe disease or death in nonhospitalized patients in a late-stage study, stated the drug maker.

The drug, known as AZD7442, was found to decrease the risk of developing severe COVID-19 or death by 50% in patients who had been symptomatic for ≤ 7 days. Executive Vice President, Biopharmaceuticals R&D, AstraZeneca, Mene Pangalos, said that an early

intervention with the antibody drug can significantly reduce progression to severe disease, with persistent protection for over 6 months.

The company is also developing the drug cocktail as a treatment for the protection of people with a weak immune response to COVID-19 vaccines... (Source: *ET Healthworld* – Reuters)

Adults 60 and Above not to Start Daily Aspirin for Prevention of Heart Disease, Stroke: US Task Force

The US Preventive Services Task Force is looking at introducing changes to its guidance on taking aspirin daily to prevent heart disease and stroke.

The task force posted a draft statement which recommends that adults, 40 to 59 years of age, having a higher risk for CVD, but no history of the disease, talk to their clinician about whether to start taking aspirin, on the basis of their individual circumstances.

The draft also states that adults 60 years of age and above should not start aspirin therapy for the prevention of heart disease and stroke, as updated evidence indicates that potential harms negate the benefits. However, the task force recommendation does not apply to people who are already on aspirin for a previous heart attack or stroke. These people must continue taking it unless advised otherwise by their clinician... (Source: *CNN*)

Omega-3 Fatty Acids Decrease Inflammation in Elderly COVID-19 Patients

According to a small randomized controlled trial, treatment with omega-3 fatty acids among frail elderly with COVID-19 may have a role in improving lipid responses and reducing the levels of proinflammatory lipid mediators.

The study, presented at the European Geriatric Medicine Society (EuGMS) annual congress, included 22 patients with several comorbidities. Patients were administered either an intravenous infusion of an omega-3 polyunsaturated fatty acid (PUFA) emulsion of 10 g fish oil/100 mL or saline placebo. Those who were given the intravenous infusion were found to have a significant reduction in the neutrophil-to-lymphocyte ratio (NLR) from baseline to the end of treatment, which suggested considerable reductions in systemic inflammation. On the other hand, patients administered a saline placebo had no significant improvements in NLR. However, omega-3 fatty acids were not significantly associated with a decrease in C-reactive protein (CRP) or interleukin (IL)-6... (Source: *Medscape*)

New MTP Rules Notified by Center

The government has notified new Medical Termination of Pregnancy (Amendment) Rules, 2021, clarifying the situations that characterize eligibility criteria for termination of pregnancy up to 24 weeks, as compared to the previous limit of 20 weeks.

The criteria for eligibility include survivors of sexual assault, rape or incest, minors, women who have physical disabilities, mentally ill women including those suffering from mental retardation and conditions where fetal malformation has a considerable risk of being incompatible with life. It also includes cases where it is assessed that if the baby is born, it may have physical or mental abnormalities, to be seriously handicapped.

Cases of those women may also be considered where there is change of marital status during the pregnancy, such as widowhood and divorce. Also included are cases of women with pregnancy in a disaster or emergency situation, as declared by the government... (Source: *ET Healthworld* – TNN)

D-dimer Assay may not be Reliable to Rule Out Pulmonary Embolism in COVID-19 Patients

The plasma D-dimer assay has long been used, in association with clinical prediction scores, to rule out pulmonary embolism (PE) in critically ill patients. However, a new study suggests that it may not be an appropriate test for patients hospitalized with COVID-19.

The study revealed that all hospitalized patients with COVID-19 and evidence of PE on radiographic evaluation had plasma D-dimer levels of 0.05 µg/mL or more, the cut-off for diagnosis.

From a sample of 1,541 patients hospitalized with COVID-19 from January 2020 through February 2021 for a suspected PE, investigators compared plasma D-dimer levels with computed tomography pulmonary angiography (CTPA) in 287 patients. A total of 118 patients (41.1%) needed ICU care, and 27 (9.4%) died during hospitalization.

Thirty-seven patients (12.9%) had radiographic evidence of PE, while 250 patients (87.1%) did not. Around 92.3% patients (n = 265) had plasma D-dimer levels of 0.05 µg/mL or more, which included all patients with PE, and 225 out of 250 patients without PE. The study is published online in *JAMA Network Open*... (Source: *Medscape*)

People with J&J Vaccine as First Shot Show Stronger Immune Response with Moderna or Pfizer Jab as Booster: NIH Study

Individuals who received Johnson & Johnson (J&J) COVID-19 vaccine as a first jab were found to exhibit a stronger immune response when boosted with Pfizer/BioNTech or Moderna vaccine in a study conducted by the National Institutes of Health.

The study included over 450 adult individuals who received initial jabs from Pfizer, Moderna or J&J COVID-19 vaccines and revealed that mixing and matching booster shots of various types is safe in adults. Mixing and matching doses for a booster led to similar side effects to those seen in primary vaccinations and were not associated with any significant safety concerns.

Using different types of vaccines as boosters was found to yield a comparable or higher antibody response compared to using the same type... (Source: Reuters)

Record High of Drug Overdose Deaths in a 12-month Period in the US: CDC

Drug overdose deaths in the United States reached a record high of over 96,000 in the 12-month period ending March 2021, suggest data from the US CDC's National Center for Health Statistics.

In the 12-month period, 96,779 drug overdose deaths were reported in the country, translating to a spike of 29.6% from March 2020 to March 2021. The CDC stated that these figures represent provisional data. The estimate for predicted deaths, accounting for delayed reporting, was more than 99,000 from March last year to March of this year.

Three states reported a decrease in drug overdose deaths from March 2020 to March 2021. These include New Hampshire, New Jersey and South Dakota. Vermont reported the largest rise in overdose deaths among the states... (Source: CNN)

Statins may Provide Slight Protection against COVID-19 Mortality

Statins, the commonly used drugs for reducing cholesterol, may be tied to a slightly lower risk of death due to COVID-19, suggest new data.

A team of researchers at Karolinska Institute, Sweden, evaluated the medical records of around 1 million

individuals in Stockholm, aged above 45 years, from March through November 2020. Around 18% of these had been prescribed a statin, such as atorvastatin and simvastatin. Individuals who had been prescribed statins had more risk factors for poor COVID-19 outcomes, including older age, more often male, more health conditions, lower education levels and less disposable income.

Taking all this into account, statin users were found to have a 12% lesser likelihood of death from COVID-19 during the study period. However, the investigators did not compare the outcomes in people who actually got infected. Additionally, the researchers only had data on prescriptions, and not on whether patients took the medicine. Therefore, a clinical trial is needed to confirm the findings, but the authors of the study still conclude that the findings point to a modest preventive effect of statin treatment on COVID-19 mortality. The findings are published in *PLOS Medicine*... (Source: Reuters)

Delhi's COVID-19 Outbreak Shows Herd Immunity against Delta Difficult, Says Study

The severe COVID-19 outbreak seen in Delhi in 2021 indicates that the Delta variant of the coronavirus can infect those who have been previously infected by a different variant of SARS-CoV-2, and brings to light the challenges in reaching herd immunity against the variant, suggested a new study.

The study noted that the Delta variant was around 30% to 70% more transmissible compared to the previous lineages of the virus circulating in Delhi. The authors noted that the city's overall seropositivity was 56.1% which could have conferred some protection from future outbreaks through herd immunity. The study was conducted by the National Centre of Disease Control (NCDC) and the Council of Scientific and Industrial Research-Institute of Genomics and Integrative Biology (CSIR-IGIB), New Delhi, in association with the University of Cambridge and Imperial College London, UK and the University, Copenhagen, Denmark.

Previous infection was found to yield only 50% to 90% of the protection against the Delta variant that it provides against previous lineages. The findings were published in the journal *Science*... (Source: ET Healthworld – PTI)

■ ■ ■ ■

The Five Interior Powers

To be in a state of happiness, bliss and ananda is what the ultimate goal of life is. Everybody is born with certain inherent powers, which if cultivated in the right direction will lead to inner happiness.

The ancient Shiva Sutra text talks about the concept of Shiva and Shakti. Shiva is silence, Shakti is power; Shiva is creativity, Shakti is creation; Shiva is love, Shakti is loving.

In computer term, Shiva is the knowledge or the information and Shakti is the operational software. Shiva and Shakti together form consciousness, in other words, the soul.

Shiva sutra – teaching about Shiva – describes five inherent powers of Shakti which everybody is born with and these are “Chitta Shakti”, “Ananda Shakti”, “Gyan (Gnana) Shakti”, “Ichha Shakti” and “Kriya Shakti”.

Kriya Shakti is the one which is most visible. Kriya is not same as karma. Karma is action born of cause and effect. Kriya Shakti is at the level of body and mind. Ichha Shakti is the inherent desire, which controls the mind. Gyan Shakti is the inherent desire to learn and is at the level of intellect. Both Ananda and Chitta Shakti are at the level of consciousness and represent the desire or aim to be blissful.

These five powers also decide the needs of a person, which can be at the level of physical body, mind, intellect, ego or the soul. The needs activate the Shakti which, in turn, leads to action. The purpose of life should be to direct the needs and the Shaktis towards the soul and not towards the ego.

The power of Kriya Shakti should have all the actions directed towards the soul; Gyan Shakti should be directed towards the knowledge of the true self; Ichha Shakti towards the desire or intention to unite with the self; Anand Shakti and Chitta Shakti towards the awareness of God and to experience the bliss of God. All thoughts, speech or actions in life should be directed on two basic goals - providing happiness to others and ending up with self-happiness. Every action and relationship in life should involve these five powers to attain inner happiness.

Most computers in the body require a key to get activated and the key in the case of Shakti is “intention or intent”. Intentions are something which are under the control of a person, or one can practice control over them.

Intention always requires the association of its buddy attention with it. Attention is the focus of action on that particular intention. The combination of intention and attention can change perceptions of life and ultimately change the reality. It has been an old Upanishad saying that you are what your thoughts are. Right intention leads to the right thought; the right thought to right action; the right action to the right habit; the right habit to the right character and the right character leads you to what you are. The punch-line, therefore, is to have right intention which should be directed towards one of the five Shaktis to acquire spiritual well-being.

Health is not mere absence of disease but a state of physical, mental, social, environmental and spiritual well-being. Spiritual well-being has now been added as the fifth dimension of health. It has been said that the body is the largest pharmaceutical armamentarium in the world and has the capacity to produce each and every drug available in the universe. This is based on the fact that no drug can go into the body without a receptor. The very fact the body has a receptor for every drug means that it has the capacity to produce that drug.

All yogic paths to liberation are also directed towards these Shaktis. One adopts Karma Marg by activating Kriya Shakti, Gyan Marg by activating Gyan Shakti and Bhakti Marg by activating Ichha Shakti.

Faulty lifestyle also involves distractions of three of these powers: Ichha, Gyan or Kriya Shakti.

Correct lifestyle involves the correct use of Kriya Shakti in doing actions, correct use of Gyan Shakti by acquiring knowledge about self and healthy behavior and correct use of Ichha Shakti by learning the dos and don'ts of life and controlling the mind towards various addictions of life which can be addition of food, sex, drugs, alcohol, smoking, sleeping, not walking and/or eating faulty Rajsik cum Tamsik high refined carbohydrate diet.



Hitting Unseen Target

Yogi Raman was a master of the art of archery. One morning, he asked his favorite disciple to witness a display of his skill. The disciple had seen this over a hundred times before, but he obeyed. They went into the woods and when they reached a beautiful oak tree, Yogi Raman took a flower and placed it on one of the branches of the tree.

He opened his bag and took out three objects: his bow made of precious wood, an arrow and a white handkerchief, beautifully embroidered with lilacs. He positioned himself one hundred paces from the spot where he had placed the flower. While he was facing his target, he asked his disciple to blindfold him with the embroidered handkerchief.

The disciple followed his teacher's instructions. Yogi Raman then asked his disciple how often he had seen him practice the ancient sport of archery. The disciple

replied that he saw him every day. He added that the teacher had always managed to hit the flower from three hundred paces away.

With his eyes covered by the handkerchief, Yogi Raman stood firm, drew back the bowstring, aiming at the flower placed on the branch of the oak tree, and released the arrow. The arrow whistled through the air, but missed even the tree and missed the target by a huge margin. Raman asked if he hit the flower, removing the handkerchief. The disciple replied that he had missed it completely. The disciple told the master that he had thought that he was going to demonstrate the power of thought and the ability to perform magic.

Yogi Raman replied that he had just taught him the most important lesson about the power of thought. He said that when we want something, we must concentrate only on that. No one can hit a target they cannot see.

■ ■ ■ ■

FDA Urges Restaurants, Food Manufacturers to Limit Sodium

The US Food and Drug Administration (FDA) has issued new guidance asking food manufacturers and restaurants to limit the amount of sodium in processed, packaged and prepared foods by 12% over the next 2½ years.

Acting FDA Commissioner, Janet Woodcock, said that the country is fighting an epidemic of chronic diseases related to the diet, such as CVD, diabetes and obesity. Meanwhile, Susan Mayne, Director of the FDA's Center for Food Safety and Applied Nutrition, stated that Americans consume more than 50% more sodium than the recommended level.

The guidance specifies voluntary short-term sodium reduction targets for restaurants, food manufacturers, as well as food service operators for 163 types of processed, packaged or prepared foods... (Source: *Medpage Today*)

Poor Sleep Quality Impacts Students' Mental Health, Finds Study

A new research has suggested that over two thirds (65.5%) of students are experiencing poor sleep quality and this is associated with mental health problems.

The study, published in *Annals of Human Biology*, included 1,113 men and women attending university full-time. The findings suggested that students reporting depressive symptoms were nearly four-fold more likely to have inadequate sleep habits. Excessive daytime sleepiness (EDS) was noted in around 55% of the students and they were about twice as likely to suffer from depression or have moderate to high-stress levels. Poor quality sleep and EDS were commonly seen among women.

The research is part of the Longitudinal Study on the Lifestyle and Health of University Students (ELESEU) and made use of data from 2016 and 2017... (Source: *HT – ANI*)

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Lighter Side of Medicine

HUMOR

BANK NAME

Mother decided that 10-year-old Cathy should get something 'practical' for her birthday. "Suppose we open a savings account for you?" mother suggested.

Cathy was delighted. "It's your account, darling," mother said as they arrived at the bank, "so you fill out the application."

Cathy was doing fine until she came to the space for 'Name of your former Bank.'

After a slight hesitation, she put down 'Piggy.'

VOTE FOR THE DEVIL

A candidate for city council was doing some door-to-door campaigning, and things were going pretty well, he thought, till he came to the house of a grouchy-looking fellow. After the candidate's little speech, the fellow said, "Vote for you? Why I'd rather vote for the Devil!" "I understand," said the candidate, "but in case your friend is not running, may I count on your support?"

TRAFFIC COURT

A New York man was forced to take a day off from work to appear for a minor traffic summon. He grew increasingly restless as he waited hour after endless hour for his case to be heard. When his name was called late in the afternoon, he stood before the judge, only to hear that court would be adjourned for the next day and he would have to return the next day. "What for?" he snapped at the judge.

His honor, equally irked by a tedious day and sharp query roared, "Twenty dollars contempt of court. That's why!" Then, noticing the man checking his wallet, the judge relented. "That's all right. You don't have to pay now." The young man replied, "I'm just seeing if I have enough for two more words."

WHOEVER TELLS THE BIGGEST LIE

Two boys were arguing when the teacher entered the room. The teacher says, "Why are you arguing?"

One boy answers, "We found a 10 dollar bill and decided to give it to whoever tells the biggest lie."

"You should be ashamed of yourselves," said the teacher, "When I was your age, I didn't even know what a lie was."

The boys gave the 10 dollars to the teacher.

MY GRADES

A high school student came home one night rather depressed.

"What's the matter, Son?" asked his mother.

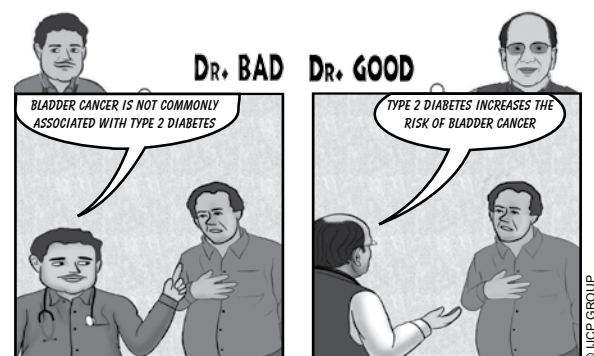
"Aw, gee," said the boy, "It's my grades. They're all wet."

"What do you mean 'all wet?'"

"You know," he replied, "...below C-level."

Dr. Good and Dr. Bad

SITUATION: A man with type 2 diabetes mellitus was told that he was at risk of developing bladder cancer.



LESSON: The PRISMA-compliant meta-analysis of cohort studies revealed a link between diabetes mellitus and increased risk of bladder cancer or cancer mortality, especially in men.

Medicine (Baltimore). 2017;96(46):e8588.



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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

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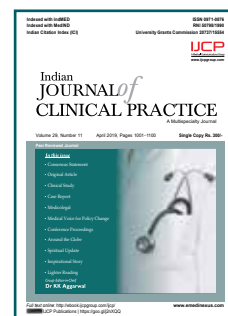
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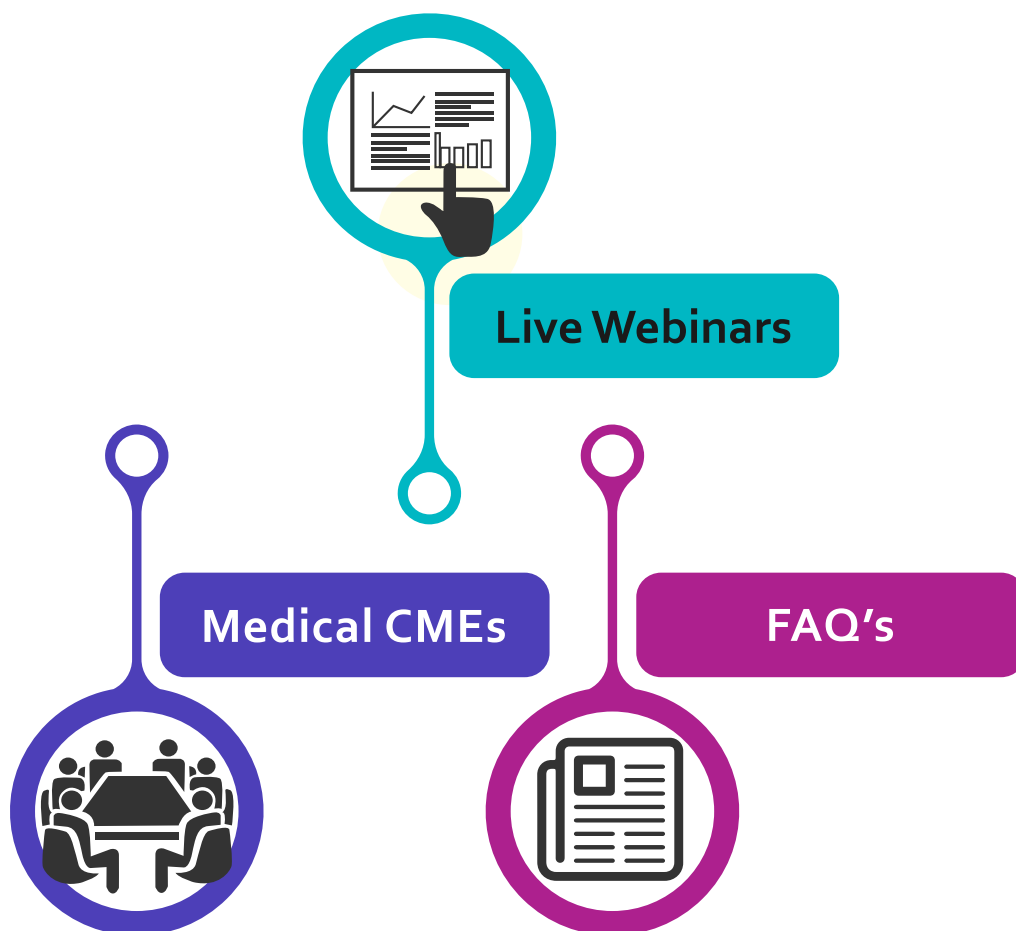
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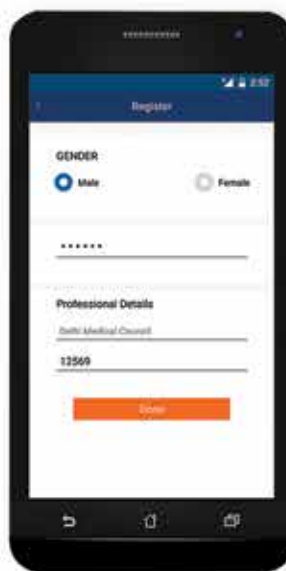
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