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

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

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Indian JOURNAL of CLINICAL PRACTICE

A Multispecialty Journal

Volume 31, Number 2 July 2020, Pages 101–200 **Single Copy Rs. 300/-**

Peer Reviewed Journal

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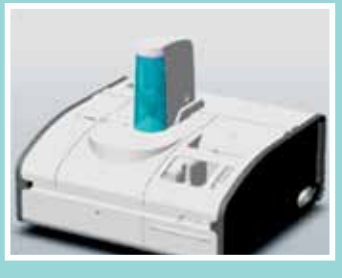

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Indian JOURNAL of CLINICAL PRACTICE
A Multispecialty Journal

Volume 31, Number 2, July 2020

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

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

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

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Airborne Transmission and WHO

NEW WHO GUIDANCE CALLS FOR MORE EVIDENCE ON AIRBORNE TRANSMISSION

- The World Health Organization (WHO) released new guidance on the transmission of the novel coronavirus acknowledging certain reports of airborne transmission; however, the agency stopped short of confirming that the virus spreads through the air.
- The agency further acknowledged that some outbreak reports pertaining to indoor crowded spaces point to the likelihood of aerosol transmission, such as during choir practice, in restaurants or in fitness classes.
- WHO stated that the coronavirus causing COVID-19 spreads through contact with contaminated surfaces or close contact with infected individuals who tend to spread the virus through saliva, respiratory secretions or droplets that are released when an infected person coughs, sneezes, speaks or sings.
- People should avoid crowds and ensure good ventilation in buildings, besides social distancing, and wear masks when physical distancing is not possible.
- The pandemic is driven by super-spreading events, and many of those events could best be explained by aerosol transmission.
- People without symptoms - to wear masks.
- Very few diseases are believed to be spread via aerosols, or tiny floating particles. These include measles and tuberculosis. These highly contagious pathogens can stay afloat in the air for hours and require extreme precautions to prevent exposure.
- WHO is using an outdated definition of droplets and aerosols and is focusing too much on the size of the droplets and the distance they travel. WHO defines aerosols as being <5 microns as only particles that small could float in the air long enough to be inhaled. However, Linsey Marr, an aerosol expert at Virginia Tech, said that a much larger range of particle size could contribute to infection. Rather than size, the differences between droplets and aerosols should be guided by how the infection occurs: If a person inhales the virus and becomes infected, it's an aerosol. If the infection occurs by contact, they are droplets. The WHO has focused on airborne transmission at long distances, but breathing in aerosols is of greater concern at close contact and when people are in the same room, says Marr. *(Reuters)*

PREDICTORS OF SURVIVAL IN COVID-19 PATIENTS TREATED WITH TOCILIZUMAB

- Administration of the interleukin (IL)-6 receptor antagonist tocilizumab within 12 days of symptom onset in patients with severe COVID-19

independently predicted in-hospital survival at 28 days, revealed a study published in the *Journal of Autoimmunity.*

- Patients were eligible for tocilizumab if they had persistent fever (38°C for >6 hours), had PaO_2/FiO_2 of <200, and exhibited persistently increasing inflammatory laboratory parameters (ferritin, D-dimer and lactate dehydrogenase [LDH]) or an elevated inflammatory laboratory parameter marked by ferritin ≥1,000 µg/L, D-dimer ≥5 mg/mL or LDH ≥500 U/L. An IL-6 level ≥5 times the upper limits of normal (≤5 pg/mL) was also evaluated.
- An 8 mg/kg IV dose of tocilizumab was administered using actual body weight with a maximum dose of 800 mg. Patients were given a second dose if persistently febrile despite treatment. Owing to medication shortages, tocilizumab dose was changed to a fixed 400 mg IV dose for all patients on March 30, 2020. All patients were followed for up to 28 days from the first dose.
- The 28-day in-hospital mortality was 43.2%, with 46 patients in the survivors and 35 in the nonsurvivors group. The sole independent predictor of 28-day in-hospital survival was receipt of tocilizumab within 12 days of symptom onset (adjusted odds ratio [OR]: 0.296, 95% confidence interval [CI]: 0.098-0.889). A sequential organ failure assessment (SOFA) score ≥8 had an independent association with 28-day in-hospital mortality (adjusted OR: 2.842, 95% CI: 1.042-7.753).
- Patients in the survivor group had higher odds of having a clinical response to the drug by Day 28 (80.4% vs. 5.7%; $p < 0.001$). Improvements in the six-point ordinal scale and SOFA score were evident in survivors after tocilizumab. The hospital length of stay was longer in the survivor group compared to nonsurvivors (27.5 days [14-31] vs. 14 days [9-20]; $p < 0.001$), while 14 (17.3%) patients remained hospitalized at the end of the study.

Source: https://www.sciencedirect.com/science/article/pii/S0896841120301347?via%3Dihub

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Loss of Smell Associated with Less Severe COVID-19 Infection

A study published in the *Annals of Allergy, Asthma & Immunology,* has revealed that loss of smell seems to be an independent positive prognostic factor of less severe COVID-19 infection.

The study enrolled 949 patients with COVID-19. The patients were assessed at Rush University Medical Center from February 1, 2020, through April 3, 2020. In all, 198 (20.9%) patients reported loss of smell. Anosmia was shown to have a significant association with younger age (mean age, 46 vs. 49 years; p = 0.02), female gender (64.7% vs. 52.8%; p = 0.003) and higher body mass index (33.6 vs. 31.5; p = 0.001).

Anosmia had a significant association with decreased hospitalization (odds ratio [OR] = 0.69), admission to intensive care unit (OR = 0.38), intubation (OR = 0.43) and acute respiratory distress syndrome (OR = 0.45). The results continued to be significant following further adjustment for allergic rhinitis and chronic rhinosinusitis.

Loss of smell was also associated with less lymphopenia and higher albumin levels, pointing to a less severe reaction to COVID-19 in patients with smell loss when compared with those with intact smell, suggested researchers.

Mean lymphocyte count was 1.84 ± 3.69 among patients with anosmia compared to 1.11 ± 0.81 among those without smell loss (p = 0.001). The levels of albumin were 3.02 ± 0.83 versus 2.77 ± 0.83, respectively (p = 0.02). Other laboratory values and inflammatory markers had no link with anosmia.

The study also revealed a significant association between anosmia and history of pre-existing smell dysfunction (OR = 4.66), allergic rhinitis (OR = 1.79) and chronic rhinosinusitis (OR = 3.70), in comparison with patients without loss of smell. *(DG Alerts Excerpts)*

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Study of COVID-19 Seroprevalence Among Healthcare Workers at Dedicated COVID Hospital in Southern Rajasthan

MAHESH DAVE*, RAHUL VIJAYVARGIYA†, LAKHAN POSWAL‡, VIKRAM BEDI*, MAYANK SHARMA#, NARENDRA DEVAL#

ABSTRACT

Background: Coronavirus disease 2019 (COVID-19), a pandemic, has affected approximately 90,000 healthcare workers (HCWs) worldwide and 548 HCWs in India with an infection rate of 6%. Seroprevalence studies can provide relevant information which is useful for assessing the level of exposure among hospital personnel, to avoid unnecessary quarantines and for healthcare resource planning. **Aims and objectives:** Study of COVID-19 seroprevalence, clinical profile and outcomes among HCWs working at a dedicated COVID hospital in southern Rajasthan. **Material and methods:** It was a cross-sectional study conducted among 100 HCWs posted in various wards of dedicated COVID hospital at the RNT Medical College, Udaipur, Rajasthan, India, over a period of 2 months from April 2020 to May 2020. **Results:** Out of 100 HCWs, 68% were male and 32% were female with mean age 31.90 years and 16% had seropositive response. Majority, i.e., 81% seropositive HCWs were asymptomatic and all had good outcome (discharged). **Conclusion:** It is advisable that this high-risk population of HCWs should follow infection prevention and control (IPC) protocol as well as institutional quarantine protocol, screening and training at timely interval to protect themselves.

Keywords: Seroprevalence, COVID-19, healthcare workers

Coronavirus disease 2019 (COVID-19) is a global health issue today. It started in Wuhan, Hubei Province, China in December 2019 and continued to spread worldwide.[1] COVID-19 is caused by SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which belongs to the family of positive-sense, enveloped, single-stranded RNA viruses with a size varying from 26 kb to 32 kb.[2] The name 'corona' was derived from the Latin word *coronae* or *crown* which means a colored circle around a luminous body such as sun or moon. The World Health Organization (WHO) declared it as pandemic on 11th March, 2020.[3] In India, the first case was reported on 30th January, 2020 in Kerala. SARS-CoV-2 is mainly transmitted through respiratory droplets and direct contact with contaminated surfaces with incubation period of 2-14 days and basic reproduction number of 2.2.[4]

A healthcare worker (HCW) delivers care and services to the sick either directly as doctors, nurses or indirectly in the form of helpers, laboratory technicians or medical waste handlers. There are over 59 million HCWs globally.[5]

Now, in the midst of COVID-19 pandemic, the *Bhagavad Gita* looks to be more relevant than ever. Here, HCWs look like *Arjuna*, hospitals are like battlegrounds for the war not only against the virus but also against the vast array of misinformation spread by mass media. Amid the chaos that the pandemic has caused, HCWs are being guided by *dharma* and a deep sense of purpose and are urged to do what is right and not to become affected by the outcome.[6]

HCWs are at the front line of the COVID-19 outbreak response and as such are exposed to hazards that put them at risk of infections. Protecting HCWs is of paramount importance and if infected, pose a great risk to vulnerable patients and fellow HCWs.

At least 90,000 HCWs worldwide are believed to have been infected with COVID-19 with average HCW infection

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rate at about 6%. This estimate is based on information collected from 30 different countries by national nursing associations, government figures and media reports.[7] Figures from China's National Health Commission showed that more than 3,300 HCWs had been infected as of early March and, according to local media, at least 22 had died. In Italy, 20% of HCWs were infected and some of them died.[8] Exact incidences of COVID-19 disease among HCWs in India is not yet officially reported but probably it has affected around 548 doctors, nurse and paramedics across the country so far.[9]

Amidst this pandemic scenario, there are a lot of expectations from HCWs and HCWs too have expectations from their higher authorities. It is the basic right of HCWs to be provided with all basic needs which can prevent infectivity, morbidity and mortality among them in the line of duty. These include:

- To provide adequate supplies of personal protective equipment (PPE) such as masks, gloves, goggles, gowns, face shields, etc.
- Refreshers training on infection prevention and control (IPC).
- Maintain appropriate working hours with breaks and followed by quarantine.

Seroprevalence studies can provide relevant information on the proportion of people who have experienced a recent or past infection. Monitoring the prevalence of infection among HCWs is useful for assessing the level of exposure among hospital personnel and identifying high-risk departments. Likewise, knowledge of past infection among HCWs could be useful for avoiding unnecessary quarantines and for healthcare resource planning.

To date, data on seroprevalence of SARS-CoV-2 antibody in HCWs is limited from India as well as from across the globe. Hence, it is our small effort, where we have tried to evaluate seroprevalence of SARS-CoV-2 antibody in HCWs working at a dedicated COVID hospital, a tertiary care hospital situated in southern Rajasthan.

AIMS AND OBJECTIVES

Aims

- Study of COVID-19 seroprevalence among HCWs at dedicated COVID hospital in southern Rajasthan.

Objectives

- To study seroprevalence among HCWs.
- To study clinical profile of seropositive HCWs.

MATERIAL AND METHODS

Study Designs and Data Collection

It was a cross-sectional study conducted among 100 HCWs posted in various wards of dedicated COVID hospital at the RNT Medical College, Udaipur, Rajasthan, India, using a descriptive model over a period of 2 months from April 2020 to May 2020.

Inclusion criteria

- All symptomatic and asymptomatic HCWs above age of 18 years.

Exclusion criteria

- HCWs already on chronic steroid, immuno-suppressant and chemotherapy.
- HCWs who were known case of people living with HIV/AIDS (PLHA) and other immune deficient diseases.
- HCWs not giving consent for study.

All participants enrolled in the present study were from RNT Medical College, Udaipur, Rajasthan and were working in dedicated COVID hospital according to their duty roster. They belonged to different departments such as Internal Medicine, Pulmonary Medicine, Otorhinolaryngology, Anesthesia, Pediatrics and Obstetrics & Gynecology. The nurses and lab technicians who were directly involved in care of COVID-19 patients were also enrolled in the present study. All these subjects were interviewed regarding their basic information, such as age, gender, professional information (occupation, hospital department, shift timing, duty hours) and significant past history, personal history, drug history, reverse transcription polymerase chain reaction [RT-PCR] testing status) were recorded.

All seropositive HCWs were grouped into 3 categories on the basis of clinical features:

- Asymptomatic having no clinical features
- Mild-to-moderate having clinical features such as cough, myalgia, fever <38°C, etc.
- Severe group with acute respiratory distress syndrome (ARDS), myocarditis, acute kidney injury, multi-organ failure, etc.

Follow-up for all seropositive HCWs was done and outcome was observed in the form of discharged and death.

Antibody-based Card Testing

Principle – Immune chromatographic assay

Test kit – Provided by SIDAK Lifecare Pvt. Ltd.

Procedure

- Place test kit on flat surface.
- Load 2 drops of blood into the sample well; then add 1-2 drop of buffer.
- Interpret the result at 15-20 minutes.

Interpretation of results – as shown in Figure 1.

- **Negative result –** If only C band is visible. The absence of any pink line in zones 1 and 2 indicate that no antibodies are present.
- **Positive result –**
  - Along with C band, a band at zone 1 indicates presence of IgM antibodies
  - Along with C band, a band at zone 2 indicates presence of IgG antibodies
  - Along with C band, a band at both zone 1 and 2 indicates presence of both IgM and IgG antibodies.
- **Invalid –** If C band does not appear, the assay is invalid.

Data Analysis

The collected data were entered in a Microsoft Excel Sheet. Graphs and tables were generated using Microsoft Word and Microsoft Excel. All interval data and proportions have been expressed as percentages.

RESULTS AND OBSERVATIONS

Out of 100 HCWs, 68% were male and 32% were female with mean age of 31.90 years. Eighty-three (83%) were in the age group of 20-40 years, while 17 (17%) were in the age group of above 40 years. In the present study, HCWs were included from various departments, including 35% from Internal Medicine, 13% from Anesthesia, 9% from Pediatrics, 7% from Otorhinolaryngology, 4% from Obstetrics and Gynecology, 3% from Surgery and 2% from Pulmonary Medicine department; 19% were Nurses and 8% were Lab Technicians (Table 1).

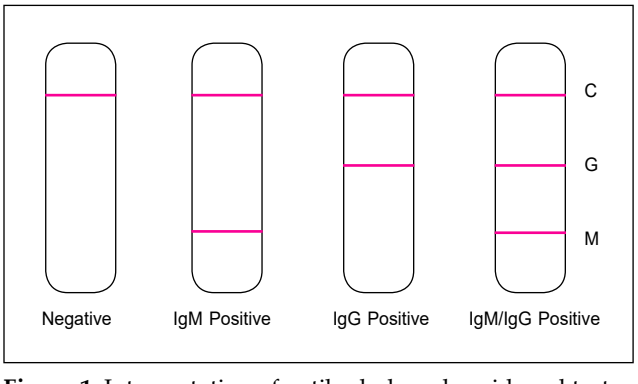

Figure 1. Interpretation of antibody-based rapid card test.

Table 2 shows the seroprevalence among HCWs. Out of 100 HCWs, only 16% developed seropositive response while rest of 84% were seronegative. In seropositive HCWs, 8% developed IgM antibody, 8% developed IgM and IgG both, while none of them had IgG antibody positivity.

Table 3 shows the clinical profile of seropositive HCWs. Majority of them, i.e., 13 (81%) remained asymptomatic,

Table 1. Epidemiological Profile of HCWs

Category	HCWs (No.)	Percentage (%)
Age		
20-40 years	83	83
Above 40 years	17	17
Sex		
Male	68	68
Female	32	32
Departments		
Internal Medicine	35	35
Nurses	19	19
Anesthesia	13	13
Pediatrics	9	9
Lab Technicians	8	8
Otorhinolaryngology	7	7
Obstetrics and Gynecology	4	4
Surgery	3	3
Pulmonary Medicine	2	2

Table 2. Seroprevalence Among HCWs

Category	Number	Percentage (%)
Total HCWs	**100**	
Seronegative	84	84
Seropositive	16	16
IgM positive	8	8
IgG positive	0	0
Both IgM and IgG positive	8	8

Table 3. Clinical Profile and Outcome Among Seropositive HCWs

Clinical profile of seropositive HCWs	Total seropositive HCWs (n = 16)	% of HCWs	Outcome
Asymptomatic	13	81	Discharged
Mild-to-moderate	3	19	Discharged
Severe	0	0	

3 (19%) developed mild-to-moderate clinical features such as cough, sore throat and fever, whereas no one had severe degree of illness.

DISCUSSION

HCWs are at the highest risk for acquiring infections during novel COVID-19 outbreaks. Thus, if transmission rises, the number of front line HCWs could become insufficient to respond to the healthcare demand. To cope with this scenario, several strategies, including periodic screenings, weekly shifts, limiting work duration per day, training program which includes proper use of PPEs and way of sanitization by which we can protect ourselves, have been suggested.

At present, to the best of our knowledge, no such a type of study is yet available from India that suggests seroprevalence rate, clinical presentation and outcome in COVID-19 disease in HCWs. Hence, we have planned to see seropositivity among front line HCWs who are working in a dedicated COVID hospital, which may be helpful in resources planning.

In the present study, 100 HCWs were included out of which 68% were male and 32% were female. They were grouped according to age and it was found that 83% were from younger age group between 20 and 40 years of age, whereas rest 17% were above the age of 40 years.

In the present study, HCWs were selected from various departments depending on the duty roster of COVID hospital - 35% were from Internal Medicine, 19% were Nurses, 13% were from Anesthesia, 9% were from Pediatrics, 8% were Lab Technician, 7% were from Otorhinolaryngology, 4% were from Obstetrics and Gynecology, 3% were from surgery and rest 2% were from Pulmonary Medicine. In a study conducted by Fujita et al,[10] a total of 92 HCWs were recruited. Of these, medical doctors, nurses and medical clerks constituted 45.7%, 52.2% and 2.2% of the participants, respectively. Fifty-nine of these (64.1%) were women with the majority of participants in their twenties and thirties. The common place of work was otolaryngology department, followed by respiratory and emergency medicine departments. The study done by Fujita et al matches with the present study in respect to age distribution but does not match regarding sex and department distribution, due the fact that the maximum subjects were selected according to duty roster of COVID hospital.

The present study was carried out among 100 HCWs out of which 16% developed seropositive response, while rest of 84% were seronegative. Among seropositive ones, 8% developed IgM antibody, 8% developed IgM/IgG both, while none of them had only IgG antibody positivity. A similar study conducted by Garcia-Basteiro et al,[11] was conducted among 578 HCWs in a large Spanish reference hospital. Investigators found that the cumulative prevalence of SARS-CoV-2 infection was 11.2% and further among those with seropositivity, they observed 6.2%, 7.6%, 9.3% had IgM, IgG and both IgG/IgM/IgA antibody response, respectively.

In the present study, seroprevalence found was lower than expected, which could be explained by sufficient availability of PPE, proper donning and doffing by HCWs because of effective training before duties, early implementation of RT-PCR screening programs in HCWs working in COVID-19 units, coupled with timely case identification and effective contact tracing and quarantines for those outside COVID-19 unit.

On analyzing clinical profile of seropositive HCWs, it was observed that majority of them, i.e., 13 (81%) were remained asymptomatic, 3 (19%) developed mild-to-moderate clinical features such as cough, sore throat and fever, whereas none of them had severe degree of illness like atypical pneumonia, ARDS, myocarditis, acute kidney injury and multiple organ dysfunction syndrome and none of them required ventilator support and ICU care while the study done by Garcia-Basteiro et al found 80% of seropositive HCWs were symptomatic with mild-to-moderate symptoms. In the present study, most of the seropositive HCWs were asymptomatic and they didn't develop complications which could be explained by low viral load, younger age groups, no associated comorbidity, good immune status, proper use of PPEs, less contact time with COVID patients, and high standard of infection control strategy at our institute.

The present study is too small to conclude the clear picture about COVID-19 infection in HCWs, but it was found that infection rate was 16% among HCWs and majority of them were asymptomatic, which may spread infection across other population groups; hence,

it is advisable that all these HCWs should undergo RT-PCR screening programs/antibody-based rapid card testing as per protocol, which may pick up disease earlier and stop spreading further.

We further say that institutional quarantine, an essential evil, still remains a dilemma as we need to balance between safety of HCWs and their family versus our limited resources.

CONCLUSION

From the present study which was carried out over 100 HCWs, we conclude that COVID-19 disease is common in HCWs with 16% found seropositive. Majority of them remained asymptomatic, i.e., 81%, whereas remaining 19% had mild-to-moderate degree of disease. No HCWs had severe illness or required ventilator support and ICU care. This may be due to proper use of PPEs and other IPC measures. It is advisable that this high-risk population of HCWs should follow IPC protocol as well as institutional quarantine protocol, screening and training at timely interval to reduce further seroprevalence rate among them.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.
2. Weiss SR, Navas-Martin S. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiol Mol Biol Rev. 2005;69(4):635-64.
3. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 – 11 March 2020. Available at: https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed March 17, 2020.
4. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med. 2020;382(13):1199-207.
5. Joseph B, Joseph M. The health of the healthcare workers. Indian J Occup Environ Med. 2016;20(2):71-2.
6. Kalra A, Michos ED, Chinnaiyan KM. COVID-19 and the healthcare workers. European Heart J. 2020;00:1-2.
7. 90,000 healthcare workers infected with COVID-19: ICN. www.aa.com.tr. Retrieved 13 May 2020.
8. The Lancet. COVID-19: protecting health-care workers. Lancet. 2020;395(10228):922.
9. 548 doctors, nurses, paramedics infected with Covid-19 across India: Report. Accessed from: https://www.hindustantimes.com/india-news/548-docs-nurses-paramedics-infected-with-covid-19-across-india-report/story-o2pM3w2adM4g3PXI6TBlkN.html
10. Fujita K, Kada S, Kanai O, Hata H, Odagaki T, Satoh-Asahara N, et al. Quantitative SARS-CoV-2 antibody screening of healthcare workers in the southern part of Kyoto city during the COVID-19 peri-pandemic period. Accessed via medRxiv preprint surver; URL https://www.medrxiv.org/content/10.1101/2020.05.12.20098962v2.article-info.
11. Garcia-Basteiro AL, Moncunill G, Tortajada M, Vidal M, Guinovart C, Jimenez A, et al. Seroprevalence of antibodies against SARS-CoV-2 among health care workers in a large Spanish reference hospital. medRxiv 2020.04.27.20082289; Accessed via medRxiv preprint surver; URL https://www.medrxiv.org/content/10.1101/2020.04.27.20082289v1

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No Improvement in Remission with Combo Therapy for IBD

Combination therapy with immunomodulators in addition to the newer biologics ustekinumab or vedolizumab was found not to improve the rates of clinical remission or response, endoscopic remission or persistence of therapy at 1 year in patients with Crohn's disease or ulcerative colitis, reported an international study published online in *Clinical Gastroenterology and Hepatology*.

Investigators noted that similar number of patients remained on treatment or exhibited endoscopic response at 12 months with either monotherapy with one of these newer non-anti-TNF (tumor necrosis factor) biologics or combination therapy with a biologic and methotrexate or a thiopurine. For patients receiving vedolizumab, adding a thiopurine or methotrexate led to no difference in clinical remission or response compared to monotherapy at Week 14 (68.2% vs. 74.1%; p = 0.22), Week 30 (74.3% vs. 75.6%; p = 0.78) and Week 54 (78.3% vs. 72.9%; p = 0.33). Additionally, in those receiving ustekinumab, no difference was evident in clinical remission or response with combination therapy at Week 14 (54.6% vs. 65.8%; p = 0.08), Week 30 (71.6% vs. 77.4%; p = 0.33) and Week 54 (62.1% vs. 67.0%; p = 0.52). About 48.9% of patients on combination therapy and 45% on monotherapy had therapy failure during the first-year follow-up… (*Medpage Today*)

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

A Study to Estimate Spontaneous Bacterial Peritonitis in Chronic Liver Disease

SANDEEP AHARWAR*, RAJA GULFAM SHAIKH†

ABSTRACT

Introduction: Spontaneous bacterial peritonitis (SBP) is an infection of initially sterile ascitic fluid without a detectable, surgically treatable source of infection. We analyzed the prevalence, clinical and laboratory features of SBP in 100 patients of chronic liver disease to identify risk factors for incidence and mortality. **Material and methods:** One hundred patients (mean age 46 years, 92% males) with chronic liver disease and ascites were studied in our prospective study during the period from October 2013 to November 2014 in Gajra Raja Medical College, Gwalior, Madhya Pradesh. Diagnosis of SBP was based on: An ascitic fluid polymorphonuclear leukocyte (PMN) count ≥250/mm^3 *and* ascitic fluid culture positive for single microorganism *With* An absence of source of infection in abdomen. Clinical features of the patients were studied on the basis of history and clinical examination. Relevant blood studies were sent as soon as possible and results analyzed. **Results:** Overall prevalence of SBP was found to be 22% in our study. Symptoms significantly associated with increased incidence of SBP were icterus (p value 0.036), altered sensorium (p value 0.012) and abdominal tenderness (p value 0.003). Higher Child-Pugh grade (Grade C 18.4%) and increased MELD (p value 0.0009) score were associated with higher risk of developing SBP. Also, increasing MELD score was associated with a higher mortality (p value 0.032). SBP +ve group was associated with an increased mortality (p value 0.01) as compared to SBP -ve group. Mortality in SBP was strongly associated with higher serum creatinine level (p value 0.0006). **Conclusion:** Icterus, altered sensorium, abdominal tenderness and raised creatinine were associated with increased risk of SBP. Child-Pugh grade and MELD score were associated with increased risk of SBP in cirrhosis in the present study. MELD score was found to be significantly associated with mortality in SBP.

Keywords: Chronic liver disease, spontaneous bacterial peritonitis, cirrhosis

Cirrhosis of liver is one of the most common conditions affecting the liver chronically and causing a very high mortality and morbidity, leading to a great burden affecting both quality of life and longevity.[1] It predisposes the patient to a number of complications, one of the most common being ascites.[2,3] Ascites itself has a number of complications, like ascitic fluid infection, cardiorespiratory embarrassment and umbilical hernia. One of the form of ascitic fluid infection is spontaneous bacterial peritonitis (SBP). SBP is an infection of initially sterile ascitic fluid without identifiable, surgically treatable source of infection.[4] This severe complication of cirrhotic ascites was first described in the mid-1960s.[5] Along with hepatorenal syndrome, it is stated as most common life-threatening complication in cirrhosis.[6] Culture-negative neutrocytic ascites (CNNA) - ascites is sterile, bacterial infection is not demonstrable by culturing; only an increased number of polymorphonuclear leukocytes (PMNs) above the limit of 250 cells/mm^3 is revealed. Monomicrobial non-neutrocytic bacterascites (or only bacterascites) has rarely been described. In this disorder, positive bacterial cultivation is presented without increased leukocytes.

SBP and CNNA are identical, both from the clinical perspective as well as therapeutic approach. The consensus conference of the International Ascites Club[7] thus recommends not to differentiate between these two entities. Even in case of CNNA, SBP is talked about, and a raised number of neutrophils in ascites is enough for the diagnosis. A spontaneous infection complicating ascites may appear even in malignant ascites;[8] however, it is found most often in cirrhotic ascites.

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SBP can present as a full blown syndrome with fever, hypotension, abdominal pain, abdominal tenderness, altered mentation or one or more of its components may be missing.[6,9-11] So, all cirrhotic patients must be screened for SBP with ascitic fluid analysis, PMN count and culture of ascitic fluid.[12-15] Patients must be treated aggressively with antibiotics as they have poor prognosis and high mortality if not treated early.

Present study was undertaken to identify SBP in chronic liver disease patients with ascites with focus on prevalence, presenting features and laboratory findings to identify risk factors for SBP in cirrhotic patients and risk factors for mortality in SBP patients.

MATERIAL AND METHODS

One hundred patients with chronic liver disease and ascites were studied during the period from October 2013 to November 2014. The results obtained were subjected to standard statistical methods for analysis and relevant conclusions were drawn from them. Results were expressed as mean (± standard deviation [SD]). Chi-square test was used wherever applicable. P value ≤0.05 was considered statistically significant.

Inclusion Criteria

- All the cases of chronic liver disease with ascites on the basis of clinical, laboratory and radiological features suggestive of chronic liver disease.

Exclusion Criteria

- Patients found to have a secondary cause of peritonitis like ruptured liver abscess, perinephric abscess, etc.
- Patients found to have more than one organism in ascitic fluid culture.
- Patients who had an antibiotic treatment within last 10 days.
- Patients having a history of recent paracentesis within 10 days.

Diagnosis of SBP

Diagnosis of SBP was based on:

An ascitic fluid PMN count ≥250/mm^3

And

Ascitic fluid culture positive for single microorganism

With

An absence of source of infection in abdomen.

All patients underwent paracentesis within 24 hours of admission. About 30 mL of ascitic fluid was aspirated with aseptic precautions; 10 mL of fluid was sent to laboratory in sterile condition for conventional culture; 10 mL of ascitic fluid was utilized for biochemical and cytological examination.

Clinical features of the patients were studied on the basis of history and clinical examination. Relevant blood studies were sent as soon as possible and results analyzed.

RESULTS

Most of the patients studied were males (n = 92; Table 1).

Age of the patients studied ranged from 22 to 85 years, with the most number of patients in the age group of 40-49 years (n = 41); mean age of the patients studied was 46.81 ± 13.18 years (Table 2).

Among 100 patients of chronic liver disease studied, 22 patients showed >250 PMN/mm^3 of ascitic fluid (Table 3). Of these 22 patients, half of them (n = 11) showed ascitic fluid culture positive for single microorganism. Including its variants, overall prevalence of SBP was found to be 22%.

This makes up the prevalence of classical SBP to be 11% and the prevalence of CNNA to be 11% as well. None of the patients who had ascitic fluid PMN count <250/mm^3 showed positive ascitic fluid culture, so there

Table 1. Gender Distribution of Patients Studied

Sex	No. of cases	Percentage (%)
Female	8	8.0
Male	92	92.0
Total	**100**	**100.0**

Table 2. Age Distribution of Patients Studied

Age in years	No. of cases	Percentage (%)
20-29	6	6.0
30-39	18	18.0
40-49	41	41.0
50-59	15	15.0
60-69	9	9.0
70-79	9	9.0
>80	2	2.0
Total	**100**	**100.0**

Table 3. Prevalence of Spontaneous Bacterial Peritonitis

Total no. of patients (100)	Ascitic PMN count >250/mm^3		Ascitic PMN count <250/mm^3		Polymicrobial bacterascites
	Culture positive	Culture negative	Culture positive	Culture negative	
	SBP	CNNA	Bacterascites	Ascites	
100	11	11	0	78	0

was no patient with monomicrobial non-neutrocytic bacterascites. None of the patients showed ascitic fluid culture positive for more than one microorganism, so no patient of polymicrobial bacterascites was seen.

All of the patients (Table 4) who were positive for SBP (n = 11) belonged to either alcohol related (n = 9) or hepatitis B related (n = 2) chronic liver disease.

Most of the patients (Table 5) were having icterus (n = 62), of which 10 were positive for SBP; 30 patients had pedal edema, of which 2 were positive for SBP; 19 had fever, of which 4 were having SBP; 15 had abdominal tenderness, of which 5 were positive for SBP; 10 patients had flapping tremors, of which 2 were positive for SBP.

Coming to the mode of presentation, most of the patients presented with increased abdominal distension (n = 72), of which 6 were positive for SBP, followed by abdominal pain in 34 patients, of which 5 were positive for SBP. Nineteen patients presented with fever, of which 4 were positive for SBP; altered sensorium was evident in 18 patients, of which 5 were positive for SBP. Sixteen presented with gastrointestinal (GI) bleeding, of which 2 were positive for SBP; vomiting was evident in 10 patients, of which only 1 patient was positive for SBP and reduced urine output presented in 6 patients, of which 2 were positive for SBP (Table 6).

Icterus (p value 0.036), altered sensorium (p value 0.012) and abdominal tenderness (p value 0.003) were found to be significantly associated with SBP +ve group as compared to those in SBP -ve group.

Abdominal pain (p = 0.39), increased abdominal distension (p = 0.17), vomiting (p = 0.91), fever (p = 0.13), reduced urine output (p = 0.074), GI bleeding (p = 0.81), pedal edema (p = 0.365) and flapping tremors (p = 0.338) were not found to be of significant value.

Seventeen of the total 100 patients belonged to Child-Pugh Grade A (Table 7), out of which none of the patients had SBP. Thirty-four patients belonged to Child-Pugh Grade B, of which 2 patients were positive for SBP making 5.9% of the patients in Grade B. Most of the patients, i.e., 49, belonged to Grade C, of which 9 patients

Table 4. Etiology in Correlation with SBP

Etiology of CLD	Total No. of cases	Positive cases (SBP)	% positivity
Alcoholic liver disease	79	9	11.4
HBsAg positive	14	2	14.2
HCV related	2	0	0.0
NASH	4	0	0.0
NCPF	1	0	0.0
Total	**100**	**11**	**11**

CLD = Chronic liver disease; HBsAg = Hepatitis B surface antigen; HCV = Hepatitis C virus; NASH = Nonalcoholic steatohepatitis; NCPF = Noncirrhotic portal fibrosis.

Table 5. Clinical Signs in Correlation with SBP

Signs	No. of cases (n = 100)	Positive for SBP (n = 11)	Percentage (%)
Icterus	62	10	16.1
Fever	19	4	21.1
Abdominal tenderness	15	5	33.3
Flapping tremors	10	2	20.0
Pedal edema	30	2	6.7

Table 6. Mode of Presentation in Correlation with SBP

Mode of presentation	Total No. of cases (n = 100)	Positive for SBP (n = 11)	Percentage (%)
Abdominal pain	34	5	14.7
Increased abdominal distension	72	6	8.3
Fever	19	4	21.1
Vomiting	10	1	10.0
Altered sensorium	18	5	27.8
GI bleeding	16	2	12.5
Reduced urine output	6	2	33.3

had SBP, making 18.4% of the patients in Grade C. So, a higher Child-Pugh grade was found to be associated with higher percentage of patients having SBP.

Mean value of MELD (Model for End-stage Liver Disease) score (Table 8) in patients who were SBP +ve was 24.4 with a SD of 6.99 as compared to 16.6 in SBP -ve group with SD of 7.16 with a p value of 0.0009, suggesting that increasing MELD score is associated with a higher risk of developing SBP.

Comparing mean laboratory investigations (Table 9) between SBP +ve and SBP -ve groups, mean total bilirubin (p value 0.002) and INR (p < 0.001) were only significantly associated with SBP +ve group.

From among 100 patients selected, total 4 patients expired. Of SBP -ve group (n = 89), 2 patients expired while in SBP +ve group also, 2 patients expired (Table 10). P value came out to be 0.010 signifying

Table 7. Child-Pugh Classification and SBP

Child-Pugh grade	Total cases	SBP +ve	SBP -ve	% positivity
A	17	0	17	0.0
B	34	2	32	5.9
C	49	9	40	18.4
Total	**100**	**11**	**89**	**11.0**

Table 8. MELD Score in Correlation with SBP

	No. of patients	Mean MELD	SD
SBP -ve	89	16.6	7.16
SBP +ve	11	24.4	6.99

Unpaired *t*-test, p value 0.0009.

Table 9. Comparison of Mean Investigations for SBP +ve and -ve Groups

Investigations	SBP +ve		SBP -ve		P value
	Mean	SD	Mean	SD	
Hemoglobin (g/dL)	8.4	2.2	8.3	2.5	0.9
WBC count (/mm^3)	7215.4	3723.8	5763.6	2136.0	0.2
Total bilirubin	**3.1**	**3.8**	**7.4**	**6.8**	**0.002**
SGOT (IU/L)	73.7	63.4	95.6	53.0	0.274
SGPT (IU/L)	53.5	37.3	79.4	76.6	0.06
SAP (IU/L)	83.5	69.7	81.6	55.2	93
INR	**1.5**	**0.4**	**2.0**	**0.4**	**<0.001**
Blood urea (mg %)	46.6	39.2	53.8	26.3	0.55
S. creatinine (mg %)	2.3	6.2	1.6	0.6	0.69
S. protein (T) (g/dL)	3.8	0.6	3.9	0.5	0.79
S. albumin (g/dL)	2.3	0.7	1.9	0.7	0.11
Ascitic fluid total protein (g/dL)	1.9	0.4	1.9	0.4	0.68
Ascitic fluid albumin (g/dL)	0.5	0.1	0.4	0.2	0.55

Unpaired *t*-test

Table 10. Correlation of SBP with Mortality

	SBP +ve	SBP -ve
Survived	9	87
Expired	2	2
Total	**11**	**89**

Table 11. Laboratory Features as Mortality Predictors in SBP

Lab investigations	SBP +ve expired (2)		SBP +ve survived (9)		P value
	Mean	± SD	Mean	± SD	
Hemoglobin (g/dL)	9.1	2.3	8.2	2.6	0.68
WBC count (/mm^3)	4350.0	919.2	6077.8	2233.1	0.14
Total bilirubin (mg %)	6.4	1.7	7.7	7.6	0.65
SGOT (IU/L)	97.5	2.1	95.2	59.2	0.91
SGPT (IU/L)	59.0	24.0	83.9	84.4	0.46
SAP (IU/L)	105.5	6.4	76.3	60.3	0.19
INR	2.0	0.2	2.0	0.5	0.97
Blood urea (mg %)	55.5	17.7	53.4	28.7	0.87
S. creatinine (mg %)	2.3	0.6	1.4	0.5	0.0006
Ascitic fluid total protein (g/dL)	2.1	0.6	1.9	0.3	0.71

Unpaired *t*-test

Table 12. MELD Score in Correlation with Mortality in SBP

SBP +ve and outcome	N	Mean MELD score	SD
Expired	2	30.50	2.121
Survived	9	23.11	7.008

Unpaired *t*-test, p = 0.032.

that SBP +ve group was associated with an increased mortality as compared to SBP -ve group.

On comparing biochemical findings (Table 11), mortality in SBP was strongly associated with higher serum creatinine level in patients who were SBP +ve (p value 0.0006).

The other biochemical parameters, i.e., hemoglobin, white blood cell (WBC) count, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum alkaline phosphatase (SAP), serum bilirubin, international normalized ratio (INR), blood urea and ascitic fluid total protein, were not found to be significantly different between survived and expired group.

Higher MELD score was found to be significantly associated with mortality group (n = 2), as compared to survived group (n = 9).

Thus, it can be said that higher MELD score is associated with increased mortality in SBP +ve patients as shown in Table 12.

DISCUSSION

The present study was conducted in 100 patients of chronic liver disease; 22 had ascitic fluid PMN count >250/mm^3 and 11 patients had ascitic fluid culture for single organism. So, prevalence of classical SBP was 11% and overall prevalence was 22%. Other studies have reported variable prevalence rate (24-30%).[16-21] In studies done by Piroth et al[16] and Dilshad et al,[17] prevalence of SBP was found to be 30%. In an Indian study by Agarwal et al,[18] the prevalence of SBP was 34.14%, while in the study by Gill et al,[19] the prevalence was 24%. In a study by Obstein et al,[20] prevalence was 26%. In a study by Andreu et al,[21] prevalence of SBP was found to be 25.45%.

In the present study, most of the patients of chronic liver disease had alcoholic liver disease (79%) followed by viral hepatitis B related (14%), HCV related (2%), nonalcoholic steatohepatitis (4%), noncirrhotic portal fibrosis (1%). In the study done by Campillo et al,[22] out of 200 patients, 175 had alcoholic liver disease, 16 were hepatitis C related, 6 hepatitis B related, 1 case was of

hemochromatosis and 1 was cryptogenic cirrhosis. In an Indian study by Mohan and Venkataraman,[23] alcoholism was seen in 55.5% and the cause was hepatitis B related in 21.8%.

SBP should be suspected when a patient with cirrhosis deteriorates, particularly with encephalopathy and/or jaundice. Patients with variceal bleeding or previous SBP are at particular risk. Clinical signs and symptoms such as fever and abdominal pain and systemic leukocytosis may be noted. In our study, icterus (p value 0.036), altered sensorium (p value 0.012) and abdominal tenderness (p value 0.003) were found to be significantly associated with SBP +ve group as compared to those in SBP -ve group.

Fever (p = 0.13), abdominal pain (p = 0.39), increased abdominal distension (p = 0.17), vomiting (p = 0.91), reduced urine output (p = 0.074), GI bleeding (p = 0.81), pedal edema (p = 0.365) and flapping tremors (p = 0.338) were not found to be of significant value.

Peripheral leukocytosis was found to be a strong indicator for presence of ascitic fluid infection. But these are also nonspecific markers for the presence of ascitic fluid infection and have not been of any statistical significance (p value 0.2) according to this study. Raised bilirubin levels (p value 0.002), and increased INR (p < 0.001) were only seen in most patients of SBP. Ascitic fluid protein levels did not significantly differ between SBP and non-SBP groups of patients and low ascitic protein was not associated with higher incidence of SBP in our study.

Advanced liver disease/Child-Pugh Class C had the highest incidence of spontaneous ascitic fluid infection among patients with cirrhosis. In the present study, 9 patients of 11 patients found to have SBP were present in Child-Pugh score Grade C while only 2 belong to Grade B, suggesting that 18.4% of Grade C patients had SBP while only 5.9% of Grade B had SBP. No patients of Grade A had SBP. In the study done by Campillo et al,[22] Child-Pugh score was associated with higher incidence of SBP and mortality in SBP (0.0011). In the study by Puri et al,[24] 95% of the patients who developed SBP belonged to Child-Pugh Grade C. In the study done by Agarwal et al,[18] 12 of the 14 patients, i.e., 85.71% with SBP belonged to Class C and 2 (14.28%) patients were in Class B Child-Pugh score.

In the present study, mean MELD score of patients with SBP +ve was 24.4 ± 6.99 as compared to 16.6 ± 7.16 for those with SBP -ve, with p value of 0.0009, suggesting that increasing MELD score is associated with a higher risk of developing SBP. In the study by Obstein et al,[20] mean MELD score for SBP +ve was 24 and without SBP was 18 (p = 0.0003). They concluded that MELD score is independently associated with a greater risk of SBP. In the study by Gill et al,[19] mean MELD score for SBP +ve group was 19 ± 2.42 and 15 ± 3.93 for SBP -ve group.

Overall mortality in present study was 4% with SBP +ve group associated with an increased mortality as compared to SBP -ve group (p value 0.01). In the present study, we found serum creatinine as strong predictor for mortality in patients of SBP with chronic liver disease. In a study by Llovat et al,[25] mortality was 17%. Factors associated with increased mortality were presence of upper GI bleeding at admission and PMN count in ascitic fluid. In another study by Rawat and Bhatnagar,[26] mortality was 39%. Factors related were jaundice, hepatic encephalopathy, total leukocyte count, total bilirubin, hyponatremia, serum albumin, INR, blood urea and serum creatinine. Musskopf et al,[27] in 2012, reported mortality of 40%. Factors associated with increased mortality were total bilirubin, serum creatinine and MELD score.

CONCLUSION

A large number of patients suffering from chronic liver disease with ascites were found to be suffering from SBP or its variant (22% in present study). This complication predisposes an individual to additional mortality risk.

Clinical features such as icterus, abdominal tenderness and altered sensorium were found to be associated with a higher risk of SBP. But none of the other clinical features was consistently associated with SBP in all the patients. None of the clinical features in expired group was found to be significantly associated with mortality in SBP. Higher serum creatinine was found to be associated significantly with expired group.

Child-Pugh grade and MELD score were associated with increased risk of SBP in chronic liver disease patients in the present study.

MELD score was found to be significantly associated with mortality in SBP.

REFERENCES

1. Hepatic cirrhosis. In: Sherlock S, Dooley J (Eds.). Diseases of the Liver and Biliary System. 11th Edition, Blackwell Publishing; 2002. pp 365-9.
2. Shah VH, Kamath PS. Portal hypertension and gastrointestinal bleeding. In: Feldman M, Friedman LS, Brandt LJ (Eds.). Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 9th Edition, Philadelphia, PA: Saunders; 2010. pp. 1489-516.

3. Runyon BA. Ascites and spontaneous bacterial peritonitis. In: Feldman M, Friedman LS, Brandt LJ (Eds.). Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 9th Edition, Philadelphia: Saunders Elsevier; 2010. pp. 1517-41.
4. Dore MP, Casu M, Realdi G, Piana A, Mura I. Helicobacter infection and spontaneous bacterial peritonitis. J Clin Microbiol. 2002;40(3):1121.
5. Conn HO. Spontaneous peritonitis and bacteremia in Laennec's cirrhosis caused by enteric organisms. A relatively common but rarely recognized syndrome. Ann Intern Med. 1964;60:568-80.
6. Nevah MI, Fallon MB. Hepatic encephalopathy, hepatorenal syndrome, hepatorenal syndrome and systemic complications of liver disease. In: Feldman M, Friedman LS, Brandt LJ (Eds.). Sleisenger and Fordtran's Gastrointestinal and Liver Disease. 9th Edition, Philadelphia, PA: Saunders; 2010. pp. 1543-55.
7. Rimola A, García-Tsao G, Navasa M, Piddock LJ, Planas R, Bernard B, et al. Diagnosis, treatment and prophylaxis of spontaneous bacterial peritonitis: a consensus document. International Ascites Club. J Hepatol. 2000;32(1):142-53.
8. Makharia GK, Sharma BC, Bhasin DK, Singh K. Spontaneous bacterial peritonitis in a patient with gastric carcinoma. J Clin Gastroenterol. 1998;27(3):269-70.
9. Barreales M, Fernández I. Spontaneous bacterial peritonitis. Rev Esp Enferm Dig. 2011;103(5):255-63.
10. Parsi MA, Atreja A, Zein NN. Spontaneous bacterial peritonitis: recent data on incidence and treatment. Cleve Clin J Med. 2004;71(7):569-76.
11. Moore CM, Van Thiel DH. Cirrhotic ascites review: Pathophysiology, diagnosis and management. World J Hepatol. 2013;5(5):251-63.
12. Riggio O, Angeloni S. Ascitic fluid analysis for diagnosis and monitoring of spontaneous bacterial peritonitis. World J Gastroenterol. 2009;15(31):3845-50.
13. Runyon BA, Umland ET, Merlin T. Inoculation of blood culture bottles with ascitic fluid. Improved detection of spontaneous bacterial peritonitis. Arch Intern Med. 1987;147(1):73-5.
14. Runyon BA, Canawati HN, Akriviadis EA. Optimization of ascitic fluid culture technique. Gastroenterology. 1988;95(5):1351-5.
15. Runyon BA, Antillon MR, Akriviadis EA, McHutchison JG. Bedside inoculation of blood culture bottles with ascitic fluid is superior to delayed inoculation in the detection of spontaneous bacterial peritonitis. J Clin Microbiol. 1990;28(12):2811-2.
16. Piroth L, Pechinot A, Di Martino V, Hansmann Y, Putot A, Patry I, et al. Evolving epidemiology and antimicrobial resistance in spontaneous bacterial peritonitis: a two-year observational study. BMC Infect Dis. 2014;14:287.
17. Husain A, Qayyum A, Dilshad M, et al. Bacteriology of spontaneous bacterial peritonitis. Professional Med J. 2007;14(4):551-5.
18. Agarwal MP, Choudhury BR, Baneerjee BD, Kumar A. Ascitic fluid examination for diagnosis of spontaneous bacterial peritonitis in cirrhotic ascites. JIACM. 2008;9(1):29-32.
19. Gill AS, Singh A, Matreja PS, Chinna RS, Mahajan R, Chhina DK. Spontaneous bacterial peritonitis in alcoholic liver chirrhosis: An Indian perspective. Euroasian J Hepato-Gastroenterol. 2012;2(1):14-9.
20. Obstein KL, Campbell MS, Reddy KR, Yang YX. Association between model for end-stage liver disease and spontaneous bacterial peritonitis. Am J Gastroenterol. 2007;102(12):2732-6.
21. Andreu M, Sola R, Sitges-Serra A, Alia C, Gallen M, Vila MC, et al. Risk factors for spontaneous bacterial peritonitis in cirrhotic patients with ascites. Gastroenterology. 1993;104(4):1133-8.
22. Campillo B, Richardet JP, Kheo T, Dupeyron C. Nosocomial spontaneous bacterial peritonitis and bacteremia in cirrhotic patients: impact of isolate type on prognosis and characteristics of infection. Clin Infect Dis. 2002;35(1):1-10.
23. Mohan P, Venkataraman J. Prevalence and risk factors for unsuspected spontaneous ascitic fluid infection in cirrhotics undergoing therapeutic paracentesis in an outpatient clinic. Indian J Gastroenterol. 2011;30(5):221-4.
24. Puri AS, Puri J, Ghoshal UC, Sharma BC, Saraswat VA, Ayyagari A, et al. Frequency, microbial spectrum and outcome of spontaneous bacterial peritonitis in north India. Indian J Gastroenterol. 1996;15(3):86-9.
25. Llovet JM, Planas R, Morillas R, Quer JC, Cabré E, Boix J, et al. Short-term prognosis of cirrhotics with spontaneous bacterial peritonitis: multivariate study. Am J Gastroenterol. 1993;88(3):388-92.
26. Rawat N, Bhatnagar MK. Study of prognostic factors in spontaneous bacterial peritonitis in Indian population. JAPI. 2005;53:350.
27. Musskopf MI, Fonseca FP, Gass J, de Mattos AZ, John JA, de Mello Brandão AB. Prognostic factors associated with in-hospital mortality in patients with spontaneous bacterial peritonitis. Ann Hepatol. 2012;11(6):915-20.

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

A Pilot Study to Assess the Knowledge, Attitude and Practice Among Healthcare Practitioners in India Regarding Tobacco Use and Cessation

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ABSTRACT

Background: Article 14 of the World Health Organization (WHO)'s Framework Convention on Tobacco Control (FCTC) recommends appropriate 'demand reduction measures concerning tobacco dependence and cessation', which includes, among others, "2(b) …. diagnosis and treatment of tobacco dependence and counseling services on cessation of tobacco use in national health and education programs, plans and strategies, with the participation of health workers, community workers and social workers as appropriate". The role of healthcare professionals (HCPs) is critical in demand reduction strategies in the domain of tobacco dependence, control and cessation. **Objective:** This study was undertaken to assess the prevalent knowledge, attitude and practices among the HCPs on tobacco use and cessation. **Methods:** Three groups of HCPs namely, medical doctors, dentists and nurses were requested to participate in the survey using a questionnaire in online and offline mode. **Results:** Significant deficiencies of knowledge, attitude and practice, in all three groups of HCPs covered in the study were found in the domain of tobacco and tobacco cessation. **Conclusions:** The findings of this pilot study highlight existence of a significant policy and practice gap in India among the HCPs' approach to tobacco cessation. Strengthening their knowledge base on tobacco, harm reduction principles and tobacco cessation practices has the potential to enhance the rate of tobacco cessation. This can aid the ongoing national effort in tobacco control to reduce the massive disease and death burden in India from current tobacco use.

Keywords: Healthcare professionals, tobacco cessation, smoking tobacco, smokeless tobacco, policy and practice gap

The Framework Convention on Tobacco Control (FCTC) of World Health Organization (WHO) refers to a comprehensive public health response to the global tobacco epidemic, which was negotiated by and adopted at the World Health Assembly (WHA) held in Geneva in May 2003 as the first WHO treaty under Article 19 of the WHO constitution.[1,2] The provisions of the treaty remain legally binding to all ratifying countries. There are 181 parties to the FCTC. As of July 2017, there were seven countries, including the USA, who had signed but not ratified the treaty, while nine countries had neither signed nor ratified it.[3] India took the lead in including the provisions of the FCTC into a legislative framework by enacting appropriate parliamentary legislations in 2005. This treaty and its legislative incorporation were developed in response to a rapid globalization of the tobacco epidemic due to multiple factors contributing to its growth in India and elsewhere. Article 14 of FCTC envisions member countries to take appropriate 'demand reduction measures concerning tobacco dependence and cessation', which includes, among others, "2(b) …. diagnosis and treatment of tobacco dependence and counseling services on cessation of tobacco use in national health and education programs, plans and strategies, with the participation of health workers, community workers and social workers as appropriate".[1] This provision highlights the important

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role of healthcare professionals (HCPs) in demand reduction strategies since they are the first-responders for any lay person who seeks help in the domain of tobacco dependence, control and cessation.

India is the second highest tobacco consuming country in the world housing ~270 million tobacco users in 2016-17.[4] This includes an estimated >11% of world's cigarette smokers, and larger sections of the population indulging in either (a) smoking tobacco in its alternative or local forms (e.g., *bidis, hookahs, chilams,* etc.), (b) chewing or masticating it in form of smokeless tobacco (SLT) such as *khaini, zarda, gutkha, betel nut/ quid,* etc. or (c) both (mixed users).[5] It is estimated that about 80% of global SLT burden is from India.[6] Consequently, it is estimated that today every 10th adult is a smoker (~100 million) and every 5th a SLT user (~199 million) in India. The economic burden of tobacco-related health issues in India is also staggering. According to the Ministry of Health and Family Welfare (MoHFW), Government of India's report for 2011, the total economic costs attributable to tobacco use for persons aged 35-69 years amounted to US$ 22.4 billion (approx. equivalent to Rs. 1,04,500 crore).[7] Therefore, India represents a complex public health challenge stemming from not only tobacco smoking in different forms, but also from the use of SLT products. Tobacco use kills an estimated million people annually in India.[8] The Government of India's plan of action in the domain formulated by MoHFW on the control of noncommunicable diseases (NCDs) aims to reduce the prevalence of tobacco by 15% by the end of the current year (2020) and further by 30% by 2025.[8]

According to WHO's assessment, since adoption of FCTC in 2005, progress towards implementation of its different articles has been uneven with implementation rates ranging from 13% to 88% for different articles in different countries, including India[9] and in 2019 the MPOWER criteria related to cessation policy in India stands fully implemented.[10] The data for India over the intervening 8-year period between the Global Adult Tobacco Survey (GATS)-1 covering 2009-10 period[11] and GATS-2 covering 2016-17 period[5] shows that the absolute tobacco usage as well as the prevalence of tobacco use among minors (15-17 years) decreased by 6% each (from 34.6% to 28.6% and from 10% to 4%, respectively). The average age of initiation of tobacco simultaneously increased by 1 year (from ~17.9 to ~18.9 years for smokers). While these are encouraging trends, GATS-2 data also shows that India had the 2nd lowest quit rate among the GATS-2 countries despite high prevalence of knowledge about the health consequences of tobacco smoking and/or chewing. GATS-2 report further illustrates that only about 55% of smokers and 50% of SLT users ever thought of or intended quitting with poor to very poor success rate.

HCPs play an important role in the Indian healthcare milieu. They are generally trusted well by their patients. Their advice carries substantial weight in the choices and decisions that people take in their health-related behaviors. Tobacco use and cessation advice is no exception. Multiple studies identified a variety of factors influencing the HCPs' services for tobacco cessation support, including location of practice and history of attending formal training programs.[12-14] Gender dynamics were mentioned in studies wherein male HCPs were confident in providing medication for tobacco cessation, whereas most female HCPs expressed lack of competence in delivering behavioral counseling services.[15] A recent study also highlighted the importance of skill building of physicians to complement their commitment to address it through their healthcare practices.[16] These facts bring to fore, once again, the critical role HCPs can play in the domain of demand reduction and cessation of tobacco. Knowledge and infrastructure empowered, and positively motivated HCPs can potentially enhance the rate of decline of tobacco consumption in India in significant measures. Only then we may be able to meet the set target of reduction of prevalence of tobacco in the country by 15% by the end of the current year (2020) and further by 30% by 2025.[8]

OBJECTIVE

This pilot survey was designed to assess the knowledge, attitude and practice (KAP) of HCPs of India in order to assess the existing gaps and lacunae as well as identify opportunities to overcome them.

METHODS

In this pilot project, a study was undertaken to assess the KAP of HCPs towards tobacco control, using a blind, online and offline survey among three sections of HCPs namely, nurses, dentists and doctors from selected regions of the country in a convenience sampling mode. Available sampling frames (e.g., local chapters of professional bodies like the Indian Medical Association [IMA], Indian Dental Association [IDA] and professional affinity groups in professional networks) purposively from the regions of Chennai, Mumbai and Shillong and their adjoining areas (covering the southern, western and the north-eastern

regions of India, respectively) were targeted for data collection. This approach introduced as much randomness in sampling as was possible within the limitations of sampling avenues and the constraints of the study. The sample size for this study was calculated by the formula, 4pq/d2, where prevalence p = 66.7%, q(1-p) = 33.3%, d = 5% (absolute error) based on Grewal et al.[17] Accordingly, we needed a minimum sample size of 355 for the study. The only inclusion criterion for recruitment was that the subject should belong to one of the three categories of a practicing HCP. Within the limits of the study, as stated, we intended to get baseline data to identify measurable indices for India in the domain of KAP of HCPs towards tobacco control and cessation.

A questionnaire comprising 32 questions was developed based on review of the published literature to assess the KAP among HCPs. The questions were based on a previously conducted feasibility study with a smaller sample of HCPs in India (unpublished), and a survey conducted among general practitioners (GPs) in Sweden and the UK.[18] The first section of the questionnaire included socio-demographic questions wherein disclosure of identity was optional. Subsequently, in the following three sections, participants were asked about their (a) knowledge, (b) attitude and (c) practice associated with tobacco and its control and cessation. The last section on 'knowledge gap' intended to assess the knowledge gap as perceived by the subjects. The links to the online questionnaire were sent to prospective subjects meeting the inclusion criteria with a request to participate in the study. In addition, the offline questionnaires were also distributed to subjects meeting the criteria and the data obtained were manually fed into the system. A sample questionnaire is provided as at the end of this article.

The study protocol was approved by the Institutional Research Committee (IRC) vide approval Ref. No: CRL/181/2020, and Approval Number: TMCH/IRC/2020/028 (date: 25/04/2020).

DATA ANALYSES AND STATISTICS

Descriptive statistical analysis was performed, with continuous variables reported as median and categorical variables reported as number or percentage. All data were analyzed using SPSS version 22.0 software. Graphs were plotted using Excel.

RESULTS AND DISCUSSION

A total of 619 HCPs participated in this study, which included 376 (~61%) female responders. The sample consisted of 133 nurses (>21% of total; 100% females; median age 27 years), 162 dentists (>26% of total consisting of 66% female dentists; median age of 24 years) and 324 doctors (>52% comprising ~42% female doctors; median age 24 years). The cohort variably represented 16 states of India with overwhelmingly dominant responses coming from HCPs belonging to Maharashtra, Meghalaya and Tamil Nadu due to the sampling approach (Table 1).

Analysis of the survey gave deep insights into different aspects of KAP of HCPs on tobacco in India. The HCPs covered in this study were predominantly (54-87%) catering to a mixed group of rural and urban patients in their current practice (Table 1). While almost all HCPs

Table 1. Demographic Details of the HCPs

Demographics indicators	HCPs			
	Nurses	Dentists	Doctors	Total
Participants (n)	133	162	324	619
Fraction of the total (%)	>21	>26	>52	100
Female HCPs (%)	100	~66	~42	>60
Median age in years	27	24	24	24
Main patient load (%) attended to: urban, rural or mixed	Mixed (~87)	Mixed (>70) & urban (~23)	Mixed (~54) & rural (~37)	Mixed (>65), rural (~13) & urban (~21)
Prevalence (%) of current tobacco use	~14	~3	~5	~7
Form of tobacco mainly used	SLT	Cigarette	Cigarette	-
Former tobacco use prevalence (%)	~11	~9	~16	~13

were aware of the deleterious effects of tobacco on health (88-92%) and the overwhelming majority of them (83-93%) enquired their patients about their tobacco habit in the routine patient medical history notes, different HCP groups understood ill-effects of tobacco differently (Table 2). A small segment of HCPs were either themselves current users of tobacco (~14% nurses, ~3% dentists and ~5% doctors) or were former users (~11%, ~9% and ~16%, respectively) (Table 1). The choice of tobacco product used by different HCP groups was variable. While nurses (100% females) predominantly used SLTs in different forms (Betel [*Areca*] nut, Oral/chewing tobacco or Betel quid/*Paan*), the dentists and doctors, mix of both genders, were mainly smokers of cigarettes (Table 1).

Among the HCPs covered in this study, the overwhelming majority, ~92% nurses, ~71% dentists and ~79% doctors, considered nicotine from any tobacco product as the main cancer causing chemical of tobacco (Table 3 and Fig. 1), while remaining had a vague understanding of the carcinogenic content of tobacco. Majority of nurses (>63%) were not aware of any tobacco de-addiction guidelines or protocols. But ~71% of dentists and >51% doctors were aware of it (Table 3). Nonetheless, overwhelming majority of all participating HCPs had never received any specific training in tobacco cessation service (Table 3 and Fig. 2). Even though as much as 88-92% of the HCPs generally believed that tobacco cessation was good for the recovery of patients from other pathophysiologies and advised cessation (Table 2), only a small segment of the HCPs offered tobacco cessation assistance supplemented with counseling and aid of medication to patients without (20-29%) or with (13-38%) follow-up (Table 4). A large majority of HCPs desired to receive tobacco cessation-specific training to augment their tobacco-specific care practices (Table 2). Most of them were unaware about tobacco de-addiction centers in their own location, and, perhaps, therefore, were unable to refer needy patients there (Table 4). They did offer some (41-52%) casual general advice to quit but hardly followed it with specific behavioral counseling, medical aids and/or follow-ups for tobacco-related behaviors among the clients (Table 4). Overwhelming majority of HCPs in all three groups had neither attended a course (90-93%) or CME (continuous medical education)/Workshop/Seminar (74-86%) in tobacco cessation, harm reduction or behavioral therapy. With the possible exception of dentists (Table 4),

Table 2. Attitude of the HCPs About Tobacco in Dealings with Patients

Attitude indicators	HCPs			
	Nurses	Dentists	Doctors	Total
Routine medical history includes tobacco habit of patients (%)	~83	~93	~89	>88
Offering any cessation advice to patients (%)	~74	~86	~80	>80
Self-perception of HCPs being qualified to offer cessation support (%)	~66	~64	~56	>60
Interest for augmentation-training in cessation support (%)	Yes: ~83	Yes: ~82	Yes: ~71; Not sure: ~17	Yes: ~76
Tobacco cessation being good (%) for recovery from other pathophysiology	~88	>92	~91	~91

Table 3. Knowledge of the HCPs on Tobacco

Knowledge indicators	HCPs			
	Nurses	Dentists	Doctors	Total
Relatively more damaging tobacco product (%)	SLT (Oral tobacco + Betel nut & quid) (~61)	Smoking tobacco (cig. + *bidi*) (>49)	Smoking tobacco (cig. + *bidi*) (~55)	-
Nicotine of tobacco being a carcinogen (%)	~92	~71	~79	>79
Awareness of tobacco de-addiction guidelines/protocol (%)	~37	>75	>51	~55
Tobacco cessation service-specific training (%)	~20	~27	~10	~17

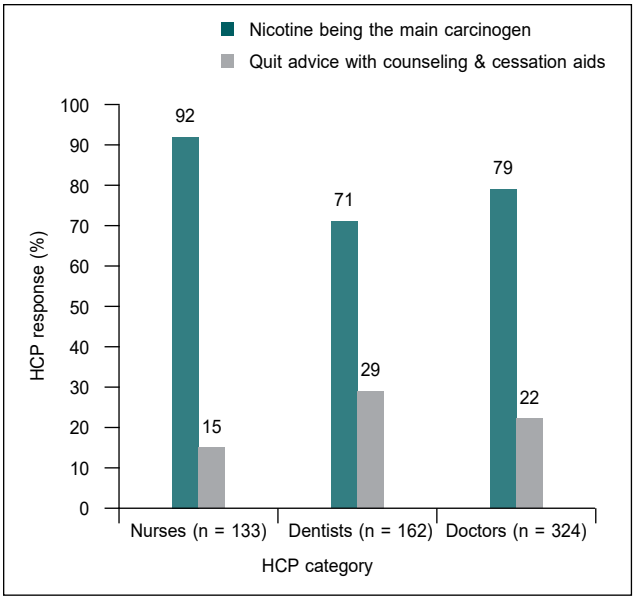

Figure 1. Bar diagram showing the % of HCPs (nurses, dentists and doctors) considering nicotine as the main carcinogen of tobacco *(green)* and the existing level of tobacco cessation service being offered by them to patients *(gray)*.

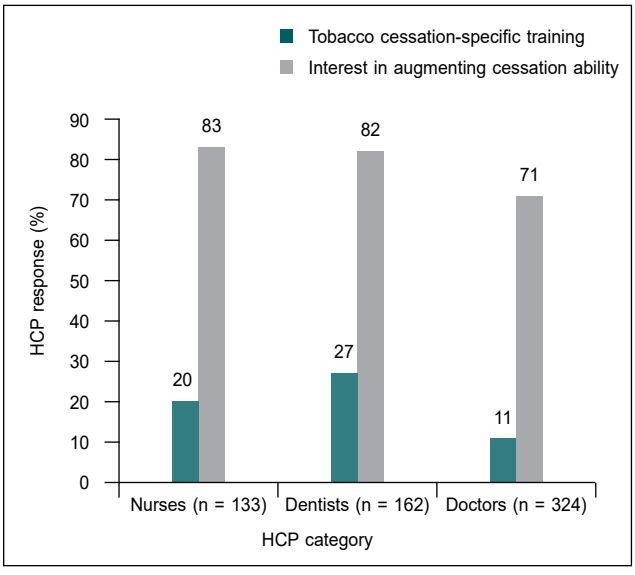

Figure 2. Bar diagram showing the % of HCPs (nurses, dentists and doctors) having received any tobacco-specific training *(green)* and their desire to receive such specific trainings to augment their ability to offer tobacco cessation assistance to patients *(gray)*.

the nurses and doctors were poorly aware of the 5 A's and R's of tobacco cessation service (Table 5).

Majority of HCPs considered nicotine as the main carcinogenic substance of tobacco (Table 3 and Fig. 1). Nicotine is a parasympathomimetic alkaloid, stimulant and the addictive component of tobacco. Like any addictive chemical, nicotine may not be entirely safe. However, apart from its consumption from tobacco products, nicotine is also used by adults worldwide in the form of medically licensed and regulated products such as nicotine patches and gums, among others, as a recommended tobacco cessation aid. According to the UK Medicines Agency,[19] "there is a large body of evidence that medicinal nicotine (in currently licensed forms) is not a significant risk factor for cardiovascular events, and does not cause cancer or respiratory disease". Also, nicotine is not classified as a carcinogen by WHO's International Agency for Research on Cancer.[20] On the contrary, nicotine replacement therapy (NRT) products are on the essential medicines list of the WHO, underscoring the importance attributed by the WHO to medicinal nicotine as a frontline drug for cessation.[21,22]

In countries such as the UK, NRT products are licensed for tobacco harm reduction. This is an important concept that needs to be understood among HCPs to inform why and how medicinal nicotine may be used for as long as necessary by smokers and users of the Indian forms of SLT to achieve tobacco cessation and prevent relapse. Prevalence of such deep and wide nicotine illiteracy among the pilot sample of HCPs surveyed in India highlights a big challenge in getting cessation products to the nearly 270 million tobacco users. The practice of HCPs is bound to be affected if their knowledge and, therefore, attitudes toward nicotine are ill informed.

The HCPs also had no clear idea of the actual carcinogenic content of tobacco, many of which are Group 1 carcinogens (proven carcinogens in humans) - estimated to be up to 60 in different tobacco products.[20,23] While the majority of them knew the potential harm tobacco might cause, they appeared to lack fully or partially the right attitude towards tobacco cessation and control due to a variety of possible reasons. The reasons could include some of themselves being current or former tobacco users, unscientific understanding of unsafe components of tobacco, lack of domain knowledge and training in tobacco de-addiction and cessation services, lack of time for engaging in tobacco cessation, lack of knowledge of availability of other support services in the domain, among others.[12-15] However, it was heartening to note that most HCPs were aware of the serious health implications of tobacco use, and its consequences on the general well-being of the patients. They did realize their lacunae and were keen on filling up the knowledge gaps in the domain by attending specialized trainings/workshops/seminars on the subject by way of CMEs (Fig. 2).

Table 4. Current Practice and Knowledge Gap of the HCPs in Tobacco Domain

Practice/Knowledge gap indicators	HCPs			
	Nurses	Dentists	Doctors	Total
Aware of any de-addiction center in your location	No: >62; Yes: ~32	No: >64; Yes: ~32	No: >64; Yes: ~32	No: >64; Yes: ~32
Referred patients to such centers	>35	>34	>42	~39
Blanket 'quit' advice towards cessation	~41	~49	~52	~49
'Quit' advice with counseling & aid towards cessation	~15	~29	>21	~22
Never attended cessation, harm reduction or behavioral therapy courses	>90	>92	>93	~92
Never attended cessation, harm reduction or behavioral therapy CMEs/ Workshops/Seminars	>86	~74	>85	~83
Unaware of 5 A's & 5 R's of cessation	~70	~26	~73	~60

Table 5. The 5 A's and R's of Tobacco Cessation Service

Attributes of intervention	Explanation
The A's	**A**sk
	Advise
	Assess
	Assist
	Arrange
The R's	**R**elevance
	Risks
	Rewards
	Roadblocks
	Repetition

The first line of defense against tobacco available to the general population is the HCP who could provide necessary information and medical intervention, including counseling, hand-holding and follow-up services.[1,24] HCPs, therefore, are the critical drivers of tobacco cessation effort globally. It is essential that clinicians such as doctors, dentists, nurses and psychiatrists offer their services to the affected population in a coordinated manner for effective tobacco control and cessation.[25] With this background, our pilot study assumes great significance because it finds significant lacunae on this front. Notwithstanding the inherent limitation of the present study based on a convenience sampling method, and small sample size, as stated earlier, the pilot study clearly highlights some startling trends that need due consideration being the very first pilot study on KAP of HCPs covering several states and regions of India. There appears to be significant deficiencies at all levels of KAP, among all three sections of the HCPs covered in the study. In order to eliminate the existing deficiencies, we need composite short-, medium- and long-term strategies of intervention specifically designed to address the three HCP groups.

In short-term strategic intervention, specific CMEs/ Workshops/Seminar on tobacco and tobacco cessation designed separately for three groups of HCPs may be the starting point. In designing such educational materials, the latest global best practice on tobacco cessation will need to be adapted for the Indian context. This should include adequate elucidation of the concept of tobacco harm reduction and the fact that medicinal nicotine is a key tool for cessation, endorsed by the WHO. Such training may be conducted by national and international experts in the domain across all platforms, including face-to-face, audio-visual and online platforms. These educational interventions and upskilling endeavors among HCPs will be the foundation stone for creating a nicotine literate society and influencer community. This has the potential to reap large dividends due to the reach and impact of HCPs on patient behavior. The medium- and long-term approaches might include, but may not be limited to, refresher CMEs, appropriate curricular modifications in medical, dentistry, nursing and allied education systems to include detailed studies on science of tobacco induced damage to health, tobacco control strategies, legal provisions and state-of-the-art of different tobacco cessation strategies practiced across the globe, among others.

Creation of sound infrastructures of tobacco cessation clinics with empowered HCPs, and development of

standard operating procedures (SOPs) for users of different tobacco products will be necessary to achieve the target of tobacco control. It is critical that the HCPs are well-equipped with up-to-date knowledge base, possess a positive attitude with empathy towards tobacco control and cessation, and are fully empowered by a SOP of global standard reflecting best-in-line practices to achieve effective and significant success in offering tobacco cessation service.[24] The complexity of tobacco usage profile prevalent in India today, and the inherent weakness of HCPs in all three domains of KAP related to tobacco, might, at least in part, explain the poor tobacco cessation outcome in India evident by comparing the GATS-1 & 2 data[5,11] as against the goal set by Government of India for the current year-end under FCTC regimen.[7,8] This can aid the ongoing national effort on tobacco control and enhance India's chances of becoming a tobacco-free nation. Based on these study findings, studies involving all zones of India, using a probability based random sampling may be undertaken.

These findings also highlight the massive policy and practice gap prevalent in India among healthcare practitioner's approach to tobacco cessation. Such a gap has serious implications on routine clinical practice as well as on the nation's health. Use of risky oral and smoked tobacco products are a key modifiable behavior that contributes to the ever growing disease burden of preventable NCDs in India. Providing cessation advice to the 270 million tobacco users of India, especially those in rural areas with limited or no access to technology and services, will remain a challenge for the foreseeable future. Enabling and empowering healthcare practitioners, including community health workers and AYUSH practitioners, to provide timely advice and follow-up on tobacco cessation has the potential to reach the diverse geography and population of India quicker. The sooner the FCTC Article 14-based global tobacco cessation policies reach and translate into healthcare practitioners' practice into the deep interiors of India, the greater the likelihood of reduction of India's NCD burden from tobacco use.

CONCLUSIONS

The tobacco usage profile prevalent in India today is highly complex. The findings of this pilot study highlight existence of a significant policy and practice gap in India among the HCPs' approach to tobacco cessation. The existing gaps of HCPs (nurses, dentists and doctors) in all three domains of KAP related to tobacco and tobacco cessation, might, at least in part, explain the poor tobacco cessation outcome in India and has serious implications on routine clinical practice as well as on the nation's health. There is an urgent need to address the issue in order to strengthen HCPs on KAP to enhance the rate of tobacco cessation in India.

Acknowledgment

Authors greatly appreciate and thank (a) Ms Mercy Marbaniang, Shillong for the arduous task of manually entering response data of offline participants on the online portal, and (b) Mr Ahmad Maaitah, doctoral candidate, University of Southampton for prompt and immaculate statistical analyses.

REFERENCES

1. WHO Framework Convention on Tobacco Control, 2003. Geneva: World Health Organization (ISBN: 9241591013).
2. Yach D. The origins, development, effects, and future of the WHO Framework Convention on Tobacco Control: a personal perspective. Lancet. 2014;383(9930):1771-9.
3. Framework Convention Alliance – Parties to the WHO FCTC. 2019. Available at: https://www.fctc.org/parties-ratifications-and-accessions-latest/. Accessed May 08, 2020.
4. GATS-2: Global Adult Tobacco Survey: Fact Sheet India 2016-17. Available at: https://www.who.int/tobacco/surveillance/survey/gats/GATS_India_2016-17_FactSheet.pdf. Accessed May 08, 2020.
5. Asma S, Mackay J, Song SY, Zhao L, Morton J, Palipudi KM, et al. "The GATS Atlas. 2015" (GATS-2), CDC Foundation, Atlanta. Available at: http://gatsatlas.org/. Accessed May 08, 2020.
6. Stepanov I, Gupta PC, Parascandola M, Yershova K, Jain V, Dhumal G, et al. Constituent variations in smokeless tobacco products in Mumbai, India. Tob Regul Sci. 2017;3(3):305-14.
7. Global Adult Tobacco Survey GATS 2 India 2016-17. Tata Institute of Social Sciences, Mumbai and Ministry of Health and Family Welfare, Government of India, New Delhi (ISBN: 978-81-937917-0-7).
8. Report on Tobacco Control in India, 2004 by Ministry of Health and Family Welfare, Government of India. Available at: https://www.who.int/fctc/reporting/Annex6_Report_on_Tobacco_Control_in_India_2004.pdf. Accessed May 08, 2020.
9. 2018 Global progress report on implementation of the WHO FCTC on tobacco control, Geneva: World Health Organization, 2018 (ISBN: 978-92-4-151461-3). Available at: https://www.who.int/fctc/reporting/WHO-FCTC-2018_global_progress_report.pdf. Accessed May 08, 2020.
10. WHO report on the global tobacco epidemic, 2019, Country profile: India. Available at: https://www.who.int/tobacco/surveillance/policy/country_profile/ind.pdf?ua=1. Accessed May 08, 2020.

11. GATS-1: Global Adult Tobacco Survey: India Report 2009-10. Ministry of Health and Family Welfare, Government of India, New Delhi. Available at: https://ntcp.nhp.gov.in/assets/document/surveys-reports-publications/Global-Adult-Tobacco-Survey-India-2009-2010-Report.pdf. Accessed May 08, 2020.
12. Pipe A, Sorensen M, Reid R. Physician smoking status, attitudes toward smoking, and cessation advice to patients: an international survey. Patient Educ Couns. 2009;74(1):18-23.
13. Singh S, Sinha SK, Saha R, Jha M, Kataria DK. Knowledge, attitude and practice related to tobacco use and its cessation among young medical professionals. Indian J Soc Psychiatry. 2014;30(1-2):35-42.
14. Katz DA, Paez MW, Reisinger HS, Gillette MT, Vander Weg MW, Titler MG, et al. Implementation of smoking cessation guidelines in the emergency department: a qualitative study of staff perceptions. Addict Sci Clin Pract. 2014;9(1):1.
15. Nagle A, Schofield M, Redman S. Australian nurses' smoking behaviour, knowledge and attitude towards providing smoking cessation care to their patients. Health Promot Int. 1999;14(1):33-44.
16. Sumana M, Sreelatha CY, Sundar M, Das N. Clinician's practices and perspectives regarding tobacco cessation in a teaching Hospital, Karnataka, India. Int J Community Med Public Health. 2017;4(3):634-9.
17. Grewal J, Isher DK, Isher PP. Knowledge regarding tobacco cessation among undergraduate, postgraduate and faculty in dental colleges of Ludhiana: A survey. Indian J Dent Sci. 2019;11(1):28-35.
18. Patwardhan S, Murphy MA. Survey of GPs' understanding of tobacco and nicotine products. Drugs and Alcohol Today. 2013;13(2):119-50.
19. UK Medicines and Health Regulatory Agency. Public Assessment Report: The use of nicotine replacement therapy to reduce harm in smokers. February 2010. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/853861/Nicotine_replacement_therapy_harm_reduction_in_smokers.pdf. Accessed May 08, 2020.
20. IARC monographs on the identification of carcinogenic hazards to humans, WHO. Available at: https://monographs.iarc.fr/list-of-classifications. Accessed May 08, 2020.
21. WHO Model list of Essential Medicines, 21st List, 2019. Available at: https://www.who.int/medicines/publications/essentialmedicines/en/. Accessed May 08, 2020.
22. Kishore SP, Bitton A, Cravioto A, Yach D. Enabling access to new WHO essential medicines: the case for nicotine replacement therapies. Global Health. 2010;6:22.
23. Hecht SS. Tobacco carcinogens, their biomarkers and tobacco-induced cancer. Nat Rev Cancer. 2003;3(10):733-44.
24. Patwardhan S, Rose, J. Overcoming barriers to disseminate effective smoking cessation treatments globally. Drugs and Alcohol Today. 2020;20(2) (In press).
25. McKay AJ, Patel RK, Majeed A. Strategies for tobacco control in India: A systematic review. PLoS One. 2015;10(4):e0122610.

SAMPLE QUESTIONNAIRE

Pilot Study on Knowledge, Attitude and Practice Among Healthcare Professionals in India: Tobacco and Tobacco-cessation Services

Purpose: This short questionnaire is to establish a baseline on the prevalence and knowledge among healthcare professionals around tobacco use and de-addiction treatments, respectively. Such a baseline will allow us to identify gaps and opportunities to empower medical professionals help their patients quit tobacco for good.

Confidentiality and Anonymity:

- Please note that your name and email are being asked only for follow-up studies !
- Data from this survey will be anonymized and analyzed by the Centre for Health Research and Education purely for research purposes and may be presented in scientific publications for educational purposes. This survey is not for commercial purposes and not sponsored by any pharmaceutical or tobacco company.

Section 1: Socio-demographics

1.1 Name of HCP & email (optional & voluntary):

_____

1.2 Age (years):_____

1.3 Gender: Female ☐ Male ☐ Other ☐

1.4 Professional qualification(s): _____

1.5 Experience (years): _____

1.6 Specialty of medical practice:_____

1.7 Patients you normally attended to are: Rural ☐ Urban ☐ Mixed ☐

1.8 Are you currently a tobacco user? Yes ☐ No ☐ Do not like to respond ☐

1.9 If yes, what tobacco product(s) do you use? Cigarette ☐ *Bidi* ☐ Oral/Chewing tobacco e.g., *Gutkha, Khaini*, etc. ☐ Betel (*Areca*) nut ☐ Betel quid or *Paan* ☐ Mixed ☐

1.10 If no, did you ever use any tobacco product? Yes ☐ No ☐ Do not like to respond ☐

Section 2: Knowledge

2.1 Based on your knowledge, please arrange the following categories of tobacco products in terms of its health damaging potential (1 being least and 5 being most damaging):

Cigarette ☐ *Bidi* ☐ Oral/Chewing tobacco such as *Gutkha, Khaini*, Betel (*Areca*) nut/*Paan*, etc. ☐

Betel (*Areca*) nut ☐ Betel quid or *Paan* ☐

2.2 Based on your knowledge, do you think nicotine from cigarette or *bidi* smoke or oral tobacco products cause cancer?

Yes ☐ No ☐ May be ☐ Do not know ☐

2.3 If no, what are the main causes of cancer from tobacco use?_____

2.4 Do you know any tobacco de-addiction guidelines or protocols? Yes ☐ No ☐

2.5 Did you ever receive any specific training on tobacco cessation service? Yes ☐ No ☐

Section 3: Attitude

3.1 Does your routine history taking include questions on the tobacco habit of a patient? Yes ☐ No ☐

3.2 To a patient using tobacco, do you provide tobacco cessation advice? Yes ☐ No ☐

3.3 If yes, average how many patients receive tobacco cessation advice per month?_____

3.4 If no, why?

You did not think it was necessary ☐ Patient did not ask for it ☐

You had no time for this in your practice ☐ No specific reason ☐ Other_____

3.5 In your own assessment, are you in a position to offer tobacco cessation support to patients?

Yes ☐ No ☐ Not sure ☐

3.6 Are you interested in getting appropriate training to enhance your ability in the domain?

Yes ☐ No ☐ Not sure ☐

3.7 Do you think tobacco cessation could help a patient in recovery from other ailment(s)?

Yes ☐ No ☐ Not sure ☐

Section 4: Practice

4.1 Which city & state do you practice? City:_____; State:_____

4.2 Do you know any tobacco de-addiction center in your city? Yes ☐ No ☐ None ☐

4.3 If yes, did you consider referring a patient to such centers for help? Yes ☐ No ☐

4.4 On an average how many patients do you refer to such centers per year?_____

4.5 In your clinical practice in the last one year, what have you mainly advised your patients using tobacco (cigarettes/*bidis*/oral tobacco such as *Gutkha, Khaini*, Betel (*Areca*) nut/*Paan*, etc.)?

☐ Nothing

☐ Asked them to quit, but did not give behavioral counseling or medication

☐ Advised to quit, and provided behavioral counseling with medications such as nicotine gums/patches

☐ Advised to quit, and provided behavioral counseling, medications such as nicotine gums/patches, and called patients for follow-ups

☐ Referred them to the nearest tobacco de-addiction center

Section 5: Knowledge gap

5.1 Have you **Ever** attended a specialized course on tobacco cessation or harm reduction or behavioral therapies (e.g., a certificate course or structured program on site or online)? Yes ☐ No ☐ Not sure ☐

5.2 If yes, name and duration of the course?

Name:_____; Duration:_____(hours/days/weeks)

5.3 Have you attended a CME/Workshop/Seminar on tobacco cessation or harm reduction or behavioral therapies? Yes ☐ No ☐ Not sure ☐

5.4 When was the last such opportunity for you to update your knowledge-base in the domain of tobacco and tobacco cessation? Month: _____ Year: _____

5.5 Are you aware of 5 A's and 5 R's strategies in tobacco cessation support? Yes ☐ No ☐ Not sure ☐

(https://docs.google.com/forms/d/e/1FAIpQLSeYSFMrVlxL8gN01RWGZ2t7g_bN583qbEWrnNtcItMV95seFw/viewform)

■■■■

Tocilizumab Improves Arthritic Kids' Quality of Life

Treatment with tocilizumab yielded significant benefits in health-related quality of life among children with juvenile idiopathic arthritis (JIA), suggests a secondary analysis of clinical trial data.

Among patients with polyarticular JIA in the phase III CHERISH trial, a reduction in the mean score on the Childhood Health Assessment Questionnaire (CHAQ) from 1.39 to 0.67 was noted at Week 16, reported researchers. Additionally, in children with systemic JIA in the phase III TENDER trial, those receiving tocilizumab had a mean change on the psychosocial summary score on the Child Health Questionnaire-Parent Form 50 (CHQ-P50) at Week 12 of 7.3 compared to 2.4 for those given placebo, reported researchers online in *Arthritis Care & Research*… (*Medpage Today*)

Belimumab Beneficial for Kids with SLE

Intravenous belimumab was found to be beneficial as a treatment for children with systemic lupus erythematosus (SLE) in the first trial of this drug for patients 5 to 17 years of age, reported researchers online in *Annals of the Rheumatic Diseases*.

At Week 52, more patients receiving belimumab compared to placebo were considered responders on the SLE Responder Index (52.8% vs. 43.6%, OR 1.49, 95% CI 0.64-3.46). The risk of severe flare was shown to be 64% lower in the belimumab group compared to the placebo group over the 52 weeks… (*Medpage Today*)

Managing Prediabetes to Ward Off Heart Disease

According to a meta-analysis published online in *The BMJ*, prediabetes was shown to be a risk factor for all-cause death and heart-related events.

Among the general population without a history of atherosclerotic cardiovascular disease, prediabetes was found to be associated with a 13% (RR 1.13, 95% CI 1.10-1.17) higher relative risk for all-cause mortality over a median follow-up of 9.8 years. Additionally, prediabetes in the general population was associated with a higher relative risk of heart events including composite of cardiovascular events: RR 1.15 (95% CI 1.11-1.18); coronary heart disease: RR 1.16 (95% CI 1.11-1.21) and stroke: RR1.14 (95% CI 1.08-1.20)… (*Medpage Today*)

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Imaging in COVID-19: A Review

PARVEEN GULATI

ABSTRACT

The coronavirus disease 2019 (COVID-19) outbreak, which started in Wuhan, China, has rapidly spread worldwide. It is a highly infectious viral disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and diagnosed by real-time reverse transcription-polymerase chain reaction (RT-PCR) of the viral nucleic acid. COVID-19 usually presents with symptoms related to respiratory system; however, lately there have been number of reports with extrapulmonary manifestations. Some patients have shown severe cardiovascular damage, acute-onset hepatitis, acute renal failure, encephalitis and myositis. Although the role of imaging has been limited in diagnosis, it is becoming more and more central to supplementing diagnosis, assessing severity, progression and in the follow-up of these patients. This article is aimed to review the role of imaging in COVID-19.

Keywords: Coronavirus infection, pneumonia, COVID-19, extrapulmonary manifestation

In December 2019, several pneumonia cases with unknown etiology were reported in Wuhan, China[1] and were subsequently confirmed to be due to a novel coronavirus - severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The disease, in shorthand, was named COVID-19 from **Co**rona**vi**rus **D**isease-20**19**. Belonging to the family Coronaviridae, the novel coronavirus is a member of the family of viruses that cause diseases ranging from the common cold to severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS).[2] The virus has since then spread to 213 countries with more than 5.7 million worldwide cases reported as of the last week of May. The virus uses widely expressed angiotensin-converting enzyme 2 (ACE2) receptors to enter cells including pneumocytes, respiratory, renal, gastrointestinal epithelial cells and the vascular endothelial cells from nasal and oral pharyngeal mucosa. The average incubation period of the disease is 6.4 days. About 20% of cases are severe with mortality of about 2-3%.[3]

The common clinical presentation includes a lower respiratory tract illness with low-grade fever, headache, generalized weakness, dry cough, dyspnea and anosmia. Old age, obesity, comorbidities like diabetes, hypertension and immunocompromised status are known risk factors for severe disease. However, several patients have shown extrapulmonary manifestations involving the cardiovascular, musculoskeletal, hepatic, renal and the nervous systems.

With changes in the presentation patterns, as well as more and more patients getting extrapulmonary system involvement, the role of imaging is increasing. The present article is an attempt to review and describe the role of imaging in the various pulmonary and extrapulmonary manifestations of the disease.

PULMONARY IMAGING IN COVID-19

Chest X-ray

Chest X-ray is the initial and remains the most commonly performed imaging in these patients. It is indicated if the patient presents with respiratory symptoms as well as for assessing the patient in follow-up. Initially, the X-ray chest remains normal, but as the disease progresses, patchy opacities in the lung fields can be noted. As the disease progresses further, these opacities may coalesce to give white lung appearance. Other findings that may be seen on radiographs during the course of illness are consolidation and may be pleural effusion.

Chest Computed Tomography Scan

Chest computed tomography (CT) scan is the most sensitive imaging modality for the evaluation of lung manifestations. Interestingly, there are studies with

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positive CT and false-negative reverse transcription-polymerase chain reaction (RT-PCR) results.[4,5] The available literature amply proves that imaging can play an important role in the evaluation of suspected COVID-19 infection. Additionally, CT imaging can help in assessing the severity, monitoring disease progression and evaluating treatment response. Due to increased incidence of deep venous thrombosis and pulmonary embolism, it is advised to go for contrast study in these cases.[6]

These patients may show varying spectrum on CT chest depending upon the time course and disease severity. There are certain CT findings which are typical for, and seen more frequently in COVID-19 patients, while there are others which are relatively uncommon. Certain findings, if present, almost rule out COVID-19 as per the disease understanding today.

Typical findings	Atypical findings
• Ground-glass opacity	• Airway changes
• Consolidation	• Pleural changes and effusion
• Reticular pattern	• Fibrosis
• Crazy paving pattern	• Vascular enlargement
• Peripheral distribution	• Air bubble sign
	• Nodules and Halo sign
	• Lymphadenopathy
	• Pericardial effusion

Lobar consolidation and lack of ground-glass opacity almost rules out COVID-19.

Ground-glass opacity is defined as a hazy area with slightly increased density with no obscuration of bronchial and vascular margins likely as a result of partial filling of air spaces or interstitial thickening. This may be unilateral or bilateral, and is usually peripheral and subpleural.[7-9] This is the earliest CT manifestation.

Consolidation is defined as alveolar air getting replaced with fluid, cells or tissues and is seen as an increase in pulmonary parenchymal density obscuring the margins of underlying vessels and airway walls.[10] The distribution is multifocal, patchy or segmental in the subpleural area or along the bronchovascular bundles. Consolidation is usually seen after 2 weeks of the onset of symptoms. It is as an indication of disease progression and should be taken as an alarming sign in management.

Reticular pattern is seen as thickening of pulmonary interstitial structures like interlobular septae and intralobular lines. These have been reported to be the most common CT finding after ground-glass opacity and consolidation in patients of COVID-19.[8] Its prevalence has been seen to have a direct correlation with duration of illness.[11]

Crazy paving pattern is seen as thickened interlobular septae and intralobular lines superimposed on a background of ground-glass opacity, giving it irregular paving stone appearance. This signals disease entering progressive or peak stage.[12]

Airway changes in the form of bronchiolectasis, bronchiectasis and bronchial wall thickening have been seen in severe disease but are not very common.[4,13,14]

Pleural and subpleural changes: Pleural thickening and pleural effusion, both have been reported, the former being relatively more prevalent; however, pleural effusion has been shown to be associated with a relatively poor prognosis.[11,15]

Vascular enlargement described as the dilatation of pulmonary vessels around and within the lesion, although not commonly reported, was seen in most of the cases reported by Ye et al.[16]

Nodules and Halo sign: A nodule refers to a rounded or irregular opacity with well or poorly defined edges measuring less than 3 cm in diameter.[10] The nodules have been associated with viral pneumonia.[17] About 3-13% of COVID-19 patients may have multifocal solid irregular nodules[12] or nodules with the Halo sign.[18] Halo sign is defined as nodules or masses surrounded by ground glass opacification.

Lymphadenopathy and pericardial effusion: Enlarged mediastinal lymph nodes (lymph node larger than 1.0 cm in short axis) have been reported in 4-8% of patients. This is considered to be a significant risk factor of severe/critical COVID-19 pneumonia. Along with pleural effusion and multiple nodules, it may suggest a superadded bacterial infection.[11,13,14]

Pericardial effusion is rare in COVID-19, but if present, it is essential to exclude infective/cardiac pathology.

Correlation Between CT Findings and Severity

The commonest CT finding in asymptomatic, mildly symptomatic, as well as severe patients is the presence of ground-glass opacities. However, consolidation, air bronchograms, pleural effusions and white lung pattern are seen in severe patients. Bilateral diffuse involvement indicates severe disease. Asymptomatic and mildly symptomatic patients show predominant involvement of the peripheral and lower lung with no multifocal segmental involvement.

Differential Diagnosis

Other viral and atypical infections including Influenza, Parainfluenza virus, Adenovirus, Respiratory Syncytial virus, Rhinovirus, SARS-CoV may show CT findings similar to COVID-19. Pulmonary edema, acute lung injury due to other causes, acute interstitial and acute eosinophilic pneumonia also may pose a diagnostic challenge on CT.

IMAGING IN GASTROINTESTINAL MANIFESTATIONS

Although respiratory symptoms are the commonest presenting complaints, an increasing number of patients are also showing gastrointestinal symptoms such as diarrhea, abdominal pain, nausea and vomiting and loss of appetite. Liver function derangement is also seen in number of patients. Bhayana et al[19] analyzed 224 abdominal imaging studies in 412 patients. Ultrasonography (USG) was the modality used in patients with deranged liver function to assess the right upper abdominal quadrant/hepatobiliary system. CT abdomen was performed in all patients with abdominal pain or sepsis.

The CT findings observed were bowel wall abnormalities in the form of small bowel and/or large bowel thickening (>3 mm in distended and >5 mm in collapsed loop) being commonest followed by pneumatosis and portal venous gas. Other findings encountered were changes suggestive of hepatitis in the form of gallbladder (GB) wall thickening and lower attenuation of parenchyma and changes suggestive of pancreatitis. The bowel findings may be due to direct viral infection, small vessel thrombosis or nonocclusive mesenteric ischemia.

USG findings observed in patients with deranged liver function tests revealed GB sludge with or without distension, GB wall thickening, pericholecystic fluid and fatty liver. Portal venous gas and portal vein thrombosis may be seen in severe/critical patients.

IMAGING IN CARDIAC MANIFESTATIONS

Acute myocardial infarction, fulminant heart failure, dysrhythmias and arrhythmia have been seen in these patients.[20,21] Patients with pre-existing risk factors like diabetes, cardiac disease or hypertension are more likely to have these problems. Echocardiography remains the main imaging modality being used so far, which may show wall motion defects including global hypokinesia. There may be associated pericardial effusion.

IMAGING IN NEUROLOGICAL MANIFESTATIONS

Loss of smell and taste are increasingly being recognized as the presenting symptoms. In one of the studies, as high as 36% of the patients had neurological symptoms.[22] Stroke, leukoencephalopathy, acute hemorrhagic necrotizing encephalopathy, Guillain-Barré syndrome have all been reported. Magnetic resonance imaging (MRI) remains the modality of choice, however, if due to logistical reasons MRI cannot be performed, plain CT is recommended. Sachs et al[23] reported leukoencephalopathy in a patient of COVID-19 where plain CT revealed low attenuation lesion in bilateral cerebral hemisphere white matter; MRI of the same patient in addition to showing white matter changes seen on CT also showed microbleeds. The findings are non-specific and may be seen number of other encephalopathies. Kandemirli,[24] in addition to white matter changes, in his study also reported venous transverse sinus thrombosis in a patient and ischemic stroke in middle cerebral artery (MCA) territory in another patient.

IMAGING, PREGNANCY AND COVID-19

USG remains the imaging modality of choice in pregnancy. A WHO mission analyzed 147 pregnant women with confirmed COVID-19 and 82 presumed cases, amongst which 8% had severe disease, and 1% were critical with multi-organ failure. They found the rate of adverse events to be less compared to the general population (13.8% severe and 6.1% critical), the mission concluded that pregnant women might not be at increased risk.[25] However, more data is required to reach a final conclusion. An increasing incidence of hydatidiform mole with the onset of the pandemic has been observed by Abbas et al. The majority of these cases were primigravidae without other risk factors.[26]

CONCLUSION

Every day new observations are being made in the COVID-19 disease spectrum and it is clear that the manifestations and involvement is not limited to the respiratory system. This also indicates that the role of imaging will not be limited to just plain X-rays; USG, CT and MRI all are going to play a role and a holistic approach will be necessary.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33.

2. Coronavirus disease 2019 [Internet]. [cited 2020 Apr 3]. Available at: https://www.who.int/emergencies/diseases/novel-coronavirus-2019.
3. Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. Euro Surveill. 2020;25(5):2000062.
4. Xie X, Zhong Z, Zhao W, Zheng C, Wang F. Chest CT for typical 2019-nCoV pneumonia: relationship to negative RT-PCR testing. Radiology. 2020;200343. [Online ahead of print]
5. Huang P, Liu T, Huang L, Liu H, Lei M, Xu W, et al. Use of chest CT in combination with negative RT-PCR assay for the 2019 novel coronavirus but high clinical suspicion. Radiology. 2020;295(1):22-3.
6. Rotzinger DC, Beigelman-Aubry C, Qanadli SD. Pulmonary embolism in patients with COVID-19: Time to change the paradigm of computed tomography. Thromb Res. 2020;190:58-9.
7. Pan Y, Guan H, Zhou S, Wang Y, Li Q, Zhu T, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. Eur Radiol. 2020;1-4. [Online ahead of print]
8. Song F, Shi N, Shan F, Zhang Z, Shen J, Lu H, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology. 2020;295(1):210-1.
9. Ng MY, Lee E, Yang J. Imaging profile of the COVID-19 infection: radiologic findings and literature review. Radiol Cardiothorac Imaging. 2020;2(1).
10. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. Radiology. 2008;246(3):697-722.
11. Shi H, Han X, Jiang N, Cao Y, Alwalid O, Gu J, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: A descriptive study. Lancet Infect Dis. 2020;20(4):425-34.
12. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology. 2020;295(3):715-21.
13. Li K, Wu J, Wu F, Guo D, Chen L, Fang Z, et al. The clinical and chest CT features associated with severe and critical COVID-19 pneumonia. Invest Radiol. 2020;55(6):327-31.
14. Wu J, Wu X, Zeng W, Guo D, Fang Z, Chen L, et al. Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features. Invest Radiol. 2020;55(5):257-61.
15. Bernheim A, Mei X, Huang M, Yang Y, Fayad ZA, Zhang N, et al. Chest CT findings in coronavirus disease-19 (COVID-19): Relationship to duration of infection. Radiology. 2020;295(3):200463.
16. Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol. 2020 Mar. [Epub ahead of print]
17. Franquet T. Imaging of pulmonary viral pneumonia. Radiology. 2011;260(1):18-39.
18. Li X, Zeng X, Liu B, Yu Y. COVID-19 infection presenting with CT Halo sign. Radiol Cardiothorac Imaging. 2020;2(1):e200026.
19. Bhayana R, Som A, Li MD, Carey DF, Anderson MA, Blake MA, et al. Abdominal imaging findings in COVID-19: preliminary observations. Radiology. 2020;201908. [Online ahead of print]
20. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020;17(5):259-60.
21. Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med. 2020:S0735-6757(20)30277-1. [Epub ahead of print]
22. Mao L, Wang M, Chen S, He Q, Chang J, Hong C, et al. Neurological manifestations of hospitalized patients with COVID-19 in Wuhan, China: a retrospective case series study. SSRN Electronic Journal, January 2020.
23. Sachs JR, Gibbs KW, Swor DE, Sweeney AP, Williams DW, Burdette JH, et al. COVID-19-associated leukoencephalopathy. Radiology. 2020;201753. [Online ahead of print]
24. Kandemirli SG, Dogan L, Zarikaya ZT, Kara S, Akinci C, Kaya D, et al. Brain MRI findings in patients in the intensive care unit with COVID-19 infection. Radiology. 2020;201697. [Online ahead of print]
25. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19), February 2020. Available at: https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf.
26. Abbas AM, Ahmed OA, Shaltout AS. Hydatidiform mole in the era of COVID-19 pandemic. Is there an association? Am J Reprod Immunol. 2020;e13253. [Online ahead of print]

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

The Mind and Body are Connected with Each Other Through Psychoneuroendocrine and Reticuloendothelial System

LEKHA L

ABSTRACT

Psychoneuroendocrinoimmunology (PNEI) is the study of the interaction between psychological, neural, endocrine and immunological responses, which was first described in 1936. There is a unity of mind and body (reflected in term mind and body medicine); and psychological factors must be taken into account when considering all disease states. Although most physical disorders are influenced by stress, conflict or generalized anxiety, some disorders are more affected than others. The concept of PNEI system propose that stressful event triggers cognitive and affective responses which, in turn induce sympathetic nervous system and endocrine changes and these ultimately impair immune function. The present review provides an overview of the fundamental literature on PNEI and its interaction with chronic low-grade cellular inflammation processes, hormetic processes, longevity with reference to resilience as a key factor in natural/pathologic evolution of aging. And consequently with the homoeopathic standpoint where dynamic, functional and structural plane been correlated.

Keywords: Psychoneuroimmunology, stress, psychiatry, allergy, longevity, specificity and non-specificity hypothesis

Psychoneuroendocrinoimmunology (PNEI) is involved in studying the interactions between psychological, neural, endocrine and immunological processes. PNEI system represents a self-regulation network implicated in the homeostasis of the organisms, in the maintenance of chemical-physical-neuropsychological balance in response to various stimuli. The concept of the PNEI system came into being in the second half of the 20th century and gained potential in the seventies and eighties when the existence of a network of immunoneuroendocrine interactions was confirmed by means of several experiments. In the nineties, Ader further disseminated the key concepts of PNEI, after the discovery that the lymphocytes (immunological cells) produce TSH (hypophyseal hormone) and other molecules with neuroendocrine activity. The confirmation of the interdependent relationship between immunological and neuroendocrine mechanisms has given way to a re-evaluation of diagnostic and therapeutic pathways in longevity medicine. The PNEI system, from the morpho-functional aspect, includes the (patho-) physiological mechanisms proper of human psyche, neurological system (limbic system and namely hypothalamus in primis), endocrine system (e.g., hypophysis and receptor glands) and immunitary system. All of these form part of an integrated self-regulation network aimed at psychosomatic homeostasis in response to endogenous and exogenous stimuli (Fig. 1).

Medicine is adapting the concept of illness and its modus operandi based on it. Emotions, mental

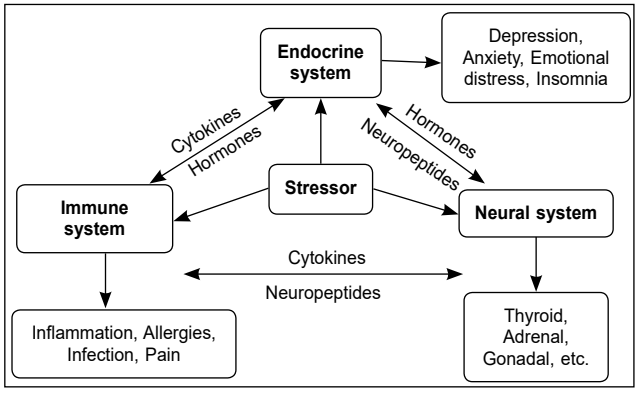

Figure 1. PNEI: Interconnections and signalling among psyche, neural, endocrine and immune systems.

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attitude, lifestyle, social support and nutrition are being increasingly appreciated as having a pivotal role in the processes of diagnosis and treatment of any disease. The way the PNEI system functions, underscores how psychosocial elements are abstract expressions of a subjective experience. Additionally, their value is also expressed through concrete pathophysiological clinical manifestations that depend on the individual-environment relationship.

Evidence indicates that chronic low-grade cellular inflammation (CLGCI), neurodegenerative and cardiovascular disorders, obesity, diabetes, cancer and senescence are all associated with PNEI system activity. Health refers to the ability to adapt to one's environment. It does not represent a fixed entity. It varies for every individual, depending on their circumstances. According to this comprehensive and modern view of health, PNEI system seems to have a significant role in the processes of aging. The imbalance between emotional and physical stimuli has a link with an ongoing series of phenomena that include and affect biological, psychological and social aspects within human life.

PNEI AND INFLAMMATION

PNEI provides the biological basis of a bidirectional relationship between the endocrine, immune and neuropsychological networks in physiological and pathological conditions. Psycho-emotional and affective state of an individual appear to affect the course of a pathological organic event. The key process through which the PNEI system intervenes in most diseases is inflammation in terms of interactions with the CLGCI. Chronic stress, or distress, is representative of the persistent disequilibrium of the PNEI system pillars. It acts on the hypothalamus-hypophysis axis and the whole endocrine system, thus altering the cortisol level. Stress promotes inflammation of the tissues due to an increase of cortisolemia and the increase of inflammatory cytokines (i.e., interleukin [IL]-1, tumor necrosis factor [TNF], IL-6). They go on to activate the immunitary system in a proinflammatory sense. Extensive innervation of lymphoid organs by neurovegetative fibers, releasing norepinephrine, acetylcholine and neuropeptides has been noted. The plexuses of sympathetic nerve fibers surrounding the arterial vessels which penetrate the lymphoid organs are also known to play a significant role. The interaction occurs through immune cells, particularly those of innate immunity that are associated with inflammation processes. Mast cells release histamine and other active substances, thus causing vasodilation and inflammation. These cells are present under the skin and the mucous membranes of the body, and also in fundamental organs, including the brain. Mast cells can be activated in an inflammatory sense by the key neuropeptides, including calcitonin-gene-related-peptide, substance P, neuropeptide Y, nerve growth factor, vasoactive intestine peptide, as well as by adrenaline, noradrenaline and other substances released by nerve fibers. The vegetative nervous system has the potential to modulate the inflammatory processes by interaction with the mast cells and other relevant immune system components.

Recently, inflammation has been recognized as one of the vital causal processes in atherosclerosis and altered lipid profile. CLGCI and hyperdyslipidemia have been tied to several causal factors. The correlation between psychic depression, chronic stress and alterations in the blood fat profile (dyslipidemia) has long been known. The science of PNEI system describes how all the compartments affect and are affected by the inflammatory processes. For instance, the immune system is affected by the alterations related to depression and dyslipidemia.

Dantzer and colleagues have shown that by the release of cytokines in the brain, an inflammatory condition is established that leads to alteration in neuronal activity causing depression and a procession of symptoms termed "sickness behavior". Chronic stress and inflammation also heighten the risk of cancer and metastasis, more so in the lymphoglandular system. Increased production of neuropeptides and stress hormones can cause an alteration in the signaling of cell proliferation (i.e., mammalian target of rapamycin [mTOR]/autophagy pathways), as well as an increase in cortisol, with consequent dysregulation of immune response, insulin and leptin. A meta-analysis involving 165 controlled studies in oncology revealed that psychosocial distress is linked with an increased incidence of cancer, worse prognosis and an increase in mortality.

Evidence thus clearly indicates that psychological emotions and stress can translate into an inflammatory process that bidirectionally involves the entire PNEI system and the target organs.

PNEI AND LONGEVITY

Chronic inflammation is involved in many pathogenetic processes. In early 2000s, Franceschi called "inflammaging" the combination of CLGCI, as the basis of any chronic degenerative process and senescence.

Several causes may be associated with the initiation and worsening of inflammatory processes. These may be of organic and psychological/social nature.

The Interaction Between PNEI and Psychophysical Aging

A study revealed that a positive childhood from the psychosocial point of view may ensure a better cardiovascular function. Another study on the psychosocial factors which interfere on healthy aging demonstrated that depression is the most relevant, while the perceived health status, ego integrity, self-achievement, self-esteem and participation in leisure activities were beneficial factors. Yet another study suggested that senescence is a process that can be enhanced by self-estimation and self-perception of own aging with an increase of 7.5 years in the lifespan, compared to the subjects who negatively interpret their aging process. This result was achieved irrespective of economic-social status, gender, loneliness and disability.

The individual level of feeling of well-being has been shown to predict greater longevity, irrespective of family, genetic and shared environment factors. One of the most relevant prospective investigation on long-term aging and its link with biological and psychosocial factors collected information on: a) The physical and mental state; b) several possible risk factors (i.e., smoking habit, alcohol consumption); c) psychosocial features such as the enjoyment of a career, the experience of retirement and the quality of family life. The study aimed to identify biological/psychosocial predictive factors of healthy aging. The Harvard grant study highlighted some key findings: a) Alcoholism had the most destructive power, strongly correlating with neurosis and depression; b) smoking was the next factor that led to early morbidity and death; c) financial success depended on warmth in human relationships and, beyond a certain level, not on subjects' intelligence; d) the human warmth of the relationship of mother-child positively impacted the rest of life; e) higher warmth of the relationship in childhood with fathers had a correlation with lower rates of anxiety for adults and greater "satisfaction of life" at 75 years of age. The study concluded that the warmth of human relationships has the greatest positive impact on life-span and satisfaction.

Telomere length is a significant longevity index and is negatively influenced by chronic stress and depression. A study assessed women with psychological tests of stress measurement and biological tests, including telomere length measurement, telomerase activity and cellular oxidative stress. Chronic stress in the mothers of sick children was found to be associated with lower telomerase activity, lower telomere length and greater cellular oxidative stress. In the same study, subjects practicing meditation (mindfulness) had greater telomerase activation and longer telomeres.

In another study, epigenetic changes related to chronic stress were highlighted among pregnant women suffering from chronic stress. The study revealed that the telomeres of the offspring are also affected, which will be statistically shorter both for infants and adults. Another study conducted on infants showed a strong difference in telomere length linked to their psychological and behavioral state. Children with greater emotional reactivity, measured by psychological tests, had increased cortisol and heart rate, and exhibited a reduction in telomere length in cells. Oxidative stress has a key role in several aging processes.

There is ample evidence on the inter-relationship between PNEI pathways, CLGCI and aging science that points to the correlation between the negative psycho-emotional factors and social chronic stress and worse longevity and a lower quality of the aging processes.

PNEI: A HORMESIS-BASED SYSTEM

Hormesis is a Greek term that means "stimulate". It was used first in 1943 by Southam and Ehrlich to indicate a specific dose/response relationship. Hormesis is a highly conserved phenomenon in the functioning evolution of animal/vegetal organisms, and is marked by a dose-dependent biphasic response. The hormetic stimulus - be it a biochemical substance, a physical stress or a psychological event - at low doses, can stimulate metabolic pathways, while at high doses, it leads to a negative effect on the metabolic processes. PNEI system responds to hormetic principles as a whole. Resilience and adaptation have a key role to play in longevity. Both these features are greatly affected by the state of health of PNEI system. Any psychological, physical or biological stressor positively or negatively alters the PNEI components and vice versa. At low doses and for a short duration, acute stressors may play a role in longevity medicine, leading to a beneficial adaptation response, thus enhancing the tolerance level to further exposure to stressors at higher doses. Stimuli that may induce a hormetic response include fasting, limited cold/heat exposure, moderate exercise, resistance respiratory training, polyphenols ingestion, oxygen deprivation or hyper-exposure, radiations, spiritual/intellectual/social stimulation.

The three main proinflammatory cytokines (IL-1, IL-6, TNF-α) are produced at low doses from microglial cells and astrocytes in the brain, especially in the hypothalamus, hippocampus, thalamus and basal ganglia, as part of the physiological processes of brain activation. Even in the presence of T cells, microglial cells take on a protective profile, which stimulates neurogenesis, especially in the hippocampus. In case of inflammatory activation with high doses of cytokines, the microglial cells adopt a distinguishable profile, giving way to blocking of neurogenesis.

An experimental study demonstrated that an immune deficiency is related to a blockage of hippocampal neurogenesis. A stimulating environment or a non-stressful physical activity, instead, lead to a moderate release of a few inflammatory mediators that stimulate neurogenesis by increasing the concentration of brain-derived neurotrophic factor (BDNF), the vital neurotrophic substance targeting neuronal growth and synapses development.

Excessive inflammation causes brain damage also as a consequence of the blockage of new neurons formation. The limbic system comprises of hypothalamus, amygdala and other neuronal structures. It rules basic urges and desires together with temperature and sleep regulation, and is strictly involved in PNEI functionality. The primary hormetic stressors which interact with limbic system are represented by caloric restriction, fasting, cold/heat exposure and other forms of required adaptation. These stimuli affect the hypothalamus and amygdala regulation. The limbic system may respond less to conventional medicine, drugs, intentional behaviors, especially at long-term. Hormetic pathways may impact the limbic system more stably. For instance, with fasting through increase of dopamine receptors, or with high/low temperature exposure through BDNF increase.

MANAGEMENT APPROACHES TO IMPROVE PNEI SYSTEM

Several procedures can have a positive impact on the PNEI system.

- Slow breathing – It leads to carotid baroreceptors regulation; blood pressure and heart rate reduction; reduction of excess cortisol.
- Contra-resistance respiratory training – It yields carotid baroreceptors regulation; reduction in blood pressure and heart rate; improves resilience.
- Meditation – It regulates carotid baroreceptors; reduces blood pressure and heart rate; reduces excess cortisol; correlation with greater telomere length and long life expectancy; resilience improvement.
- Prayer – It is associated with carotid baroreceptors regulation; blood pressure and heart rate reduction; excess cortisol reduction; improvement of resilience.
- Autogenic training – It leads to carotid baroreceptors regulation; blood pressure and heart rate reduction; excess cortisol reduction; resilience improvement.
- Vagus nerve stimulation (neural therapy, acupuncture, massages) – It regulates peripheral inflammation; TNF-α reduction.
- Nutrition and nutraceuticals (polyphenols, omega-3 fatty acids) – They reduce oxidative stress; activate anti-inflammatory pathways; activate hormetic processes; protect against cognitive decay and mood alterations.
- Melatonin supplementation – It is associated with regulation of sleep-wake cycle; cerebral and immune-endocrine metabolism support and controls chronic stress (cortisol).

PSYCHONEUROIMMUNOLOGICAL EFFECTS

Communication between the brain and immune system:

- Stimulation of brain sites alters immunity
- Damage to brain hemispheres alters immunity (hemispheric lateralization effects)
- Immune cells produce cytokines that act on the central nervous system (CNS)
- Immune cells respond to signals from the CNS.

Communication between neuroendocrine and immune system:

- Glucocorticoids and catecholamines impact immune cells
- Endorphins from pituitary and adrenal medulla act on the immune system
- Activity of the immune system is correlated with neurochemical/neuroendocrine activity of brain cells.

Connections between glucocorticoids and immune system:

- Anti-inflammatory hormones enhance the organism's response to a stressor
- Prevention of the overreaction of the body's own defense system
- Regulators of the immune system
- Impact cell growth, proliferation and differentiation

- Lead to immunosuppression
- Suppress cell adhesion, antigen presentation, chemotaxis and cytotoxicity
- Increase apoptosis.

Corticotropin-releasing hormone (CRH):

Release of CRH from the hypothalamus is affected by stress.

- CRH regulates the hypothalamic-pituitary-adrenal (HPA) axis/stress axis
- CRH regulates the secretion of adrenocorticotropic hormone (ACTH)
- CRH is widely distributed in the brain and periphery
- CRH regulates the actions of the autonomic nervous system (ANS) as well as the immune system. Stressors that increase the release of CRH tend to suppress the function of the immune system. On the other hand, stressors that depress CRH release potentiate immunity.
- Centrally-mediated as peripheral administration of CRH antagonist does not affect immunosuppression.

CONCEPT OF EVOLUTION OF DISEASE FROM HOMOEOPATHIC STANDPOINT

Variegated forms and expressions of phenomenon of life are due to susceptibility. Susceptibility refers to an inherent quality of all the living beings to react to a stimuli in the environment. The sophisticated control system of psychoneuroendocrine system and reticuloendothelial system help to maintain an effective harmony over a wide range of environmental circumstances to balance the functioning of the vital force or spiritual dynamic at all levels and in all areas is thus assured. Disease evolves from dynamic plane to functional plane and then to structural plane. Man is a complete psychobiological unit of life and disease evolves centrifugally from center to periphery or from within outwards. At the level of spirit, when the will is altered, misdirected, weakened and distorted, there occurs a loss of hold of value system. Erosion of value system and ethical norms leads to thinking and thinking perceptions and discriminations get blunted as a result. This gives rise to indecision which leads to unbalanced, uncontrolled, ungoverned, exotic, spasmodic, irrational, contrary, contradictory, inappropriate and ambivalent attitude and behavior, functions and activities.

When intellect level is affected, first of all, learning responses are erased. The conflict arising from blocked desires, impulses, urges drive expressions through various channels such as: a) Altered imaginations, b) altered psychological functions, c) drop in performance and efficiency, d) disturbed intellectual performance, e) emotional disturbance, f) altered psychophysiological functions, g) structural alterations and h) altered behavior.

From peripheral expressions, one has to project backwards to perceive the mental state to treat the patient. At physical level, disease evolves in centripetal manner, i.e., from periphery to center, from less vital organ to more vital organ.

Dr Hahnemann, about 200 years back, observed that disease is not simply an affection of a part but its existence is due to combination of various factors like emotional sphere, genetic predisposition and various morbific agents.

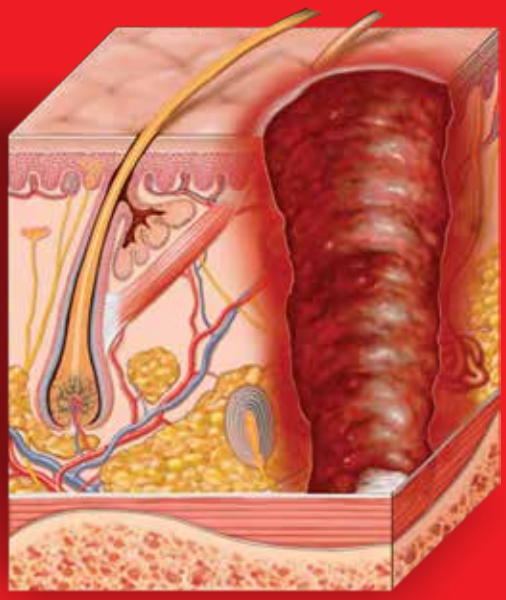
CONCLUSION

Since the seventies, data have pointed to a role for PNEI in the aging process and in degenerative diseases. Lately, a significant role has been attributed to PNEI system in psychiatric diseases. Chronic stress and psychological/social discomfort may lead to pathophysiological clinical manifestations and interfere with the immune system and favor CLGCI and inflammaging, where the latter process is known to play a key role in different pathologies, from autoimmune diseases, diabetes, atherosclerosis to neurodegeneration and cancer.

Literature evidence points to several measures improving PNEI function, such as stress management, nutrition, nutraceuticals (e.g., polyphenols, melatonin), that may have a role in targeting CLGCI and aging processes. Hormetic stressors may represent a potential mechanism to stimulate PNEI system, eventually leading to an improvement in terms of resilience and healthy aging.

SUGGESTED READING

1. Lesser Writings of Prof. (Dr.) N. Mohanty, IB1408, 404 pages, HB Publication 2005.
2. Cavezzi A, Ambrosini L, Quinzi V, Roberto C, Colucci E. Psychoneuroendocrineimmunology (PNEI) and longevity. Healthy Aging Research. 2018;7:12.
3. Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J, et al. World Allergy Organization guidelines for the assessment and management of anaphylaxis. World Allergy Organ J. 2011;4(2):13-37.
4. A Short Textbook of Psychiatry. 7th Edition.
5. Sadock BJ, Ahmad S, Sadock VA. Kaplan & Sadock's Pocket Handbook of Clinical Psychiatry. 6th Edition, Philadelphia: Wolters Kluwer; 2019.



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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Prevention and Treatment of Pressure Ulcer – A Serious Complication of Multimorbidity and Immobility

ARUN BHATT

ABSTRACT

Pressure ulcers (PU) are a serious complication of immobility as well as multimorbidity, with global prevalence rates ranging from 8.8% to 53.2%. PUs are usually difficult to manage and have a negative impact on the patient's quality of life; however, PUs are often preventable. This article provides an overview of PUs, their epidemiology, clinical pattern, risk factors, mechanism of action and management. The article also focuses on the role of silicone-based dressings in the management of PU.

Keywords: Pressure ulcers, risk factors, prevention, management, silicone dressings

Pressure ulcers (PU), a serious complication of immobility as well as multimorbidity, is a wound which begins in the upper layers of the skin due to sustained pressure, or pressure combined with shear, and then extends into the deeper tissue layers.[1,2] PU or bed sores occur when patients cannot reposition themselves to relieve pressure on bony prominences. PUs are usually difficult to manage, painful and costly. PUs have negative impact on the patient's quality of life but are often preventable.

EPIDEMIOLOGY

Globally, prevalence rates of PU range from 8.8% to 53.2% and incidence rates vary from 7% to 72.5%.[1-3] However, there are large variations observed between clinical settings - acute care, aged care and community care (Table 1).[3]

Prevalence and incidence rates are higher in special high-risk populations, such patients in palliative care, or with spinal cord injuries, neonates and infants and people in critical care. PUs occur in up to 23% of patients in long-term and rehabilitation facilities.[4]

Table 1. Rate of PU Prevalence and Incidence Under Different Care Settings

Population	Prevalence (%)	Incidence (%)
Acute care	0-46	0-12
Critical care	13.1-45.5	3.3-53.4
Geriatric care	4.1-32.2	1.9-59
Pediatric care	0.47-72.5	0.27-27
Operating room	-	5-53.4

Prevalence is about 30% in geriatric settings and about 20% in nursing-dependent patients in home care.[2] The incidence of PUs in intensive care unit (ICU) setting is 10-41%.[4]

In India, there are very few systematic studies of PU. Chauhan et al reported PU prevalence of 4.94% in 445 hospitalized in medical and surgical wards.[5] Mehta et al reported prevalence of 7.8% in all hospitalized patients.[6] Prevalence in intensive care was 24.3%. Sacrum and heels were most commonly affected. Most common ulcers were Grade III - 42.8%.[6]

CLINICAL PATTERN

PUs are graded, based on extent and depth of involvement, as per National Pressure Ulcer Advisory Panel (NPUAP)-European Pressure Ulcer Advisory Panel (EPUAP) International classification system (Table 2).[2]

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Common sites for PUs are:

- Patients lying on back – sacrum, coccyx, spinous processes, heels, ankles and elbows
- Patients lying on side – iliac crest, trochanters, helix of the ear.

Most common PU sites are the sacrum and the heels, and majority of PUs are stage I or stage II in severity.[1]

Pain and discomfort are most important problems. PUs have a profound impact on emotional, physical, mental and social domains of life.[1] PUs pose a major burden of illness and reduced quality of life for patients and their caregivers.[3] In USA, the development of a single PU in hospital can increase the patient's length of hospital stay fivefold.[3]

PUs are associated with increased mortality. Amongst patients with PU, there is a twofold increase in death compared to those who do not have pressure ulcers.[1] In US, >60,000 patients die each year as a direct result of PUs.[4]

RISK FACTORS

PUs occur when risk factors which prevent repositioning to relieve pressure on bony prominences. The risks could be: 1) Intrinsic - patient-related or 2) Extrinsic - related to the patient's environment (Table 3).[2,6]

Table 2. NPUAP-EUPAP International Classification System for Pressure Ulcer

Category/ Stage	Title	Description
I	Nonblanchable redness of intact skin	• Intact skin with nonblanchable erythema of a localized area usually over a bony prominence. • Discoloration of the skin, warmth, edema, hardness or pain may also be present. • Darkly pigmented skin may not have visible blanching. • The area may be painful, firm, soft, warmer or cooler than adjacent tissue. • May be difficult to detect in individuals with dark skin tones. • May indicate 'at risk' persons.
II	Partial thickness skin loss or blister	• Partial thickness loss of dermis that presents as a shallow open ulcer with a red pink wound bed, without slough. • May also present as an intact or open/ruptured serum filled or serosanguinous filled blister. • Presents as a shiny or dry shallow ulcer without slough or bruising.
III	Full thickness skin loss (fat visible)	• Full thickness tissue loss. • Subcutaneous fat may be visible, but bone, tendon or muscle are not exposed. • Some slough may be present. • May include undermining and tunneling. • Depth varies by anatomical location. ▸ Bridge of the nose, ear, occiput and malleolus do not have (adipose) subcutaneous tissue; ulcers can be shallow. ▸ Areas of significant adiposity can develop extremely deep pressure ulcers. • Bone/tendon is not visible or directly palpable.
IV	Full thickness tissue loss (muscle/bone visible)	• Full thickness tissue loss with exposed bone, tendon or muscle. • Slough or eschar may be seen. • Often include undermining and tunneling. • Depth varies by anatomical location. ▸ Bridge of the nose, ear, occiput and malleolus do not have subcutaneous tissue; ulcers can be shallow. • Can extend into muscle or supporting structures (such as fascia, tendon, joint capsule) causing osteomyelitis or osteitis likely to occur. • Exposed bone/muscle is visible or directly palpable.

Table 3. Risk Factors Contributing to Development of Pressure Ulcers

Intrinsic - Patient-related	Extrinsic - Related to the patient's environment

• Elderly
• Critical care
  ▸ ICU
  ▸ Acute illness
  ▸ Mechanical ventilation
• In long-term homes/home care
• Trauma
  ▸ Spinal-cord injuries
  ▸ Fracture hip
• Neurological disease
  ▸ Impaired consciousness
  ▸ Impaired perception
  ▸ Motor disturbances
  ▸ Sensory disturbance
  ▸ Diminished pain perception
• Cardiovascular diseases
  ▸ Peripheral arterial occlusive disease
  ▸ Congestive heart failure
• Nutritional problems
  ▸ Anemia
  ▸ Cachexia
  ▸ Malnutrition
  ▸ Inadequate fluid replacement
• Diabetes mellitus
	• Undue and prolonged pressure
	• Friction
	• Shear
	• Moisture
	• Abnormal posture
	• Impaired mobility

MECHANISMS OF PU FORMATION

PU occurs because of complex interplay of:[1-3]

- Pressure – develops on bony prominences, as immobile patients cannot reposition themselves.
- Friction – can disturb the barrier function of the stratum corneum and is an additional risk for infection to occur concurrently with PUs.
- Shearing – is the mechanical stress seen when a patient is sliding down the bed, but his skin remains in the same place since it sticks to the bed linen.
- Moisture – causes softening of the upper layers of the skin and makes skin vulnerable to dermal erosion and increased risk of pressure ulceration.

In patients at high risk of PU formation, there is a lower threshold for occlusion of blood vessels causing ischemia-induced damage and a higher threshold for direct deformation-induced damage.[3] When a patient is exposed to sustained external mechanical forces – prolonged pressure, friction and shear forces – there is local ischemia, reperfusion injury to cells, impairment of interstitial fluid flow and lymphatic drainage, and prolonged deformation of cells.

Friction can result in PU indirectly and directly.[7] In the indirect sense, friction is essential to create the shearing forces. When skin is damaged by pressure ischemia, it may become more susceptible to friction. Friction and pressure ischemia will work together to accelerate breakdown of skin. Prolonged pressure, friction and shear forces, alone or combined, lead to reduction in the oxygen and nutrient supply to cells, impairment of the removal of waste products following cell metabolism, causing cell damage and inevitable tissue destruction.

MANAGEMENT OF PU

- Evaluate risk factors[3] – Utilize a well-defined approach to risk assessment which includes assessment of activity/mobility and skin status – category/stage of PU.
- Assess impact of perfusion and oxygenation, e.g., blood pressure, diabetes, edema, smoking.
- Consider impact of poor nutritional status.
- Evaluate impact of increase in skin moisture, e.g., urinary incontinence, fecal incontinence, urinary catheter *in situ*.
- Review potential impact of increased body temperature, advanced age, sensory perception, abnormal hematology and general health status.

Use of scales, e.g., Braden, Norton, Waterlow, can support clinical judgment in systematic assessment of risk factors.

Treatment of PU

Treatment of existing PU requires consideration of:[3]

- Effective assessment of ulcer
- Monitoring of healing by measuring ulcer area
- Management of pain
- Wound management – cleansing, debridement, infection, dressings and surgery.

Prevention of PU

Preventive measures require attention to all risk factors – nutritional care, repositioning and skin care.

Nutritional care

Malnutrition is linked to the risk of developing PUs, PU severity and impaired healing of wounds.[3] Hence, all patients at high-risk of developing PU should be screened for any nutritional deficiencies. A dietitian should carry out detailed and comprehensive nutrition assessment, focusing on: 1) weight status, 2) patient's ability to eat and 3) adequacy of total nutrient intake. The dietitian should consult other medical and paramedical experts, and develop an individualized nutrition intervention plan considering caloric, protein, vitamin and mineral requirements and hydration. The nutrition plan should be monitored regularly.

Repositioning and early mobilization

Repositioning and mobilization of patients is a vital part of prophylactic management of PU.[3] Regular repositioning helps to reduce the duration and amount of pressure over vulnerable parts of the body and to provide comfort, improve hygiene, maintain dignity and functional ability. If regular repositioning is not possible, an alternative prevention strategy using a high specification mattress or bed may be useful. Positioning the patient on bony prominences should be avoided if there is nonblanchable erythema at the site. As sacrum and heels are common sites of PU, special attention should be given to the sites while repositioning the patient. The heels can be kept free of the surface of the bed by using suspension devices that elevate and relieve pressure on the heel completely.

Support surfaces

These are specialized devices, e.g., special mattresses, for pressure redistribution with characteristics of immersion, envelopment and heat and moisture permeability. Support surfaces are an important component of PU treatment as they provide an environment that improves perfusion of injured tissue. Selection of support surfaces should be individualized considering several factors, e.g., level of immobility and inactivity, need for microclimate (temperature and humidity of the interface between the support surface and the patient) control and shear reduction, and risk of developing new PU.[3]

Skin care

Maintaining skin integrity is vital in the prevention of PU.[3] Maintaining healthy skin requires detailed assessment and planning of care.

Preventive skin care includes:

- Avoid positioning the patient on an area of erythema whenever possible.
- Maintain cleanliness and dryness of skin by using pH balanced skin cleanser, e.g., emollient, deodorant and water-repellent barrier.
- Avoid massaging or vigorously rubbing the skin which is at risk of PU.
- Implement a plan to manage continence problems. Skin should be cleansed immediately after any episode of incontinence.
- Use a barrier product, e.g., silicone gel, which provides protection to the skin from exposure to excessive moisture and helps in reduction of friction and pressure damage.

Prophylactic dressings/Topical applications

Prophylactic topical applications have a role in reducing friction and decreasing localized shear forces.[3] Prophylactic ability of such topical applications depends on: 1) type of dressing - elastic adhesive silicone, 2) the number of layers and their construction and 3) the size of the selected dressing.

Mechanism of Action of Barrier Application

Prophylactic topical application/dressing of silicone-based therapies work in multiple ways to help in prevention of PU. One such silicone-based protectant and soothing translucent gel contains several active components, with diverse attributes.[8]

- Cyclopentasiloxane, the most commonly used silicone in the cosmetic industry, has high volatility and mild solvent properties, thus making it ideal to be used in topical formulations. Its low heat of vaporization suggests that it has a 'dry feel' when applied to the skin.
- Dimethicone is antifoaming agent, emollient, and water repelling agent.
- Dimethicone polymer is a viscosity increasing and dispersing agent.
- Magnesium Aluminum Metasilicate is lubricant, emulsifier and coating agent.
- Silica silylate is a hydrophobic white, fluffy powder, which has a very high sebum/oil absorption capacity.

These components of the gel impart special properties relevant to prevention of PU. These are:

- Adhesiveness – smooth adhesive film which sticks to the skin, forming an invisible, dry, silky-smooth, protective, anti-friction barrier, preventing heat and skin tear due to friction.
- Abrasion resistance – ability to be retained on the skin when exposed to forced abrasion.

- Resistance to friction – lowering of friction on the skin surface helps to reduce the friction on the skin.
- Moisture – a nonocclusive barrier which is comfortable to the user as it allows skin to breathe and sweat to escape.

These ingredients are used regularly as cosmetic ingredients in most of the personal care products and are listed as safe in literature.

Within seconds of application, the gel dries to form a long-lasting, flexible, water-repellent and protective anti-friction film. The film reduces friction by 80% between skin and clothing/bedding, thereby helping prevent PUs. It protects skin exposed to irritation from moisture such as sweat, urine or fecal matter. This barrier film is breathable that provides comfort to the patient without hampering regular function of skin.

CLINICAL TRIALS: SILICONE APPLICATION

Clinical trials of prophylactic topical applications face many challenges:

- Recruitment of patients to achieve homogeneity in acute care settings where patients have diverse medical conditions.
- Difficulty of deciding statistically relevant sample size due to nonavailability of data on background incidence of PU at Indian hospitals.
- Difficulty of blinding/masking the topical application and ensuring randomization.
- Need to standardize other factors, e.g., nutrition, repositioning, beds, bed sheets.
- Training of nursing/other staff in consistency in use of scales for assessing wounds for frequent observations of bed sore at multiple sites.
- Difficulty of detecting early redness in dark skin.
- Ethical consideration – As efficacy of silicone-based topical applications in prevention of PU is well-established with all studies favoring use of such dressing/applications,[3] it would be unethical and risky to deprive the patient the benefits of preventive topical application.

Several clinical trials have shown reduction in occurrence of PU at high-risk anatomical locations – heels, sacrum - when a prophylactic polyurethane foam soft silicone dressing was applied (Table 4).[1,9-13]

In view of such evidence of preventive effect of silicone-based foam dressing, all patients at risk of developing PU should be offered application of polyurethane foam dressing – silicone - to bony prominences (e.g., heels, sacrum) for the prevention of PU in locations frequently subjected to friction and shear.

Table 4. Clinical Trials of Silicon-based Preventive Therapy for Pressure Ulcer

Study	Control incidence (%)	Silicone dressing incidence (%)
Kalowes et al[9]	5.9	0.7
Park[10]	46	6
Santamaria et al[11]	17.8	4.3
Brindle and Wegelin[12]	11.4	2
Chaiken[13]	13.6	1.8

CONCLUSIONS

Pressure ulcers are a serious complication of immobility and are associated with high morbidity. All efforts should be made to prevent PUs in high-risk patients combining nutritional care, repositioning and skin care and prophylactic application of silicone-based topical applications.

REFERENCES

1. Moore ZE, Webster J. Dressings and topical agents for preventing pressure ulcers. Cochrane Database Syst Rev. 2013;(8):CD009362.
2. Anders J, Heinemann A, Leffmann C, Leutenegger M, Pröfener F, von Renteln-Kruse W. Decubitus ulcers: pathophysiology and primary prevention. Dtsch Arztebl Int. 2010;107(21):371-82.
3. National Pressure Ulcer Advisory Panel, European Pressure Ulcer Advisory Panel and Pan Pacific Pressure Injury Alliance. Prevention and Treatment of Pressure Ulcers: Clinical Practice Guideline. Emily Haesler (Ed.). Cambridge Media: Osborne Park, Western Australia; 2014.
4. Bauer K, Rock K, Nazzal M, Jones O, Qu W. Pressure ulcers in the United States' inpatient population from 2008 to 2012: Results of a retrospective nationwide study. Ostomy Wound Manage. 2016;62(11):30-8.
5. Chauhan VS, Goel S, Kumar P, Srivastava S, Shukla VK. The prevalence of pressure ulcers in hospitalized patients in a university hospital in India. J Wound Care. 2005;14(1):36-7.
6. Mehta C, George JV, Mehta Y, Wangmo N. Pressure ulcer and patient characteristics - A point prevalence study in a tertiary hospital of India based on the European Pressure Ulcer Advisory Panel minimum data set. J Tissue Viability. 2015;24(3):123-30.
7. Bhattacharya S, Mishra RK. Pressure ulcers: Current understanding and newer modalities of treatment. Indian J Plast Surg. 2015;48(1):4-16.

8. Rustomjee MT. An Anti Chafing Gel Composition Indian Patent application no 201721025474. 14 Dec 2018.
9. Kalowes P, Messina V, Li M. Five-layered soft silicone foam dressing to prevent pressure ulcers in the intensive care unit. Am J Crit Care. 2016;25(6):e108-e119.
10. Park KH. The effect of a silicone border foam dressing for prevention of pressure ulcers and incontinence-associated dermatitis in intensive care unit patients. J Wound Ostomy Continence Nurs. 2014;41(5):424-9.
11. Santamaria N, Gerdtz M, Sage S, McCann J, Freeman A, Vassiliou T, et al. A randomised controlled trial of the effectiveness of soft silicone multi-layered foam dressings in the prevention of sacral and heel pressure ulcers in trauma and critically ill patients: the border trial. Int Wound J 2015;12(3):302-8.
12. Brindle CT, Wegelin JA. Prophylactic dressing application to reduce pressure ulcer formation in cardiac surgery patients. J Wound Ostomy Continence Nurs. 2012;39(2):133-42.
13. Chaiken N. Reduction of sacral pressure ulcers in the intensive care unit using a silicone border foam dressing. J Wound Ostomy Continence Nurs. 2012;39(2):143-5.

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Polyvalent Mechanical Bacterial Lysate: A Polyvalent Respiratory Vaccine

JYOTI YADAV

ABSTRACT

Polyvalent mechanical bacterial lysate (PMBL) is a mixture of antigens derived from 13 strains of inactivated pathogenic bacteria. PMBL exerts therapeutic as well as preventive effects in acute and recurrent respiratory infections by activating and enhancing both immunoglobulin (Ig)M memory B cells and interleukin (IL)-2 receptor expressing T lymphocytes. PMBL is active as an immunomodulating agent and is used in acute, subacute, recurrent and chronic infections. It reduces number and intensity of episodes. It can be combined with antibiotics and mucolytic agents to get very good results.

Keywords: Polyvalent mechanical bacterial lysate, antigens, inactivated pathogenic bacteria, chronic obstructive pulmonary disease

Polyvalent mechanical bacterial lysate (PMBL) is a mixture of antigens derived from 13 strains of inactivated pathogenic bacteria. These strains include *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus viridans*, *Klebsiella pneumoniae*, *Klebsiella ozaenae*, *Haemophilus influenzae B*, *Neisseria catarrhalis* and *Streptococcus pneumoniae* (type 1, 2, 3, 5, 8 and 47). These 13 strains are commonly occurring pathogens, which cause respiratory tract infections. Although most of the upper respiratory tract infections are due to viruses, nevertheless epiglottitis and laryngotracheitis are due to *H. influenzae* and majority of the bacterial pharyngitis is due to *S. pyogenes*.

COMPOSITION

Total concentration of active ingredient is 50 mg out of which 7 mg is bacterial fraction (each strain concentrated at 6 billion) and 43 mg of glycoll, which acts as a support of freeze drying. Excipients present in PMBL include colloidal hydrated silica, microcrystalline cellulose, calcium hydrogen phosphate dehydrate, magnesium stearate, ammonium glycyrrhizate and essence of mint powder.

ACTIONS

PMBL acts both on innate as well as adaptive immunity.[1] Braido et al demonstrated that bacterial lysates have protective effect in respiratory tract infections.[2] Cazzola et al observed that PMBL exerts therapeutic as well as preventive effects in acute and recurrent respiratory infections by activating and enhancing both immunoglobulin (Ig)M memory B cells and interleukin (IL)-2 receptor expressing T lymphocytes.[3] PMBL stimulates both T and B lymphocytes.[4,5]

Chronic obstructive pulmonary disease (COPD) patients having acute exacerbations of *S. pneumoniae, N. catarrhalis* and *H. influenzae* show beneficial effect when treated with PMBL.[6] PMBL is active as an immunomodulating agent and is used in acute, subacute, recurrent and chronic infections. It reduces number and intensity of episodes. It can be combined with antibiotics and mucolytic agents to get very good results. It can easily be given from 3 years age onwards. PMBL is recommended for prevention when given in combination with inhaled corticosteroids and long-acting β_2-agonists. PMBL strengthens immune system, increases all subsets of natural killer cells, which play major role in destruction of cells infected by viruses.

It also induces production of opsonizing immunoglobulins, which destroy pathogenic bacteria through granulocytes.[7,8] PMBL is found to be effective

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in post-tubercular as well as COPD patients in reduction of exacerbation rate and lower the risk of development of concomitant respiratory infections in tuberculosis.

DOSAGE AND LOCAL ACTION

PMBL is recommended for first 10 days of the month for 3 consecutive months to have an efficient protection during winter and it's use is extended during follow-up of 9 months in COPD patients. PMBL tablets do not have lifelong effect, as immunoglobulins have very short half-life between 6 and 21 days. PMBL tablets allow production of secretory IgA at application site resulting in mucosal protection against bacterial infections.[9] PMBL intake increases IgA, IgM and IgG. On swallowing, PMBL tablet acts on gastrointestinal mucosa through gut associated lymphoid tissue and via systemic circulation of immunoglobulins and cytokines it treats respiratory tract infections. PMBL tablets can be given sublingually, which cause loco-regional action of antigens present in PMBL with immunocytes. The time of complete disintegration of PMBL tablet in oral cavity is 1.5-2 minutes. Sublingual route allows direct contact of antigens with mucosal immunocytes of mouth and larynx, thus inducing loco-regional activation of immune system. PMBL tablets act on all actors of immunological cascade to stimulate both innate and adaptive immunity. PMBL tablets should be taken before meals and should not exceed recommended dose. PMBL tablet is superior to it's chemical lysates. PMBL offers protection starting from first week of intake and provides protection for an additional 3 months after the end of 3 months treatment.[10-12]

Morandi et al observed that PMBL activates both circulating as well as plasmacytoid dendritic cells.[7] Braido et al found that PMBL activates natural killer cells, which play important role in destruction of cells infected by viruses.[8] PMBL activates dendritic cells and also increases the secretion of efficient IgA.[1,13]

Therapeutic Uses

Most of the seasonal flu vaccines like flu vaccine are trivalent vaccines, while PMBL vaccine is polyvalent having 13 various inactivated strains, thus it prevents most commonly occurring pathogens of upper and lower respiratory tract infections. PMBL's mechanical lysis ensures attainment of particulate antigens which is 10-100 times more immunogenic than soluble antigens.

PMBL is also found effective in community-acquired polymicrobial pneumonia in intensive care unit patients.[14] PMBL when used in immunocompromised patients was found to be useful with no safety concern.[15] Potential activity of PMBL in other therapeutic areas like allergies or cancer immunotherapy has not yet been tried but theoretically, it may prove beneficial in these patients. It has not yet been used in autoimmune diseases.

Side Effects

There are very minimal side effects except laryngitis; however, more trials need to be done to ascertain other side effects.

Contraindications

PMBL should be avoided in first 3 months of pregnancy.

COST OF VACCINATION

Retail price of one 50 mg tablet is ₹ 40, thus cost of vaccination of 3 consecutive months will be about ₹ 1,200. If it is as effective as claimed, vaccination is cost-effective.

REFERENCES

1. Palmieri G. Prophylaxis of airways viral infections: role of the enhancement of the immune defenses. Giorn It Mal Tor. 2003;57:46-51.
2. Braido F, Tarantini F, Ghiglione V, Melioli G, Canonica GW. Bacterial lysate in the prevention of acute exacerbation of COPD and in respiratory recurrent infections. Int J Chron Obstruct Pulmon Dis. 2007;2(3):335-45.
3. Cazzola M, Rogliani P, Curradi G. Bacterial extracts for the prevention of acute exacerbations in chronic obstructive pulmonary disease: a point of view. Respir Med. 2008;102(3):321-7.
4. Lanzilli G, Falchetti R, Tricarico M, Ungheri D, Fuggetta MP. In vitro effects of an immunostimulating bacterial lysate on human lymphocyte function. Int J Immunopathol Pharmacol. 2005;18(2):245-54.
5. Lanzilli G, Falchetti R, Cottarelli A, Macchi A, Ungheri D, Fuggetta MP. In vivo effect of an immunostimulating bacterial lysate on human B lymphocytes. Int J Immunopathol Pharmacol. 2006;19(3):551-9.
6. Cazzola M. A new bacterial lysate protects by reducing infectious exacerbations in moderate to very severe COPD: a double-blind, randomized, placebo-controlled trial. Trends in Med. 2006;6:191-9.
7. Morandi B, Agazzi A, D'Agostino A, Antonini F, Costa G, Sabatini F, et al. A mixture of bacterial mechanical lysates is more efficient than single strain lysate and of bacterial-derived soluble products for the induction of an activating phenotype in human dendritic cells. Immunol Lett. 2011;138(1):86-91.

8. Braido F, et al. Polyvalent mechanical bacterial lysate treatment in COPD: new immunological evidence. IV World Asthma and COPD Forum, 2011.
9. Braido F, et al. A good clinical outcome following therapy with a polyvalent mechanical bacterial lysate (PMBL) correlates with the capacity of inducing a specific loco regional immunoresponse in patients with recurrent upper respiratory tract infections. XXVII Congress of the European Academy of Allergology and Clinical Immunology, 2008.
10. Tricarico D, Varricchio A, D'Ambrosio S, Ascione E, Motta G. Prevention of recurrent upper respiratory tract infections in a community of cloistered nuns using a new immunostimulating bacterial lysate. A randomized, double-blind clinical trial. Arzneimittelforschung. 2004; 54(1):57-63.
11. Boris VM. Prophylaxis of episodes of winter airways infection with a sublingual antibacterial vaccine obtained by mechanical lysis PMBL (ISMIGEN Zambon): clinical trial in patients with a case history of tuberculosis. Giorn It Mal Tor. 2003;57:210e5.
12. Macchi A, Vecchia LD. Open comparative, randomized controlled clinical study of a new immunostimulating bacterial lysate in the prophylaxis of upper respiratory tract infections. Arzneimittelforschung. 2005;55(5):276-81.
13. Rossi GA, Peri C, Raynal ME, Defilippi AC, Risso FM, Schenone G, et al. Naturally occurring immune response against bacteria commonly involved in upper respiratory tract infections: analysis of the antigen-specific salivary IgA levels. Immunol Lett. 2003;86(1):85-91.
14. Cillóniz C, Ewig S, Ferrer M, Polverino E, Gabarrús A, Puig de la Bellacasa J, et al. Community-acquired polymicrobial pneumonia in the intensive care unit: aetiology and prognosis. Crit Care. 2011;15(5):R209.
15. Petrunov B, Nenkov P, Shekerdjiisky R. The role of immunostimulants in immunotherapy and immunoprophylaxis. Biotechnol Biotechnol Equip. 2007; 21(7):454-8.

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Cancer Immunotherapy Linked to Severe COVID-19 Outcomes

Cancer patients receiving immunotherapy were found to be at a heightened risk for severe outcomes from COVID-19, suggest retrospective findings from Memorial Sloan Kettering Cancer Center in New York City.

Among more than 400 cancer patients with symptomatic COVID-19, those treated with immune checkpoint inhibitors had around three-times higher risk of hospitalization (HR 2.84, 95% CI 1.24-6.72, p = 0.013) and severe respiratory illness (HR 2.74, 95 CI 1.37-5.46, p = 0.004) in a multivariate analysis, reported researchers in *Nature Medicine*… (*Medpage Today*)

Results from Two Phase 3 Trials of Bimekizumab Reported

Results from two late-breaking phase 3 trials of the investigational interleukin-17A and IL-17F inhibitor bimekizumab have revealed that most patients with moderate-to-severe psoriasis could achieve clearance at Week 16 and maintained clinical response at 1 year.

About 85% patients achieved PASI 90 and 84.1% achieved an IGA of 0/1 in the bimekizumab arm at Week 16 compared to 49.7% and 53.4%, respectively, in the ustekinumab arm and 4.8% and 4.8%, respectively, among those on placebo ($p < 0.001$ for all associations). Furthermore, 58.6% of patients in the bimekizumab arm achieved PASI 100, compared with 20.9% of those in the ustekinumab arm and none in the placebo group. The findings were presented at the virtual annual meeting of the American Academy of Dermatology… (*Medscape*)

Russia Preparing Mass Vaccination Against Coronavirus for October

Moscow: According to local news agencies, Russia's health minister is preparing a mass vaccination campaign against the novel coronavirus for October, after a vaccine completed clinical trials.

Health Minister Mikhail Murashko said that a state research facility in Moscow had completed clinical trials of the vaccine and paperwork was on to get it registered. According to the minister, doctors and teachers would be the first to receive the vaccination. According to a source, Russia's first potential COVID-19 vaccine would obtain local regulatory approval in August and would be administered to health workers soon thereafter… (*Reuters*)

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

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

Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

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

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

About Sameer Malik Heart Care Foundation Fund

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

Objectives

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

Activities of the Fund

Financial Assistance

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

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

Drug Subsidy

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

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

Who is Eligible?

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

Important Notes

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

Check List of Documents to be Submitted with Application Form

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

Free Diagnostic Facility

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

Free Education and Employment Facility

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

Laboratory Subsidy

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

Help Us to Save Lives

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

Donate Now...

About Heart Care Foundation of India

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

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

Objectives

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

Heart Care Foundation Blood Donation Camps

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

Committee Members

Chief Patron

Raghu Kataria

Entrepreneur

President

Dr KK Aggarwal

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

Governing Council Members

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

Advisors

Mukul Rohtagi
Ashok Chakradhar

Executive Council Members

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

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

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

http://heartcarefoundationfund.heartcarefoundation.org

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Women's and Providers' Experiences with Injectable Contraceptives (Depo-Provera): A View from Vadodara, India

PRAKASH V KOTECHA*, SANGITA V PATEL†, RAJENDRA K BAXI‡, SHAGUFA KAPADIA#, KEDAR MEHTA$

ABSTRACT

Objective: To compare users' and providers' perspectives on injectable contraceptives (IC). **Methods:** This qualitative study employed semi-structured in-depth interview technique. Sixty women with experience of using IC and 10 doctors involved in providing IC were selected. Telephonic interviews of doctors were also conducted. **Results:** Over 50% of the women had side effects and had discontinued use within 1 year. The most common 'likes' according to women included ease of use, being tension free for 3 months and being effective and those of the providers were that it reduced anemia, privacy could be maintained, noncontraceptive benefits, good substitute, not to be taken daily like pills, safe and effective. The most common 'dislikes' reported by providers and clients were excessive bleeding, amenorrhea, irregular periods, spotting, weight gain and frequent pregnancy tests. **Conclusion:** Although certain distinct advantages of IC have been expressed, the associated problems are equally significant and therefore IC should not be an over-the-counter contraceptive.

Keywords: Clients' and providers' perspectives, depo-provera, injectable contraceptives, India, qualitative study

Choice of contraceptive methods is a key element of family planning that benefits both women and providers. Offering client's choices can help increase contraceptive prevalence rates. Data from 36 developing countries indicate that making one additional modern method widely available could increase contraceptive prevalence by about 12%.[1] Hence, there is a need to expand contraceptive choices. Progestin-only injectable contraceptives (POIC) i.e., Depo-medroxyprogesterone acetate (DMPA) and Norethisterone enanthate (NETEN) are newer contraceptives.Awareness about POIC is low in India (19%) with near-zero usage for contraception.[2] Early attempts for clinical trials of DMPA by the Indian Council of Medical Research (ICMR) in the 1970s were abandoned due to unacceptable high rates of bleeding disorders in DMPA users. After the US Food and Drug Administration (FDA) approval of DMPA for contraceptive use in 1992, the Drug Controller of India licensed NETEN (1986) and DMPA (1993) for restricted use in the private sector with a condition that the manufacturers carry out post-marketing surveillance amongst Indian women.[3] The present study, thus was undertaken to compare women's and providers' perspectives on IC and to identify whether to include IC in our National Family Welfare Program or not as policy making decisions.

MATERIAL AND METHODS

Sample Selection

Women, who had experience of using IC either at the time of study or in the past, were selected for the study from the list provided by IC providers. The providers comprised of doctors involved in providing IC, many of them were involved with IC projects. Telephonic

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interviews were also conducted and information was elicited from different gynecologists of the city, irrespective of whether they prescribe IC to their clients at present or not.

Enrollment

Obstetrics and Gynecology specialists who prescribed IC were asked to give their voluntary consent for participation after taking consent from their clients. A total of 10 doctors who prescribed IC to their clients and 60 women were studied. To ensure that, we get total picture of users' perspective we enrolled both types of users - current and past and to assure positive recall adequately we decided to take them in the ratio of 3:1 as far as possible and obtained them from government and private practitioners. While interviewing the doctors who prescribed IC, it was realized that how many doctors prefer use of IC as contraceptive method, would not be possible to find out from interviewing only those doctors who prescribed IC. Thus in an effort to have a quick data on these aspects, a telephonic interview was attempted by picking up telephone numbers of all obstetricians from doctor's directory. For the telephonic interviews, 85 doctors irrespective of whether they prescribed the injection or not, were interviewed. Five doctors refused to give consent for telephonic interview.

Study Tools

Women who consented were assured of confidentiality and interviewed by co-investigators using semi-structured in-depth interview technique. Similarly, semi-structured interviews of 10 providers who prescribed IC to their clients were conducted by the senior investigator. The research staff noted down the interviews and later translated them into English after reviewing for accuracy. Transcripts were content analyzed using the technique of open coding to discover conceptual patterns or themes, in the text. Themes found to be both salient and repeated in the text were defined and used as codes to organize the text into categories. The quantitative study was done by telephonic interview.

RESULTS

Demographic Profile of IC Users

Of the 60 women interviewed, 16 were those who had taken IC in the past and were no longer continuing it, whereas 44 were those who were currently taking IC. Most of the women belonged to the age group of 25-29 years. Four out of the 60 women were nonliterate. Most of the women (45%) had at least secondary education. More than three-fourths of the women were housewives. Majority (53%) of women using IC belonged to relatively better socioeconomic class.

Reasons for Using IC

The influence of the doctor was evident in the responses of 23% of the women who reported 'no other option left' as one of the reasons for using IC. It was interesting to see that 78% of the women had negative perceptions about one or more contraceptive methods without ever using them! About three-fourths of the women did not want to use Copper T. There were many women who admitted that it would be difficult for them to remember taking pills daily and hence had found IC as a suitable alternative.

A 29-year-old woman with one child reasoned, "Taking pills everyday is a problem, and on top of it I feel uneasy, have nausea and headache".

Another woman explained, "We both are not comfortable using condoms, there was white discharge due to Copper T and by using pills I used to get excessive bleeding. So, I had to take injections".

Women's Likes

'Likes' about IC were reported by 97% of the women, understandably more current than past users.

Voices of IC Users

"There is no tension for 3 months and only some people suffer from side effects while others may not".

"It is better than taking pills daily. IC is simple and convenient".

"It is good that after taking the injection I don't get periods so I get more time to worship God".

What Doctors Like About IC

Majority of the doctors viewed IC as a better option as compared to pills or Copper T. More than half reported "not having to take the pains of remembering it daily like in case of oral contraceptive (OC) pills" as the major point in favor of IC. Almost half of the doctors pointed out that irregular menstruation perceived as a problem by the IC users, was in a way advantageous to them.

A senior lady gynecologist observed, "Since menorrhagic patients lose so much blood, amenorrhea due to IC could be beneficial to them".

Some doctors believed that the use of IC is gradually increasing.

One of the prominent lady gynecologists practicing since more than two decades stated, "IC gives 100% safety and assurance. I advise my clients to try IC first before going to OC pills or Copper T".

Majority of them preferred giving IC to post-delivery cases.

As mentioned by one of the lady gynecologists, "During the lactation period, clients do not mind amenorrhea due to IC, as they are mentally prepared for amenorrhea. They are happy about it, as their main concern is that they should not get pregnant".

Dislikes and Problems

When asked regarding their dislikes 57% of the total women reported having dislikes about IC, which were more in past users than current users.

A school teacher troubled with the problem of spotting said, "I am scared, what if something happens when I am at the school?"

A 23-year-old woman, who did not get periods for a year, explained: "If we do not get our periods then the uterus may get infected, tumor or cancer of uterus may also occur."

A woman fed-up of excessive bleeding said, "Husband wife's relation gets disturbed due to continuous bleeding."

Frequent visits to doctor due to continuous bleeding were also a matter of concern. The prevalence of problems was almost the same in both current and past users. The problems reported were the side effects of IC experienced by the women.

A woman with three children, who had continuous excessive bleeding for 16-17 days retorted, "It would be alright even if I would have conceived again, but at least I would have not faced such problems".

A woman, who discontinued taking IC, reasoned, "I felt there is no guarantee of the injection. I did not get periods for 2-3 months so, I felt as if I have conceived".

The side effects of IC were the major cause of concern for the doctors as well. Menstrual irregularity was reported as the most common complaint by their clients. According to some of the doctors, amenorrhea due to IC is quite stressful for their clients as they are always in confusion whether amenorrhea is just a side effect of IC or is it because they have conceived.

A senior lady doctor said, "If I just examine and say that they have not conceived, they do not believe it. I have to do a pregnancy test. So, there is an additional expense".

Apart from this, the doctors also highlighted the socio-cultural impact and psychological stress of menstrual irregularity and amenorrhea in particular.

"In our society it is strongly believed that menstrual cycle should be regular".

Return of fertility was also a concern mentioned.

One doctor emphasized this saying, "Return of fertility is the most important research aspect of IC and it should be done".

Perceptions of Providers Obtained by Quantitative Survey

Out of the 83 doctors who were interviewed on phone, about 16% never prescribed IC, while 84% had prescribed IC at some time during their practice and 41% were currently prescribing IC. Only about one-fifth of the doctors reported positive qualities regarding IC (20.4%). Positive qualities were reportedly higher in case of doctors who currently prescribe the injection (35.3%) as compared to those who used to prescribe IC in the past (14%) and those who have never prescribed IC to their clients till now (7.7%). However, negative qualities were reported by a majority of the doctors (94%) and among them the percentage of doctors who used to prescribe IC in the past was the highest (36/36) as compared to those who presently prescribe IC (31/34). Among the 13 doctors who had never prescribed IC in the past, 11 of them had negative perceptions regarding IC. This might be one of the reasons for not prescribing IC to their clients.

A doctor who had never prescribed IC said, "I know that due to injection side effects are obvious then why should it be given and why should one try".

Some doctors were in favor of IC even though they were aware of the side effects that it caused. As can be expected, most of the doctors who currently prescribed IC reported these qualities as compared to those who had stopped prescribing IC.

According to a senior lady gynecologist, "IC is good as there is no fear of getting pregnant for 3 months. Although I am willing to give, my clients hesitate because of side effects".

Even though some doctors mentioned the favorable points, most of them expressed their dissatisfaction regarding IC due to its side effects, which is similar to our findings from the in-depth interviews. Out of the 83 doctors interviewed, 78 of them had negative perceptions about IC-based on the problems faced by their clients after using it. Amenorrhea and irregular bleeding were the two major complaints of the clients, as reported by most doctors.

This was followed by substantial dissatisfaction of the clients due to various side effects of IC for which they blamed the doctors.

As one lady doctor who prescribed IC in the past puts it, "Clients with amenorrhea which did not even get cured by medicines, used to come and complain about it and blame me for it. It was such a headache. This was the main reason for me to stop prescribing IC".

Psychosocial stress associated with menstrual irregularity was another important concern with the clients.

Referring to this, one of the doctors endorsed this view, "Every woman wants 1 monthly cycle. If they do not get periods, they are always in a dilemma whether they are pregnant or not".

DISCUSSION

The 'likes' reported by clients for using IC were being tension free after having taken it, simple, comfortable and no botheration in doing routine work. The most common likes by providers and clients were that of the convenience of having to take the injection only once in 3 months, effective in preventing pregnancy and good substitute when other contraceptives give problem. However, the side effects or problems due to IC were the major cause of concern for all the doctors, even though they acknowledged the benefits of IC. One study showed likes of DMPA are independent of intercourse and also independent of the user's memory (and thus of continuing motivation).[4]

Higher percentage of past users had 'dislikes' than current users implying that for the past users these dislikes were perhaps the reasons for having discontinued IC. Over 50% of the women reported some or the other complaints. The problems presented were mainly the side effects of IC experienced by the women. The most common dislikes reported both by women and providers were excessive bleeding, amenorrhea, irregular periods, scanty bleeding, spotting, weight gain and frequent pregnancy tests as shown in Figure 1. Psychological stress due to problems in menstrual cycle, religious restrictions, severe backache and possibility of damage to uterus were mentioned as dislikes particularly by women. While for the doctors delayed fertility and lack of data related to it was a major concern. Over half of the doctors from quantitative survey had stopped prescribing IC as their clients had adverse problems out of proportion to the possible advantages that they could perceive.

Three different studies reported irregular bleeding, spotting and amenorrhea as the common side effects.[5-7] However, rising popularity of injectable contraceptives in Sub-Saharan Africa has also been documented.[8]

The most commonly reported reasons for method discontinuation are side effects, primarily menstrual irregularities and weight gain.[6,9] DPMA carries a higher risk of amenorrhea than NETEN and may be recommended to women who prefer minimal menstrual bleeding.[10]

Women's likes

- Good for those who cannot swallow pills
- No monthly tension of periods
- No botheration in doing routine work
- Simple and comfortable

Common likes

- Effective in preventing pregnancy
- Not to be taken daily like pills but just once in 3 months
- Good substitute when other contraceptives give problem

Doctor's likes

- Reduces anemia
- Good for menorrhagic patients
- Privacy can be maintained
- Noncontraceptive benefits

Women's dislikes

- Severe backache and headache
- Possibility of damage to uterus
- Problem in going to religious places
- Mental tension due to problems in menstrual cycle

Common dislikes

- Excessive bleeding
- Amenorrhea
- Irregular periods
- Scanty bleeding
- Spotting
- Weight gain
- Frequent pregnancy tests

Doctors' dislikes

- Break through bleeding
- Delayed fertility and lack of data related to that

Figure 1. Likes and dislikes of IC according to women and doctors.

Dr C Sathyamala in her monograph articulates that it is not suitable for nulliparous women, adolescents, breastfeeding women.[11]

Studies thus far have not shown any serious long-term effects of DMPA or NETEN. However, both have been used for a relatively short time and the potential long-term effects (over >15 years) are not yet known.[12] Hence, counseling provided by the doctors plays an important role in the acceptance of IC as a reliable and convenient method. Inadequate counseling leading to lack of knowledge regarding possible side effects of IC brings about substantial dissatisfaction among IC users and hence is likely to affect its continuation rate. Doctors were not in favor of making IC 'over-the-counter' available to women and believed that it was suitable only for a particular group of clients and IC should be given to the clients only under their supervision.

A large number of providers also believe that IC is very unsafe and is a banned contraceptive and should not be used. Based on the complaints of side effects by the clients, quite a few of those who started prescribing with enthusiasm have now backed out from their routine prescription. This study was only carried out in one region of India and is thus not necessarily representative of all of India.

Acknowledgments

We express sincere thanks to

- UNFPA, New Delhi office in general and Dr Dinesh Agrawal in particular for financial and technical assistance for this study.
- And practicing gynecologists, doctors and their clients whose support and co-operation made this study a reality.

REFERENCES

1. Ross JA. Management strategies for family planning programs. Centre for Population and Family Health, School of Public Health, Columbia University, New York, 1989.
2. National Family Health Survey. International Institute for Population Science. Mumbai, India, 1993.
3. SAMA. Unveiled reality: a study on women's experiences with Depo-Provera, an injectable contraceptive. SAMA, Delhi, 2000.
4. Bigrigg A, Evans M, Gbolade B, Newton J, Pollard L, Szarewski A, et al. Depo Provera. Position paper on clinical use, effectiveness and side effects. Br J Fam Plann. 1999;25(2):69-76.
5. Hirve S. Injectables as a choice - evidence-based lessons. Indian J Med Ethics. 2005;2(1).
6. Polaneczky M, Guarnaccia M, Alon J, Wiley J. Early experience with the contraceptive use of depot medroxyprogesterone acetate in an inner-city clinic population. Fam Plann Perspect. 1996;28(4):174-8.
7. Sarojini NB, Murthy L. Why women's groups oppose injectable contraceptives. Indian J Med Ethics. 2005;2(1).
8. Adetunji J. Rising popularity of injectable contraceptives in Sub-Saharan Africa. Population Association of America, Los Angeles, Office of Population and Reproductive Health, Bureau for Global Health, US Agency for International Development (USAID). 2006 Mar. 30–Apr. 1.
9. Sangi-Haghpeykar H, Poindexter AN 3rd, Bateman L, Ditmore JR. Experiences of injectable contraceptive users in an urban setting. Obstet Gynecol. 1996;88(2): 227-33.
10. Draper BH, Morroni C, Hoffman M, Smit J, Beksinska M, Hapgood J, et al. Depot medroxyprogesterone versus norethisterone oenanthate for long-acting progestogenic contraception. Cochrane Database Syst Rev. 2006;(3):CD005214.
11. Sathyamala C. An Epidemiological Review of the Injectable Contraceptive Depo-Provera. Medico Friend Circle and Forum for Women's Health. Mumbai, 2000 and 2001.
12. Facts about injectable contraceptives: memorandum from a WHO meeting. Bull World Health Organ. 1982;60(2): 199-210.

■■■■

DCGI Approval to Serum-Oxford COVID-19 Vaccine for Phase 2, 3 Clinical Trials

New Delhi: The Serum Institute of India (SII) has received permission from the Drugs Controller General of India (DCGI) to conduct phase 2 and 3 human clinical trials in India on the potential COVID-19 vaccine, stated a senior government official.

It is following an extensive evaluation that the DCGI has granted approval to SII to perform phase 2, 3 clinical trial based on the recommendations of the Subject Expert Committee (SEC), mentioned the official. According to the study design, all subjects will receive two doses 4 weeks apart - first dose on Day 1 and second dose on Day 29 – followed by assessment of the safety and immunogenicity at predefined intervals… (*ET Healthworld – ANI*)

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Megakaryocyte in Peripheral Blood Smears – A Report of Two Cases

HARSHITA DUBEY*, AMAR RANJAN†, LAWANYA RANJAN‡, PRANAY TANWAR†, GARIMA JAIN#, CHANDAN KUMAR#

ABSTRACT

Myeloproliferative neoplasm (MPN), a clonal hematopoietic stem-cell disorder, results from the proliferation of one or more hematopoietic series of cells like erythroid, granulocytic or megakaryocytic series. Megakaryocytes (MGK) are large polypoidal cells seen within bone marrow aspirate (BMA) smears. We are presenting here two cases of MGK in peripheral blood smears (PBS), one with MPN and the other in a case of chronic myeloid leukemia (CML) with blast crisis. MGK in PBS is rare and is not always associated with neoplasm. It can be due to increased MGK differentiation due to reactive etiology.

Keywords: Megakaryocyte, myeloproliferative neoplasm, bone marrow aspirate, myeloid leukemia, stem-cell disorder

Myeloproliferative neoplasms (MPN) consist of a group of disorders. It is caused by abnormally excessive growth and proliferation of bone marrow stem cells resulting into production of excessive numbers of one or more types of blood cells (red cells, white cells and/or platelets). These cells are compromised in terms of functions. It is a chronic condition that may remain stable for years or may gradually progress to myelodysplastic syndrome (MDS) or to blastic phase of disease over time.

It is a clonal blood stem-cell disorder, caused by mutation, in DNA of stem cell. It is a rare disease. Most common age group is over 50 years, but can occur in any age group.[1]

Megakaryocytes (MGK) are large cells (50-100 μm) that constitute 0.05% of cell population in human bone marrow.[2] Autopsy studies done on tissue sections show that the normal concentration of MGK in bone marrow are 25-32.5 per 10,000 nucleated cells.[3]

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Megakaryocyte is routinely seen in bone marrow aspirate (BMA) smear, not in peripheral blood smear (PBS).

However, presence of MGK in PBS has exceptionally been reported in case reports, most of which have been seen in reactive conditions.[4] We, while working at a cancer hospital, found 2 cases of PBS with MGK in it, one with MPN and the other in a case of chronic myeloid leukemia (CML) with blast crisis.

CASE REPORTS

Case 1

A 59-year-old male presented with mass in left upper abdomen with on and off fever for 12 months. Clinical examination showed hepatosplenomegaly. Routine hemogram showed hemoglobin - 11.6 gm%, total leukocyte count (TLC) - 15.3 × 10^9/L and platelet count - 301 × 10^9/L. PBS showed left shift with myelocytes and metamyelocytes comprising of 25% of all nucleated cells. In the PBS, a well-formed MGK was seen at the tail end of the smear (Figs. 1-3).

BMA was markedly diluted, showed hematopoietic cells of all series with Myeloid: Erythroid (M:E) ratio 8:1, 3% blasts and 1% basophils.

Bone marrow biopsy showed marrow fibrosis. Hematopoietic elements were markedly reduced. No dysplasia was noticed. With the suspicion of CML, *BCR-ABL* was done, which was negative. Chronic myeloproliferative neoplasm (CMPD) was considered.

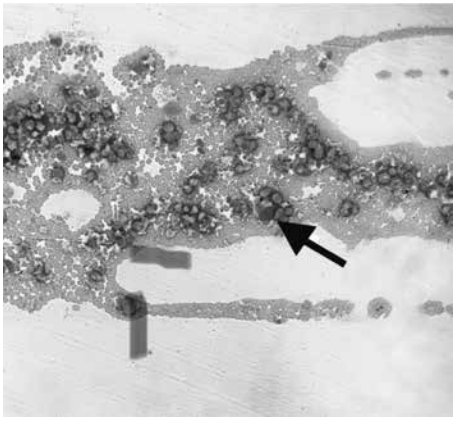

Figure 1. PBS showing megakaryocyte, 10X, Mac-Grunwald Giemsa stain.

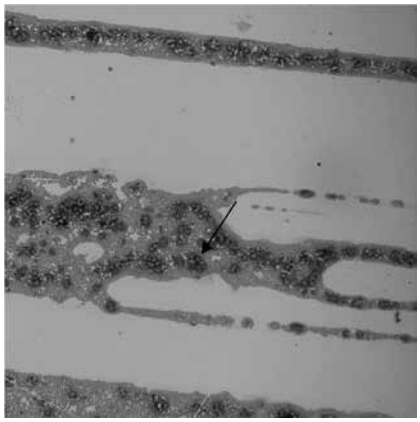

Figure 2. PBS showing megakaryocyte, 4X, Mac-Grunwald Giemsa stain.

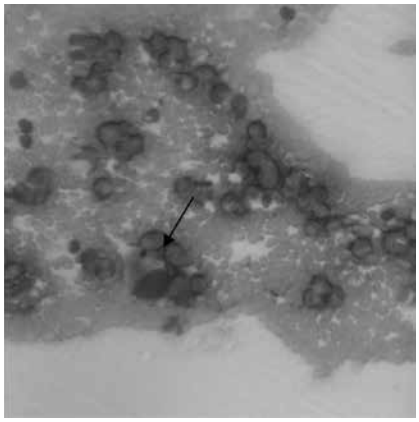

Figure 3. PBS showing megakaryocyte, 20X, Mac-Grunwald Giemsa stain.

Serum level of vitamin B12 was 12.7 (low) (normal range 25-165 pmol/L). During clinical evaluation, it was noticed that the patient was on imatinib 400 mg OD dose for 18 days, but he discontinued it without medical advice for last 15 days. He had complaint of imatinib intolerance (fever and diarrhea). Now, the case was started with imatinib 200 mg/day dose. After 15 days, the patient died.

The case was CMPD, who had two unique presentations: MGK in PBS and imatinib intolerance.

Case 2

A 60-year-old female presented with generalized weakness for 4 months, low-grade fever for 2 months and history of weight loss for 2 months. Pallor, mild hepatosplenomegaly and left cervical lymphadenopathy were present. Hemogram showed TLC - 15 × 10^9/L, hemoglobin - 8.7 gm% and platelet count - 170 × 10^9/L. Differential count of PBS showed blasts (85%) and neutrophil (15%). Interestingly, the PBS showed a well-formed large MGK at the tail of the smear (Fig. 4).

BMA smear examination showed 80% blasts. Bone marrow biopsy showed hypercellular marrow with near total replacement by blasts, which were positive for CD34 and negative for CD3, CD20 and CD138.

Flow cytometry revealed 51% blasts positive for CD19, CD34, CD10, HLA-DR, dim positive for CD79a and TdT and negative for CD45, CD20, CD38, CD33, CD13, CD117, CD64, CD3, CD4, CD5, CD7, CD8 and MPO. Diagnosis of acute lymphoblastic leukemia (ALL) was made and management was started, but no significant improvement was seen. On repeat (thrice) hemogram estimation, it was observed that platelet count was on higher side (>200 × 10^9/L). This raised suspicion of any other associated disease, mainly CML, with blast crisis or Ph-positive ALL. Cytogenetic study revealed chromosome XY, t (9, 22). Reverse-transcriptase polymerase chain reaction (RT-PCR) showed p210 positive. Finally, the diagnosis of CML with blast crisis was considered.

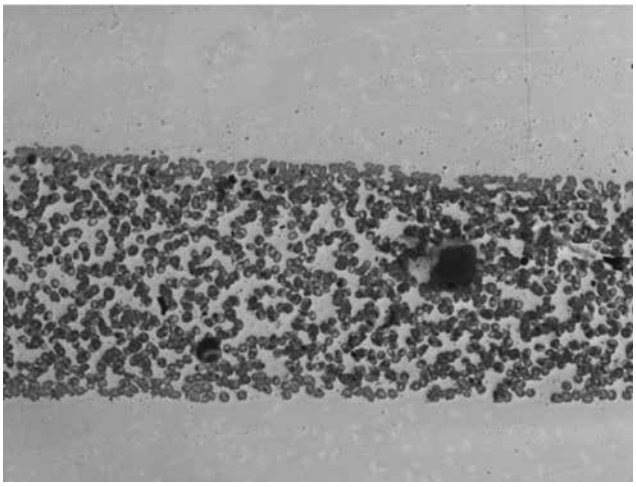

Figure 4. PBS showing megakaryocyte, 20X, Mac-Grunwald Giemsa stain.

A diagnosis of CML with blast crisis was made and treated accordingly.

Till date, the differentiation between CML with blast crisis and Ph-positive ALL is a challenge. On the basis of normal platelet count repeatedly, the diagnosis CML with blast crisis was suggested in this case.

DISCUSSION

Our first case was diagnosed as CMPD, who faced early mortality. So, a confirmatory diagnosis couldn't be made, which required further molecular testing like *JAK-2, MPL,* etc. Bone marrow biopsy showed fibrosis, which raised suspicion of polycythemia vera or

primary myelofibrosis. The two were excluded due to normal level of hemoglobin or platelet count. Essential thrombocythemia (ET) was excluded due to normal platelet count or normal MGK in BMA or bone marrow biopsy. It showed no feature of chronic eosinophilic leukemia. With available studies it may be placed in the category of MPN-Unclassifiable.[5]

MPN–Unclassifiable: It is the least common subtype of MPN. Very little knowledge is available about its incidence, presentations and management. It is diagnosed when an MPN has features of MPN but it does not meet diagnostic criteria of any specific entity. It may overlap two or more entities of MPN.[6]

MPN–Unclassifiable also needs exclusion for the presence of genetic mutation of platelet-derived growth factor receptor alpha (*PDGFRA*), platelet-derived growth factor receptor beta (*PDGFRB*) and fibroblast growth factor receptor 1 (*FGFR1*).

MDS-MPN (chronic myelomonocytic leukemia [CMML]/atypical CML/juvenile myelomonocytic leukemia [JMML]), etc. or MDS was excluded in this case due to absence of atypia. MDS (MDS-SLD/MLD/Ring sideroblasts/excess blasts) was excluded due to absence of atypia. MN with germ line predisposition (*CEBPA*/*DDX41*/*RUNX*/*ANKRD26*/*ETV6*/*GATA2* mutations) is rarely seen and shows positive family history. No such history was found in the patient's family.

Reactive bone marrow response is seen towards alcohol, drug or toxin, folate or vitamin B12 deficiency.[7]

Garg et al, in 2019, showed 4 cases of MGK in PBS. They reported it in 10-year and 14-year-old males. The first presented with reactive thrombocytosis and the other was a burn patient. Other cases were 30-year and 15-year-old females, who presented with thrombocytopenia. The first was positive for dengue serology and the other case was suffering from *Plasmodium vivax* infection. None of their cases had hepatosplenomegaly or evidence of hematological neoplasm.[4]

Ku et al (2017) has shown MGK in PBS in a case of ET that progressed to post-ET myelofibrosis. Platelet count was within normal limit. They proposed an unclear clinical significance for the finding of MGK in PBS.[8]

Erber et al (1987) have shown circulating MGK in PBS in cases of aggressive type of myelodysplasia.[9]

MGK in PBS may be seen in thrombocytosis, thrombocytopenia or with normal platelet count. It may not be associated with hematological disorder. Possibly, it has no clinical significance; however, it requires more study.

In our second case, MGK in PBS may be a presentation of CML in which blast crisis may be the first presentation.

CONCLUSION

Detection of MGK in PBS is rare and it is not always associated with neoplasm. It can be due to increased MGK differentiation due to reactive etiology. Its importance in prediction of any underlying disease needs study on more cases.

REFERENCES

1. Myeloproliferative neoplasms information. Leukaemia Foundation [Internet]. [cited 2020 May 24]. Available at: https://www.leukaemia.org.au/disease-information/myeloproliferative-disorders/
2. Noetzli LJ, French SL, Machlus KR. New insights into the differentiation of megakaryocytes from hematopoietic progenitors. Arterioscler Thromb Vasc Biol. 2019;39(7):1288-300.
3. Ebaugh FG Jr, Bird RM. The normal megakaryocyte concentration in aspirated human bone marrow. Blood. 1951;6(1):75-80.
4. Garg N, Gupta RJ, Kumar S. Megakaryocytes in peripheral blood smears. Turk J Haematol. 2019;36(3):212-3.
5. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, et al. The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: document summary and in-depth discussion. Blood Cancer J. 2018;8(2):15.
6. Korkmaz S. Non-classic myeloproliferative neoplasms: Are we really aware of these rare diseases in daily practice? Euro Med J. 2017;2(3):113-20.
7. Hasserjian RP. Reactive versus neoplastic bone marrow: problems and pitfalls. Arch Pathol Lab Med. 2008;132(4):587-94.
8. Ku NK, Rashidi H. Unusual finding of a megakaryocyte in a peripheral blood smear. Blood. 2017;130(23):2573.
9. Erber WN, Jacobs A, Oscier DG, O'Hea AM, Mason DY. Circulating micromegakaryocytes in myelodysplasia. J Clin Pathol. 1987;40(11):1349-52.

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Hyperhomocysteinemia – A Death Warrant in Young

MANISH N MEHTA*, AMI TRIVEDI†, SNEHA VADHVANA‡, ARJUN CHANDRASEKHARAN#, JEMIMA BHASKAR¥

ABSTRACT

Patient with atherosclerotic narrowing of blood vessels develop thrombotic occlusion and present clinically with cerebrovascular accidents, coronary artery disease, chronic kidney disease and peripheral vascular disease, with the main risk factors for atherosclerosis being diabetes mellitus, dyslipidemia, systemic hypertension, advanced age, male sex, obesity and smoking. But there are many other causes of arterial occlusion in the young, such as nonatherosclerotic angiopathies, thrombophilias, genetic disorders, inflammatory and infectious vasculitis. This is a case where thrombotic occlusion has occurred in the coronary and cerebral circulation in a young patient due to thrombophilia.

Keywords: Hyperhomocysteinemia, arterial and venous thrombosis, coronary artery disease and stroke in young patients, vitamin B12, folic acid

Hypercoagulability of the blood occurs in various diseases causing vascular occlusion. Compared to thrombotic occlusion due to atherosclerosis, it occurs in younger age group, it can be venous or arterial, can be recurrent and can occur in blood vessels which are not usually involved in atherosclerosis. Here is one such case.

CASE REPORT

A 21-year-old male was admitted with generalized tonic-clonic seizures. The patient gave 4 months history of coronary artery disease (CAD) - acute anterior wall myocardial infarction (AWMI) with left ventricular (LV) dysfunction and echocardiography showed LV clot. The patient was started on aspirin 75 mg, warfarin 2 mg, enalapril 5 mg, metoprolol 25 mg and diuretics. Due to the LV clot, the patient developed an embolic stroke about 2 months later with a neurological deficit as left-sided hemiparesis. Following treatment, hemiparesis improved and the patient was able to walk without support. The patient was treated for the seizures and there was no recurrence.

The following investigations were done:

- Hemoglobin - 11.8 g/dL
- White blood cell (WBC) - 7,000/mm^3
- Platelets - 1,83,000/mm^3
- Serum creatinine - 0.8 mg/dL
- Blood urea - 28 mg/dL
- Serum glutamic-pyruvic transaminase (SGPT) - 18 U/L
- Prothrombin time (PT) - 22.6 seconds
- Activated partial thromboplastin time (aPTT) - 46 seconds
- PT: International normalized ratio (INR) - 2.05
- Serum cholesterol - 143 mg/dL
- Serum triglycerides - 176 mg/dL
- Serum homocysteine - 18.53 μmol/L (1-15.39)
- Antiphospholipid IgG - 1.3 GPL U/mL (0-10)
- Antiphospholipid IgM - 1.6 GPL U/mL (0-10)
- 2D Echocardiography – CAD - AWMI with severe LV dysfunction, EF - 35%, LV apical thrombus, akinetic septum and lateral wall
- Coronary angiogram – Proximal left anterior descending artery - 50% lesion with Grade 2

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thrombus and Thrombolysis In Myocardial Infarction (TIMI) Grade 2 flow distally.

The patient was again readmitted with history of fever, vomiting, abdominal pain and loose stools. The patient was clinically stable but on the third day after admission, his condition deteriorated. He was shifted to intensive care unit (ICU). The patient became dyspneic with a drop in oxygen saturation and blood pressure. He was further managed with invasive ventilation and inotropic support with noradrenaline and dopamine. Echocardiography showed an ejection fraction (EF) of 20% with moderate mitral regurgitation and generalized LV hypokinesia. Despite treatment, the patient did not improve and died of cardiac failure. Previous investigations had already revealed hyperhomocysteinemia in plasma. Treatment was given with both vitamin B12 and folic acid.

Table 1. Causes for Nonatherogenic Occlusion of Blood Vessels

Nonatherosclerotic angiopathies	Cervicocephalic arterial dissection
	Cerebral amyloid angiopathy
	Moyamoya disease
	Fibromuscular dysplasia
	Reversible cerebral vasoconstriction syndrome
	Susac's syndrome
	Sneddon's syndrome
	Migraine-induced stroke
Hematologic conditions	Hypercoagulable state due to deficiencies of protein S, protein C or antithrombin; factor V Leiden mutation, prothrombin gene G20210A mutation
	Acquired hypercoagulable state (e.g., cancer, pregnancy, hormonal contraceptive use, exposure to hormonal treatments such as anabolic steroids and erythropoietin, nephrotic syndrome)
	Antiphospholipid syndrome
	Hyperhomocysteinemia
	Sickle cell disease
	Myeloproliferative disorders (e.g., leukemia, lymphoma)
Genetic	Fabry disease
	CADASIL
	MELAS
	Marfan syndrome
	Neurofibromatosis
	Sturge-Weber disease
Inflammatory and infectious	Vasculitis (primary angiitis of the CNS, Sjogren's syndrome, Wegener's granulomatosis)
	Temporal arteritis
	Takayasu disease
	Behcet's syndrome
	Neurosarcoidosis
	Neurocysticercosis
	HIV
	Varicella zoster virus
	Neurosyphilis
	Tuberculous meningitis

CADASIL = Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; MELAS = Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episode; CNS = Central nervous system; HIV = Human immunodeficiency virus.

This young patient was admitted four times within a span of 5 months and had both cerebrovascular accident (CVA) and acute myocardial infarction and had occlusion of both cerebral and coronary arteries leading to death despite treatment for hyperhomocysteinemia, which is vitamin B12 and folic acid replacement.

DISCUSSION

There are many causes for nonatherogenic occlusion of blood vessels leading to CVA, CAD and other vaso-occlusive diseases in young individuals. Table 1 shows the major causes of such events.

Thrombophilia is an inherited or acquired tendency to develop thrombosis. Thrombophilia can cause thrombosis by manufacturing too much clotting proteins, making abnormal clotting proteins that are resistant to breakdown, producing too little of proteins that prevent thrombosis or damaging the walls of blood vessels.

This patient is a case of thrombophilia due to hyperhomocysteinemia. Elevated levels of homocysteine produce arterial and venous thrombosis as well as the development of atherosclerosis. In the other causes of thrombophilia, the pathology is more of hypercoagulability of blood causing thrombosis and atherosclerosis does not play a major part.

The prothrombotic effects of homocysteine are due to thioester linkages formed between homocysteine metabolites and many proteins, including fibrinogen. Marked elevation of homocysteine may be caused by an inherited deficiency of cystathionine beta-synthase. Much more common is a variant form of 5,10-methylenetetrahydrofolate reductase which causes mild homocysteinemia in 5-15% Caucasians and eastern Asians. It is characterized by increased concentration of sulfur-containing amino acid homocysteine in the blood and urine. Many patients present in childhood. Life-threatening vascular complications of coronary, renal and cerebral arteries can occur. Some patients develop a marfanoid habitus and radiological evidence of osteoporosis. Hyperhomocysteinemia has 9 distinct clinical disorders. The classic disease shows evidence of elevated free homocysteine in plasma. Homocysteine acts not only as a thrombophilic agent but also as an atherogenic agent. Vascular occlusions can occur in the arteries and veins.

Treatment involves giving folate and vitamin B12 supplements. They reduce the homocysteine levels but have limited effects on cardiovascular disease.

CONCLUSION

Homocysteinemia often goes undiagnosed as a cause of CAD and stroke. It has to be ruled out in all young patients with arterial and venous thrombosis. But the sad state of affairs is such that although treatment is with only vitamin B12 and folic acid replacement, which is freely available, patients often succumb to the disease.

SUGGESTED READING

1. Smajlović D. Strokes in young adults: epidemiology and prevention. Vasc Health Risk Manag. 2015;11:157-64.
2. Harrison's Principles of Internal Medicine. 19th Edition; 2018. p. 434.
3. Kumar V, Abbas A, Fausto N, Aster J. Robbins and Cotrans Pathologic Basis of the Disease. 8th Edition. Philadelphia: Saunders; 2010. p. 122.

■■■■

Common Causes of Pediatric Allergic Contact Dermatitis

The leading three contact allergens in patients below 18 years of age include hydroperoxides of linalool, nickel sulfate and methylisothiazolinone, suggests an analysis of data from the Pediatric Allergic Contact Dermatitis Registry.

This registry is the first multicenter prospective database in the United States focusing on pediatric allergic contact dermatitis. Investigators obtained data on 218 patients below 18 who were referred for an evaluation of allergic contact dermatitis at one of the 10 participating sites from January 2016 through June 2020. The mean number of allergens patch tested per child was 78. Nearly 81% of the children had one or more positive patch test reactions, with the rate being more or less similar among those with and without a history of AD (80% vs. 82%, respectively). The five top allergens were hydroperoxides of linalool (22%), nickel sulfate (19%), methylisothiazolinone (17%), cobalt chloride (13%) and fragrance mix I (12%). The findings were presented at the virtual annual meeting of the Society for Pediatric Dermatology… (*Medscape*)

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Spontaneous Intracranial Hypotension

CJ SELVAKUMAR*, SHRADDHA LAXMIDHAR MOHANTY†, V SADEESHKUMAR‡, N SHOBANA¥

ABSTRACT

Introduction: Out of all the painful conditions, headache is one of most common cause of patients coming to hospital. Usually few patients present with orthostatic headache, which signifies low cerebrospinal fluid pressure. **Case description:** A 38-year-old female presented with intense headache in upright position, relieved on lying down in supine position. She was treated with analgesics and epidural blood patch. **Discussion:** Spontaneous intracranial hypotension is one of the treatable causes of headache. It can be detected by magnetic resonance imaging, which can reduce the morbidity and improve quality of life. **Conclusion:** As there is increase in availability of MRI, spontaneous intracranial hypotension can be detected easily.

Keywords: Orthostatic headache, subdural hygroma, epidural blood patch

Spontaneous intracranial hypotension is one of the rare causes of headache. The most characteristic feature is the relative change in intensity of headache with change in posture. The intensity of headache is more in the upright and standing position, relieved in the recumbent position (orthostatic headache). The headache occurs due to lowering of intracranial pressure caused by leakage of cerebrospinal fluid (CSF).

CASE HISTORY

A 38-year-old lady presented with headache for 2 weeks, which was severe in intensity, in bitemporal and occipital region, persisting throughout the day, aggravated in sitting and standing position, relieved by supine position. The headache was associated with pain in upper part of neck and vomiting. She had past history of hypertension with regular treatment with antihypertensives. She had no history of previous lumbar puncture, spinal surgery, congenital disease, connective tissue disorders and type 2 diabetes mellitus. No significant family history obtained.

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On neurological examination, she was conscious, oriented to time, place and person; cranial nerves, motor system, sensory system, cerebellar system, autonomic nervous system were normal. No meningeal signs were present. She was initially treated with analgesics, antidepressants, antihypertensives and intravenous fluid. But her headache was not getting relieved with the medications. Neurosurgery and ear, nose and throat opinion were normal. Routine blood investigations were done (blood and radiological). Her blood parameters were hemoglobin - 11.3 g/dL, total leukocyte count - 8,400/mm^3, random blood sugar - 108 mg/dL, serum creatinine - 1 mg/dL. Magnetic resonance imaging (MRI) of brain revealed thin subdural hygroma in both the frontal convexity, prominent venous sinus and draining cortical veins, especially right transverse sinus. Left lateral ventricle narrowed at the frontal horn (slit-like frontal horn) (Figs. 1 and 2).

These findings were suggestive of intracranial hypotension. She was treated with oral analgesics tablet paracetamol and diclofenac, tablet propranolol, capsule omeprazole and intravenous fluids, but there was not significant improvement. A follow-up MRI of brain revealed increase in volume of subdural collection in right frontoparietal convexity with maximum thickness of 16 mL and left frontoparietal, occipital convexity with maximum thickness of 3 mL (Fig. 3). The lesion showed areas of blooming. Since MRI of brain did not reveal any site of leakage, MRI of whole spine with CSF sequence was done, which revealed hyperintense area at the level T7 (thoracic) vertebra suggestive of CSF leak (Fig. 4). After localization of site of CSF leak, epidural

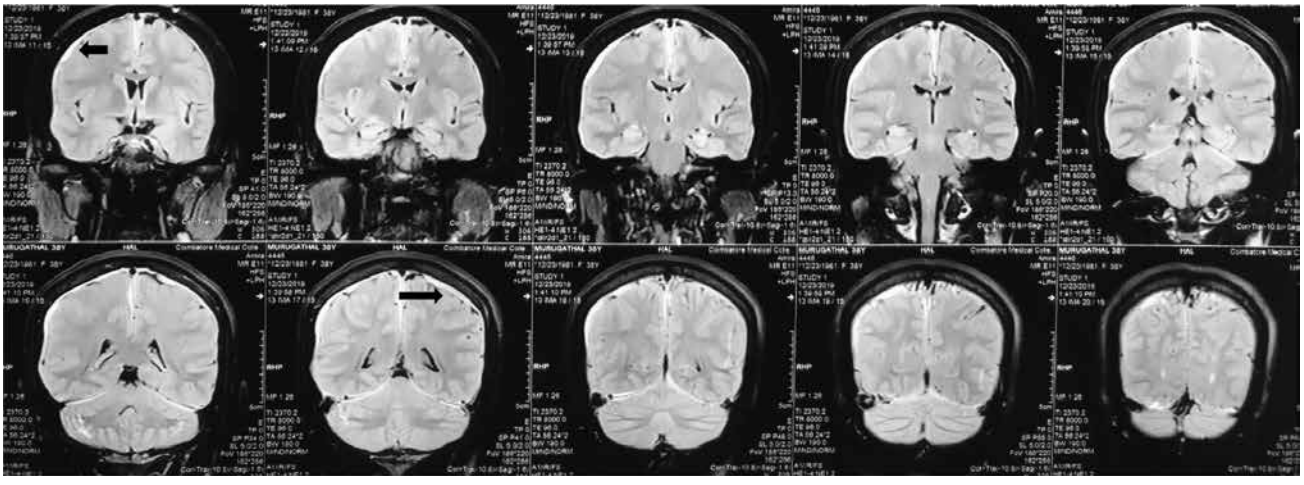

Figure 1. T2 Flair coronal section of MRI of brain - Bilateral subdural hygroma.

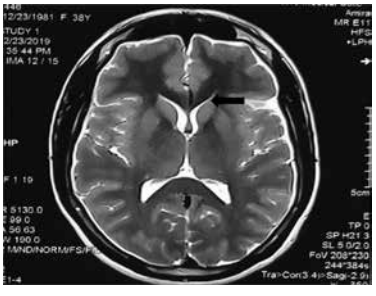

Figure 2. T1 Axial section of MRI of brain – Slit-like frontal horn of left lateral ventricle.

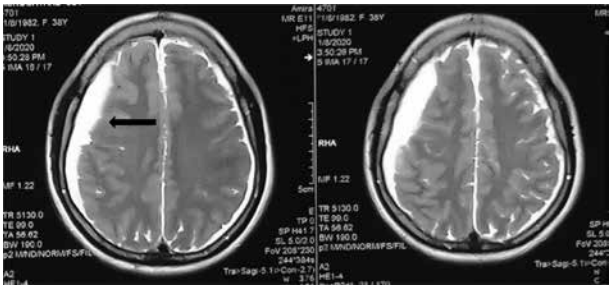

Figure 3. T2 Axial section MRI of brain - Increase in volume of subdural collection in right frontoparietal convexity and left frontoparietal, occipital convexity (follow-up scan).

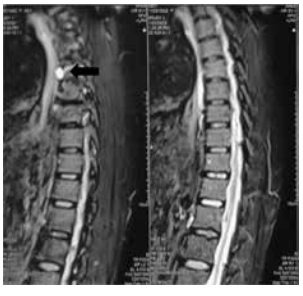

Figure 4. MRI of spine with CSF flow sequence showing leak at T7 vertebral level.

blood patch with patient's own blood was put. After the procedure, her headache reduced tremendously within 2 days.

DISCUSSION

There are various causes of intracranial hypotension. The CSF leak can be caused by lumbar puncture (CSF trickles into the paravertebral muscles), spinal surgery and spinal trauma (tear in the arachnoid surrounding a nerve root). Spontaneous intracranial hypotension can be caused due to low intracranial pressure by leakage of CSF with unknown cause. It is a rare disease occurring in 1 in 50,000 people. It is more common in women than men. The most common cause of spontaneous intracranial hypotension is the leak of CSF through a tear in spinal dura. Marfan and Ehlers-Danlos syndrome, autosomal dominant polycystic kidney disease are genetic risk factors for spontaneous CSF leak.

Orthostatic headache is cardinal presentation of spontaneous intracranial hypotension. It may be associated with diplopia (due to 6th cranial nerve palsy or self-audible bruit from turbulence in the intracranial venous system). There can be sagging of the frontal lobes in low CSF pressure caused by leakage of the CSF (brain sagging syndrome), which can lead to brainstem lesions with stupor, gaze palsies and cranial nerve palsies. Patients are apathetic and disinhibited with prominent daytime somnolence.

To localize the site of the leak, radionuclide cisternography or CT (computed tomography) myelography can be done. CT myelography is the preferred diagnostic test. Dynamic CT myelography is useful for detecting high flow leaks. As there are technological advancements and availability of MRI, MRI of brain with gadolinium contrast is done, which shows prominent dural enhancement (due to dural venous dilation) or diffuse pachymeningeal enhancement described by Fishman and Dillon et al. Other additional features seen are subdural effusions on cerebral convexities, temporal lobes, optic chiasma or cerebellar tonsils. In order to find leak, MRI of spine can be done which may show spinal fluid collection, dural enhancement, dilated epidural veins, enlarged epidural venous plexus, attenuation of spinal canal or compression of spinal cord and contrast

extravasation. MRI of spine helps us find the site of leak present in the spinal dura.

A diagnostic criteria for headache in spontaneous intracranial hypotension was framed by Schievink et al as:

- Orthostatic headache
- The presence of at least one of the following: low opening pressure (≤60 mm water), sustained improvement of symptoms following epidural blood patching, demonstration of an active spinal CSF leak, cranial MRI changes suggestive of intracranial hypotension (brain sagging or pachymeningeal enhancement)
- No recent history of dural puncture
- Not attributed to another disorder.

CONCLUSION

Our patient had orthostatic headache, with relief of headache after blood patch and MRI of brain showing dural enhancement.

The definitive treatment is epidural blood patch with approximately 20 mL of patient's blood at the site of leak, which relieves the headache. After blood patch, there has been no recurrence; very few cases had repeated episodes of orthostatic headache.

As there is increase in availability of MRI, spontaneous intracranial hypotension can be detected easily. It can be treated easily, preventing long-term morbidity as well as preventing the inappropriate usage of analgesics.

SUGGESTED READING

1. Disturbances of cerebrospinal fluid, including hydrocephalus, pseudotumor cerebri and low-pressure syndromes (Chap 29). In: Ropper AH, Samuels MA, Klein JP, Prasad S (Eds.). Adam and Victor's Principles of Neurology. 11th Edition, McGraw-Hill; 2019. pp. 654-6.
2. Gordon N. Spontaneous intracranial hypotension. Dev Med Child Neurol. 2009;51(12):932-5.
3. Vaidhyanath R, Kenningham R, Khan A, Messios N. Spontaneous intracranial hypotension: a cause of severe acute headache. Emerg Med J. 2007;24(10):739-41.
4. Mokri B. Spontaneous intracranial hypotension. Continuum (Minneap Minn). 2015;21(4 Headache):1086-108.
5. Limaye K, Samant R, Lee RW. Spontaneous intracranial hypotension: diagnosis to management. Acta Neurol Belg. 2016;116(2):119-25.
6. Tosaka M, Sato N, Fujimaki H, Tanaka Y, Kagoshima K, Takahashi A, et al. Diffuse pachymeningeal hyperintensity and subdural effusion/hematoma detected by fluid-attenuated inversion recovery MR imaging in patients with spontaneous intracranial hypotension. AJNR Am J Neuroradiol. 2008;29(6):1164-70.
7. Wu JW, Wang YF, Fuh JL, Lirng JF, Chen SP, Hseu SS, et al. Correlations among brain and spinal MRI findings in spontaneous intracranial hypotension. Cephalalgia. 2018;38(14):1998-2005.
8. Mokri B. Spontaneous CSF leaks: low CSF volume syndromes. Neurol Clin. 2014;32(2):397-422.
9. Medina JH, Abrams K, Falcone S, Bhatia RG. Spinal imaging findings in spontaneous intracranial hypotension. AJR Am J Roentgenol. 2010;195(2):459-64.
10. Schievink WI, Dodick DW, Mokri B, Silberstein S, Bousser MG, Goadsby PJ. Diagnostic criteria for headache due to spontaneous intracranial hypotension: a perspective. Headache. 2011;51(9):1442-4.
11. Zheng Y, Lian Y, Wu C, Chen C, Zhang H, Zhao P. Diagnosis and treatment of spontaneous intracranial hypotension due to cerebrospinal fluid leakage. Springerplus. 2016;5(1):2108.

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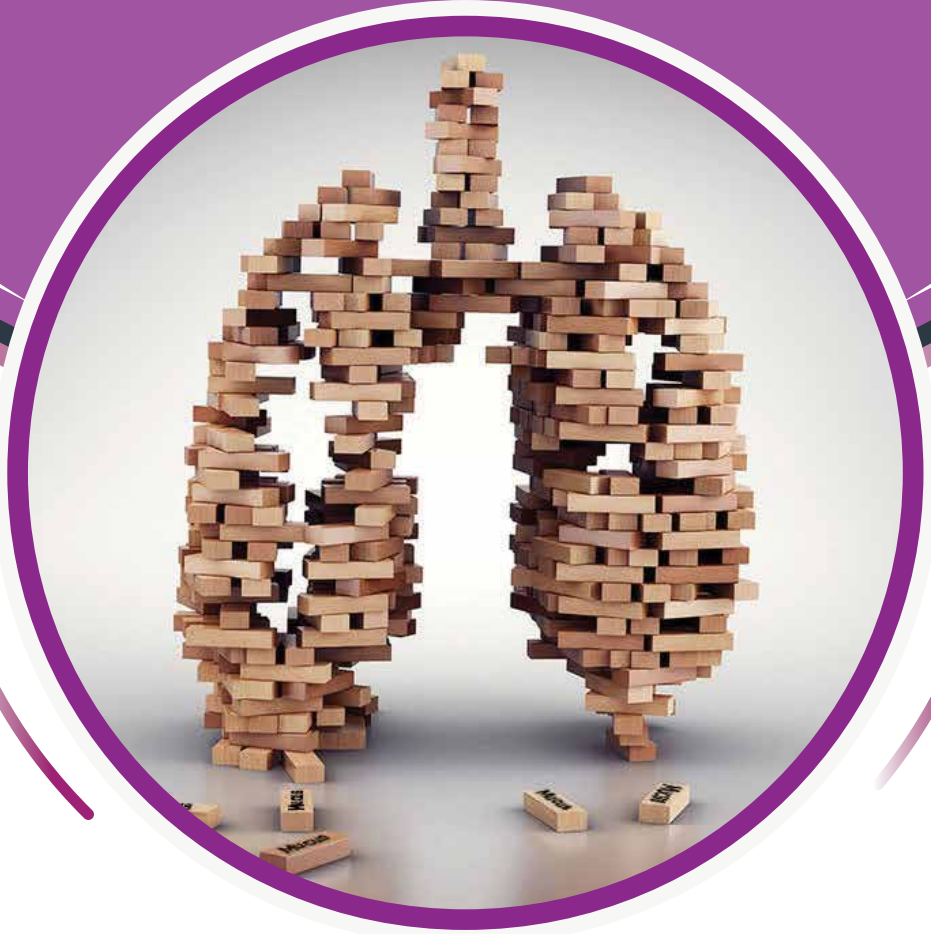
Moist Heat Treatment of N95 Masks Eliminates COVID-19, Says Study

Moist heat treatment of N95 masks tends to eliminate the novel coronavirus, suggest scientists.

The study revealed that moist heat treatment of masks for 60 minutes at 70°C in a humid condition did not impair their structure or impact function. According to investigators, this low-cost reprocessing strategy could be applied 10 times without affecting the mask's filtration, breathing resistance, fit and comfort. This strategy could possibly help curb the global shortage of masks during the pandemic. The findings are published in the *Canadian Medical Association Journal (CMAJ)…* (*HT – PTI*)

Breaking Mucus Accumulation



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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

A Rare Case of Intrathyroid Dermoid Cyst in a Middle-aged Female

RAXITH S RAGAVENDRA*, NARAYAN I HEBSUR†, NARAYAN Y KABADI‡

ABSTRACT

Introduction: The term 'dermoid cyst' describes a cystic lesion comprising of stratified squamous epithelium with epidermal appendages. **Presentation of case:** A dermoid cyst arising in the left lobe of the thyroid gland in a 35-year-old female was managed with a left hemithyroidectomy. **Discussion:** While congenital lesions feature frequently in the differential diagnosis of childhood neck masses, dermoid cysts presenting as a unilateral neck mass are rare. **Conclusion:** When dermoid cysts are found within the thyroid, their pathogenesis may be explained by a disruption of normal thyroid development. Excision appears the treatment of choice.

Keywords: Dermoid cyst, stratified squamous epithelium, thyroid gland, congenital lesions, excision

The term 'dermoid cyst' describes a cystic lesion comprising of stratified squamous epithelium with epidermal appendages. DeMello referred to midline cervical lesions of the above morphology, originally classified as thyroglossal duct cysts, as dermoids. This classification remains controversial, but true midline dermoids in the cervical region are not uncommon. Clearly, these lesions remain clinically distinct from cervical teratoma which represents a tumor of germ cell origin containing all three layers of the trilaminar embryo.

Dermoids located within or immediately adjacent to the thyroid gland appear rare. A dermoid cyst presenting as a midline, cold thyroid nodule in a 9-year-old girl has been previously reported. We describe an intrathyroid dermoid cyst presenting as a solitary thyroid nodule in a middle-aged female.

CASE PRESENTATION

A 35-year-old female presented with a left-sided neck mass. She noticed a swelling 1 year back. It had been gradually increasing in size since then. There were no other symptoms or signs suggestive of thyroid disease. There was no history of dysphagia, hoarseness of voice or additional neck masses. Obstetric history, she was married with two children and tubectomized 4 years back, menstrual cycles were regular. There was no past history of irradiation or iodides. The family history was unremarkable, although her mother had an excision of nonfunctioning thyroid nodules several years earlier.

Examination revealed a 3 × 2 cm oval-shaped, firm to hard mass left of the midline, medial and anterior to the sternocleidomastoid muscle (Fig. 1). It did not extend into the mediastinum and moved on swallowing but not on protrusion of the tongue. There was no cervical lymphadenopathy.

Investigation

An ultrasound revealed a 3.4 × 1.9 cm hypoechoic nodule arising from within the left lobe of the thyroid (Fig. 2). Color duplex revealed no blood flow within the nodule. Thyroid function tests were within normal limits. Chest radiography was normal. Fine needle aspiration cytology (FNAC) was performed, which revealed few inflammatory cells.

Operative Findings

A large smooth whitish color cystic mass was seen within and adherent to the left lobe of the thyroid gland (Fig. 3). There was evidence of a chronic inflammatory reaction around the mass. A left hemithyroidectomy was performed.

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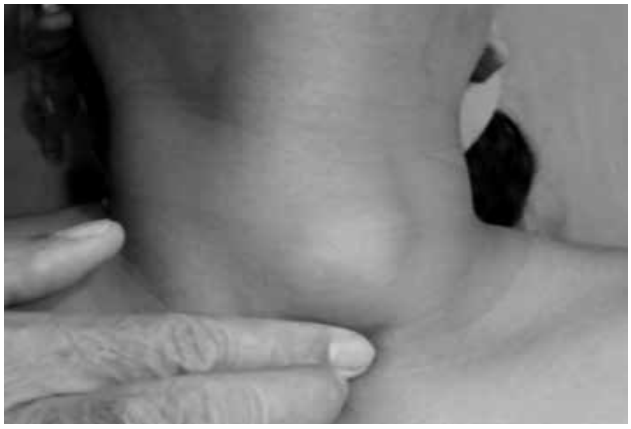

Figure 1. Patient with solitary thyroid nodule.

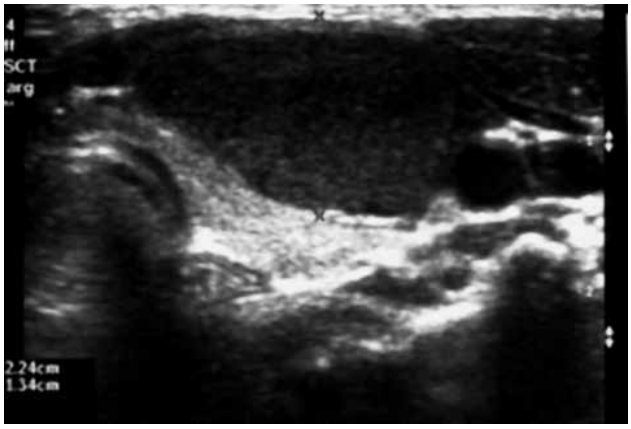

Figure 2. Ultrasound of intrathyroid lesion.

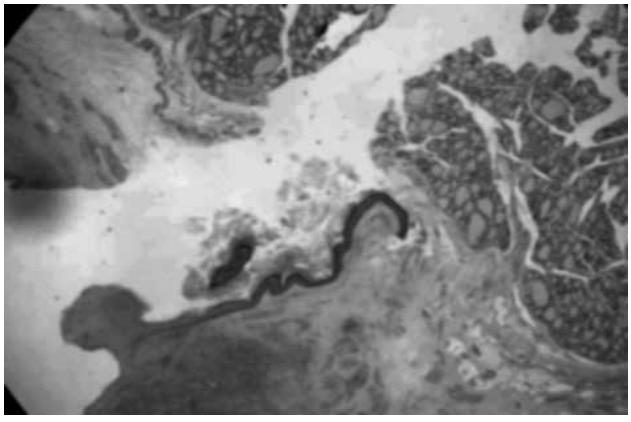

Figure 3. Showing operative intrathyroid cyst.

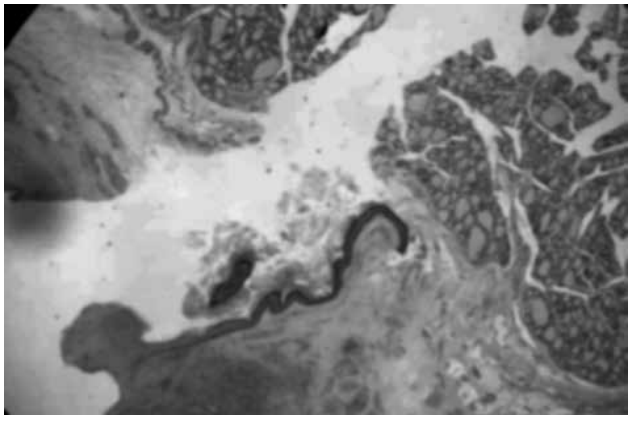

Figure 4. Histopathology of dermoid cyst with adjacent thyroid tissue.

Histopathological Examination

The microscopic examination showed a dermoid cyst. The wall consisted of stratified squamous epithelium with few associated sebaceous glands. There were focal areas of rupture with an associated foreign body-type giant cell-reaction around keratin. Histologically, the adjacent thyroid was unremarkable and the cyst appeared attached to it (Fig. 4).

The postoperative recovery was uneventful. Repeated thyroid function tests 6 weeks postoperatively were normal.

DISCUSSION

The thyroid gland develops during the 3rd week of gestation, as a midline diverticulum from the ventral surface of the pharynx. Elongation of the embryo with growth of the pharynx and tongue leaves the thyroid caudal to its point of origin. The diverticulum forms the majority of the gland but receives lateral contributions from the fourth ultimobranchial bodies that form the calcitonin-producing C cells.

A palpable neck mass is a commonly encountered clinical problem. Meticulous clinical history and physical examination may suggest the clinical diagnosis. Imaging is increasingly performed to confirm the clinical diagnosis and assesses the anatomical extent of involvement before any form of treatment. Apart from its location, the distinction between solid and cystic or cyst-like neck masses helps in the definitive diagnosis or to narrow the differential diagnoses. Cystic masses of the neck include a wide range of congenital and acquired lesions. The vast majority of cystic lesions in infants and children are congenital or developmental in origin, whereas inflammatory and neoplastic diseases constitute the majority of cystic or cyst-like neck masses in adults.

An asymptomatic left-sided mass evident low in the anterior cervical triangle may represent lymphadenopathy in the pre-tracheal lymphatic chain with a single predominant node. A congenital anomaly such as a true cervical dermoid or third or fourth branchial cleft cyst must be considered as these, together,

comprise 55% of cervical neck masses in children. Thymic cysts may occasionally present just lateral to the midline but are very rare. Lymphatic malformations such as cystic hygromas occur predominantly in the posterior triangle but may present in this manner. They are usually fluctuant and brilliantly translucent. A thyroglossal duct cyst would tend to present as a midline mass that elevates on tongue protrusion.

A dermoid cyst is the most common of the teratomatous lesions in the head and neck region, approximately 7% occur of all dermoids occurring in this region. Histologically, it contains two germ cell layers and skin appendages (e.g., hair follicles and sebaceous glands). An epidermoid cyst is less common in the neck as compared to a dermoid cyst and is comprised solely of ectoderm. In this case, the nodule appeared to move with swallowing but did not elevate with protrusion of the tongue. The ultrasound scan suggested an intrathyroid mass and radionuclide scanning confirmed the presence of normal-appearing functioning thyroid tissue surrounding the mass. The mass was therefore thought to arise from the left hemithyroid.

The intrathyroid location of the lesion is of particular interest with regard to the etiology of dermoids in the head and neck. A hypothesis for this entity is entrapment of cells within disparate layers during embryogenesis. This explains the appearance of components of ectoderm within a predominantly endodermal organ such as the thyroid. Yet another explanation has been the traumatic implantation of ectodermal cells within deeper tissues. This applies in the context of dermoid cysts identified around surgical incisions or near scars but would not be applicable to our patient.

CONCLUSION

Dermoid cysts should be included in the differential diagnosis of a lateral neck mass in adults, even when apparently within the thyroid gland. Given the rarity of this lesion, the true diagnosis may only be made at operation. Because of the risk of infection and progressive enlargement, excision remains the treatment of choice.

SUGGESTED READING

1. Cox CA, Nguyen DL, Medina J, Leonard JC. Dermoid cyst presenting as a "cold" thyroid nodule. Clin Nucl Med. 1996;21(5):395.
2. deMello DE, Lima JA, Liapis H. Midline cervical cysts in children. Thyroglossal anomalies. Arch Otolaryngol Head Neck Surg. 1987;113(4):418-20.
3. De Ponte FS, Brunelli A, Marchetti E, Bottini DJ. Sublingual epidermoid cyst. J Craniofac Surg. 2002;13(2):308-10.
4. Mahmood S, Moody H. Dermoid, teratoma or choristoma? A rare lesion of the tongue in an adult. Br J Oral Maxillofac Surg. 2003;41(2):117-9.
5. Mazzaferri EL. Management of a solitary thyroid nodule. N Engl J Med. 1993;328(8):553-9.
6. Raab SS, Silverman JF, Elsheikh TM, Thomas PA, Wakely PE. Pediatric thyroid nodules: disease demographics and clinical management as determined by fine needle aspiration biopsy. Pediatrics. 1995;95(1):46-9.
7. Skandalakis JE, Gray SW. Embryology for surgeons (Chapter 2). In: The Pharynx and its Derivatives. 2nd Edition, Baltimore: Williams and Wilkins; 1994.
8. Tapper D, Sawin R, O'Neill JA Jr, Rowe MI, Grosfeld JL, Fronkalsrud EW, et al. Teratomas Andother Germ Cell Tumours Pediatric Surgery. 5th Edition, Chapter 29, Mosby: St. Louis; 1998.
9. Thompson NW, Geiger JD, O'Neill JA Jr, Rowe MI, GrosfeldJL, Fronkalsrud EW, et al. Thyroid/Parathyroid Pediatric Surgery. 5th Edition, Chapter 48, Mosby: St. Louis; 1998.
10. Torsiglieri AJ Jr, Tom LW, Ross AJ 3rd, Wetmore RF, Handler SD, Potsic WP. Pediatric neck masses: guidelines for evaluation. Int J Pediatr Otorhinolaryngol. 1988;16(3):199-210.

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A Third of World's Children have High Lead Levels

Lead poisoning is affecting children on a huge scale that was previously unknown, suggests a new study by the United Nations Children's Fund (UNICEF) and Pure Earth, an international non-profit organization that focuses on pollution issues.

This first of its kind report has revealed that about 1 in 3 children, which amounts to about 800 million worldwide, have blood lead levels at, or above, 5 μg/dL, the amount at which action needs to be taken.

Around half of these children are in South Asia. The report has also stated that informal and inadequate recycling of lead-acid batteries has a huge contribution to lead poisoning in children in low- and middle-income countries… (*UN*)

Significance of Peripheral Blood Smear in Diagnosis of Blood Parasitic Infection

GOPAL RAVAL*, DEVANG PATVARI*, D KOTHARI*, P JOSHI*, M PANDYA*

ABSTRACT

Bancroftian filariasis is a tropical and subtropical disease caused by *Wuchereria bancrofti* and transmitted by the Culex mosquitoes. It is conventionally diagnosed made by demonstrating microfilariae in the peripheral blood smear. Microfilariae and adult filarial worm have been incidentally detected in the blood. We here report an unusual case of Bancroftian microfilariasis in a 28-year-old male coming from endemic area with history of fever since 1 month. Patient had history of yellowish discoloration of skin and sclera.

Keywords: Microfilaria, *Plasmodium falciparum*, jaundice

Filariasis is caused by slender thread-like nematodes belonging to super family Filarioidea. Filariasis is endemic in India and South-East Asia. Present estimate suggest that over 120 million people in 80 countries are affected by filariasis and more than 1.1 billion people live in areas where there is risk of infection.[1,2] Individuals having circulating microfilariae are outwardly healthy but have the ability to transmit the infection to others through mosquito bites. Those with chronic filarial infection suffer severely from the disease but no longer transmit the infection. Diagnosis of filarial infection is frequently made on clinical grounds in endemic areas, but demonstration of microfilariae in circulating blood is the only means by which one can make definitive diagnosis.[2,3]

CASE REPORT

A 28-year-old male patient presented at Dr Jivraj Mehta Hospital with complaint of fever on and off since 1 month. Fever was associated with chills, and high-grade in nature. Patient also had a history of yellowish discoloration of skin and sclera since 1 month. Patient had past history of traveling to Madhya Pradesh 1 month before. He stayed there for 15 days. After returning to Ahmedabad, he had developed all these complaints. Patient had no any other sign and symptoms suggestive of filariasis like swelling, enlargement of limb except traveling and staying at an endemic area. So, when patient came with this complaint to Dr Jivraj Mehta Hospital, blood investigation was advised in form of complete blood count (CBC), peripheral smear for malaria parasite (PSMP), liver function test (LFT) and renal function test (RFT).

Peripheral Smear Findings

Blood sample collected at routine time (no night blood sample). Blood smear examination of patient

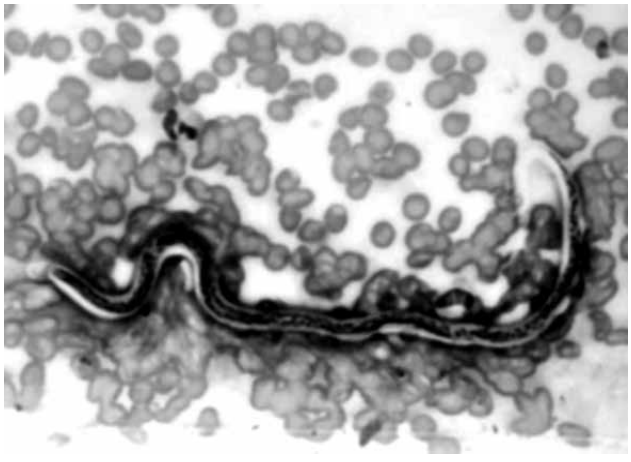

Figure 1. Microfilaria of *Wuchereria bancrofti.* Note the cephalic and tail tip free from nuclei (Fields stain, 40x).

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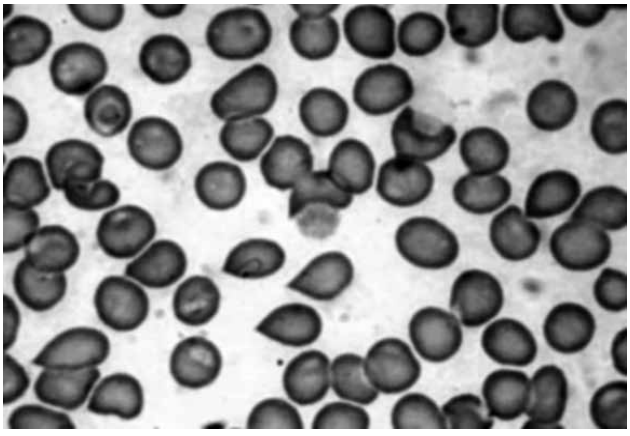

Figure 2. Trophozoites of *P. falciparum* (oil immersion field 100x Fields stain).

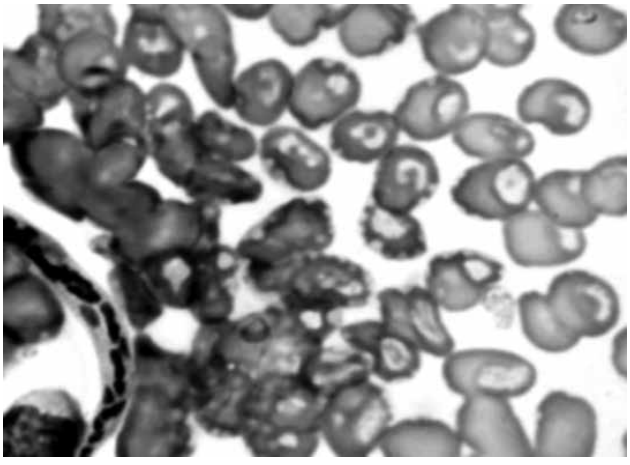

Figure 3. Trphozoites of *P. falciparum* and microfilaria of *W. bancrofti* (oil immersion field 100x Fields stain).

revealed the trophozoite of *Plasmodium falciparum* and scattered microfilariae in background of lymphocytes, neutrophils and eosinophils (Figs. 1 and 2). Morphologically the microfilaria showed presence of hyaline sheath (Fig. 1), cephalic space length: breath ratio of 1:1. Nuclei were spherical, regularly placed, appeared in row, well-separated without any overlapping (Figs. 2 and 3) and absent at cephalic end and tail tip (Figs. 1 and 2). The results of laboratory findings are summarized in Table 1.

Table 1. Other Laboratory Findings

Lab investigations	Results
Differential count	
Neutrophils	77%
Lymphocytes	21%
Eosinophils	01%
Monocyte	2%
Platelets counts	1,55,000/mm^3
Serum bilirubin	
Total	7.91 mg%
Direct	6.17 mg%
Indirect	1.74 mg%
SGPT	451 IU/L
Parasites	Trophozoite of *P. falciparum* Grade II and microfilaria of *W. bancrofti* are seen

DISCUSSION

Filariasis is a major public problem in tropical countries, especially India, China, Indonesia and parts of Africa. Clinically, filariasis can be of two major categories:

- Filariasis of skin and subcutaneous tissue
- Lymphatic filariasis.

Onchocerca volvulus and *Loa loa* are most common organisms reported in former and *W. bancrofti* and *Brugia malayi* are the two most common species in latter.[4]

The life cycle of *W. bancrofti* is found in two hosts. Man is definitive host and mosquito is an intermediate host. Adult worm resides in lymph nodes where the gravid female releases a large numbers of microfilariae. These larvae pass through the thoracic duct and pulmonary capillaries to the peripheral circulation.[5] Our case, *W. bancrofti* infection (filariasis) associated with *P. falciparum* infection. *P. falciparum* and *W. bancrofti* are transmitted by the same mosquito vector, *Anopheles gambiae* and interaction between the two species in the vector may have important implications for transmission of these two infections.[6] Patient also had raised serum glutamic-pyruvic transaminase (SGPT) and eosinophil counts were within normal range, which has also been reported by Varghese et al.[7]As in this case, patient had no other history suggestive of filarial infection except traveling and staying at an endemic area, this case would have been missed if peripheral smear was not properly examined. So, if a patient has any history of traveling and staying at an endemic area peripheral smear should be carefully examined for filarial infection. Patient was referred to physician and given falcigo 120 mg IV stat as loading dose on the first day followed by 60 mg IV twice-daily for 5 days and diethylcarbamazine (6 mg/kg) for 21 days. Patient was advised to come for follow-up after 21 days. Patient improved with the above treatment.

CONCLUSION

The main purpose of this case report is to raise the awareness that in tropical countries like India where filariasis is endemic, it should always be considered as a differential diagnosis of fever with history of traveling and staying at an endemic area. As patient also had an infection of *P. falciparum*, filarial infection would have been easily missed if the smear had not been examined properly. Careful examination of peripheral smears is very important in prompt recognition of the disease and institution of specific treatment especially in unsuspected cases.

REFERENCES

1. Sivakumar S. Role of fine needle aspiration cytology in detection of microfilariae: report of 2 cases. Acta Cytol. 2007;51(5):803-6.
2. Park K. Textbook of Preventive and Social Medicine. 18th Edition, Jabalpur, India: M/S Banarsidas Bhanot Publishers; 2005. pp. 211-6.
3. Rawat V, Rizvi G, Sharma N, Pandey H. An unusual presentation of Wuchereria bancrofti infection. Indian J Med Microbiol. 2009;27(4):382-3.
4. Mallick MG, Sengupta S, Bandyopadhyay A, Chakraborty J, Ray S, Guha D. Cytodiagnosis of filarial infections from an endemic area. Acta Cytol. 2007;51(6):843-9.
5. Kishore B, Khare P, Gupta RJ, Bisht SP. Microfilaria of Wuchereria bancrofti in cytologic smears: a report of 5 cases with unusual presentations. Acta Cytol. 2008;52(6): 710-2.
6. Marsh K, Kinyanjui S. Immune effector mechanisms in malaria. Parasite Immunol. 2006;28(1-2):51-60.
7. Varghese R, Raghuveer CV, Pai MR, Bansal R. Microfilariae in cytologic smears: a report of six cases. Acta Cytol. 1996;40(2):299-301.

■■■■

Low Vitamin D Tied to Increased COVID-19 Risk

Low plasma vitamin D level was found to be an independent risk factor for COVID-19 infection and hospitalization in a large, population-based study.

Individuals positive for COVID-19 had a 50% higher likelihood of having low versus normal 25(OH)D levels in a multivariate analysis controlling for other confounders. Investigators evaluated data for 7,807 individuals; of these, 10.1% were COVID-19 positive. About 90% of COVID-19 positive patients had low plasma 25(OH)D concentrations compared to 85% of participants negative for COVID-19. The findings are published online July 23 in *The FEBS Journal*… (*Medscape*)

Mothers Unlikely to Pass Coronavirus to Newborns with Proper Safety Techniques

Mothers infected with the novel coronavirus will not likely pass the infection to their newborns if appropriate health precautions are taken, suggests a study published in *The Lancet Child & Adolescent Health.*

There were no cases of viral transmission among 120 babies born to 116 COVID-positive mothers, reported researchers, even when they shared a room and the babies were breastfed. Precautions were taken; for instance, babies remained in enclosed cribs, 6 feet away from their mothers, except at the time of breastfeeding. Additionally, mothers wore surgical masks when handling the child and followed appropriate hand and breast washing procedures… (*CNN*)

COVID-19: WHO Chief Scientist Sees No Herd Immunity Yet

According to World Health Organization (WHO) chief scientist, nearly 50-60% of the population needs to be immune to the novel coronavirus for protective "herd immunity" effect to set in.

In a social media event, Dr Soumya Swaminathan mentioned that studies from some hard-hit countries suggest that about 5-10% of people have antibodies; some countries have shown it to be as high as 20%. She added that in order to achieve herd immunity through natural infection, you need to have several waves… (*HT*)

Role of Atmospheric Pressure as a Trigger for Subarachnoid Hemorrhage

EZEQUIEL GARCÍA-BALLESTAS*, LUIS RAFAEL MOSCOTE-SALAZAR†, AMIT AGRAWAL‡

Studies suggest that there is a link between temperature decline from the highest of the previous day (TDP) to the lowest of the event day with the incidence of subarachnoid hemorrhage (SAH).[1] The impact of weather conditions, particularly the atmospheric pressure, on the occurrence of cerebral hemorrhage is well described in the literature. Several studies have reported a potential correlation between environmental factors and SAH onset, while certain others have not found a significant association, resulting in controversy due to different assessment of meteorological factors, patient selection, target geographical area and study design.[2-8] The atmospheric pressure is related to the temperature variation and atmospheric pressure determines nature of temperature fluctuation, magnitude of change and persistence duration. However, using prefecture-wide survey data amassing all patients with SAH in the defined area, has minimized referral and selection biases and proved the correlation of TDP with the incidence of spontaneous SAH. The triggering effect of TDP was prominent in younger women patients <65 years old. Interestingly, variations in barometric pressure are reported to be associated with the development of intracerebral hemorrhages, including SAH. It is possible that the effect depends on the change of magnitude of the barometric pressure, and secondary manifesting, as temperatures changes in preceding days and onset of new-onset SAH ictus. This aspect has been evaluated by various authors.[5,8-10]

Previous studies from the Netherlands, Japan and Northern France revealed significant associations between low daily temperatures and SAH.[2,3,11] Conversely, such an association was not found to be significant in studies from Germany and the US.[4,6] Although the study has many concerns (a small sample size; flack of atmospheric pressure trend over SAH ictus and limited information about exposure to cold, usage of protective clothing and living room modifications),[7] to add further, investigating environmental factors not only will help to know the impact of atmospheric pressure as a risk factor to trigger SAH but also shall help in deciding how the environment around these patients needs to be managed in critical care settings. The biggest challenge for the researcher would be to identify whether it is low pressure,[12] or high atmospheric pressure,[5] which is more important. Additionally, it will help to guide how the patients with diagnosed, yet unruptured, aneurysms can be managed and what kind of day-to-day activities in what weather conditions they can participate in.

REFERENCES

1. Fukuda H, Ninomiya H, Ueba Y, Ohta T, Kaneko T, Kadota T, et al. Impact of temperature decline from the previous day as a trigger of spontaneous subarachnoid hemorrhage: case-crossover study of prefectural stroke database. J Neurosurg. 2019;1-9.
2. Abe T, Ohde S, Ishimatsu S, Ogata H, Hasegawa T, Nakamura T, et al. Effects of meteorological factors on the onset of subarachnoid hemorrhage: a time-series analysis. J Clin Neurosci. 2008;15(9):1005-10.
3. Backes D, Rinkel GJ, Algra A, Vaartjes I, Donker GA, Vergouwen MD. Increased incidence of subarachnoid hemorrhage during cold temperatures and influenza epidemics. J Neurosurg. 2016;125(3):737-45.
4. Beseoglu K, Hänggi D, Stummer W, Steiger HJ. Dependence of subarachnoid hemorrhage on climate conditions: a systematic meteorological analysis from the dusseldorf metropolitan area. Neurosurgery. 2008;62(5):1033-8; discussion 1038-9.
5. Buxton N, Liu C, Dasic D, Moody P, Hope DT. Relationship of aneurysmal subarachnoid hemorrhage

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to changes in atmospheric pressure: results of a prospective study. J Neurosurg. 2001;95(3):391-2.

6. Cowperthwaite MC, Burnett MG. The association between weather and spontaneous subarachnoid hemorrhage: an analysis of 155 US hospitals. Neurosurgery. 2011;68(1):132-8; discussion 138-9.
7. Inagawa T. Seasonal variation in the incidence of aneurysmal subarachnoid hemorrhage in hospital- and community-based studies. J Neurosurg. 2002;96(3):497-509.
8. Landers AT, Narotam PK, Govender ST, van Dellen JR. The effect of changes in barometric pressure on the risk of rupture of intracranial aneurysms. Br J Neurosurg. 1997;11(3):191-5.
9. de Steenhuijsen Piters WA, Algra A, van den Broek MF, Dorhout Mees SM, Rinkel GJ. Seasonal and meteorological determinants of aneurysmal subarachnoid hemorrhage: a systematic review and meta-analysis. J Neurol. 2013;260(2):614-9.
10. Rué M, Camiade E, Jecko V, Bauduer F, Vignes JR. Relations entre hémorragies sous-arachnoïdiennes par rupture anévrysmale et paramètres météorologiques à partir d'une série française de 236 patients. Neurochirurgie. 2014;60(5):222-6.
11. Lejeune JP, Vinchon M, Amouyel P, Escartin T, Escartin D, Christiaens JL. Association of occurrence of aneurysmal bleeding with meteorologic variations in the north of France. Stroke. 1994;25(2):338-41.
12. Honig A, Eliahou R, Pikkel YY, Leker RR. Drops in barometric pressure are associated with deep intracerebral hemorrhage. J Stroke Cerebrovasc Dis. 2016;25(4):872-6.

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Small Study Suggests Rapid Decay of Anti–SARS-CoV-2 Antibodies in Persons with Mild COVID-19

DG Alert: Findings from a study published in *The New England Journal of Medicine* "raise concern" that humoral immunity against SARS-CoV-2 may not be long lasting in persons with mild illness. Javier Ibarrondo, David Geffen School of Medicine at University of California, Los Angeles, California, and colleagues evaluated 34 persons (20 females and 14 males; mean age: 43 years, [range, 21-68]). Of these, 30 participants had their infection confirmed by PCR, while the other 4 participants had CLI. Most of the participants had mild illness.

A total of 31 of the 34 participants had two serial measurements of IgG levels, while the remaining 3 participants had three serial measurements. The first measurement was obtained at a mean of 37 days after the onset of symptoms (range, 18-65), and the last measurement was obtained at a mean of 86 days after the onset of symptoms (range, 44-119).

The initial mean IgG level was 3.48 $\log_{10}$ ng per milliliter (range, 2.52-4.41). On the basis of a linear regression model that included the participants' age and sex, the days from symptom onset to the first measurement, and the first $\log_{10}$ antibody level, the estimated mean change (slope) was reported to be −0.0083 $\log_{10}$ ng per milliliter per day (range, −0.0352 to 0.0062). The authors noted that this corresponds to a half-life of approximately 73 days over the observation period. Further, they reported that the 95% confidence interval for the slope was −0.0115 to −0.0050 $\log_{10}$ ng per milliliter per day (half-life, 52-120 days).

The protective role of antibodies against SARS-CoV-2 is unknown, but these antibodies are usually a reasonable correlate of antiviral immunity, and anti–receptor-binding domain antibody levels correspond to plasma viral neutralizing activity. Given that early antibody decay after acute viral antigenic exposure is approximately exponential, we found antibody loss that was quicker than that reported for SARS-CoV-1.

Reference: https://www.nejm.org/doi/10.1056/NEJMc2025179

Treatment of AMI and Acute Stroke will be Tenecteplase

The COVID-19 pandemic could hasten the switch to tenecteplase for stroke and acute myocardial infarction (AMI) treatment because it is given as a single, 5-second IV bolus that takes about 2 minutes to mix, prepare and administer rather than the more than 1 hour for weight-based bolus and subsequent infusion of alteplase.

Selenium and Brain Tumors

EZEQUIEL GARCÍA-BALLESTAS*, LUIS RAFAEL MOSCOTE-SALAZAR†, AMIT AGRAWAL‡

The evidence shows that selenocysteine (one of the most prevalent among the 25 selenoproteins encoded by the human genome) exerts a regulatory role in the growth of cancer cells, triggering apoptosis mediated by oxidative damage,[1] attacking the topoisomerase enzymes and the microtubular apparatus[2] and altering the expression of metalloproteinases in the matrix.[3] Spengler et al,[2] in their study published in 2019, showed that selenoproteins have a great capacity to interact with anticancer drugs, especially vincristine, affecting, among other targets, the formation of microtubules and enzymatic action of topoisomerases blocking tumor cell growth. Clark et al,[4] in a randomized, double-blind, multicenter, placebo-controlled study, proposed to determine whether supplementation with selenium decreases the incidence of cancer. They established, as a primary point, the incidence of squamous cell carcinoma in conjunction with the administration of selenium and as a secondary endpoint, the incidence and total mortality of cancer. From this study, we highlight that after 8 years of follow-up, it was demonstrated that selenium, although it does not protect specifically against the development of squamous cell carcinoma, does exert a protective effect against the incidence and mortality from cancer in general.[4]

Malignant gliomas (WHO Grade IV) represent the most common tumor in the brain with a survival between 12 and 16 months[1,3] and are considered as one of the most highly invasive and chemotherapy-resistant tumors. Search has been encouraged for new alternatives with low side effects,[1] that concomitant with chemical treatment, provide higher quality and life expectancy.[2] The current literature suggest that selenium and its compounds can serve as a promising alternative as add-on to chemotherapy in the treatment of these cases. Also, it can help to check the progression of the disease and could be associated with substantial reduction in short- and long-term side effects of chemotherapy agents and thus can enhance the quality of life.

REFERENCES

1. Fan CD, Fu XY, Zhang ZY, Cao MZ, Sun JY, Yang MF, et al. Selenocysteine induces apoptosis in human glioma cells: evidence for TrxR1-targeted inhibition and signaling crosstalk. Sci Rep. 2017;7(1):6465.
2. Spengler G, Gajdács M, Marć MA, Domínguez-Álvarez E, Sanmartín C. Organoselenium compounds as novel adjuvants of chemotherapy drugs - A promising approach to fight cancer drug resistance. Molecules. 2019;24(2):336.
3. Yakubov E, Buchfelder M, Eyüpoglu IY, Savaskan NE. Selenium action in neuro-oncology. Biol Trace Elem Res. 2014;161(3):246-54.
4. Clark LC, Combs GF Jr, Turnbull BW, Slate EH, Chalker DK, Chow J, et al. Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin. A randomized controlled trial. Nutritional Prevention of Cancer Study Group. JAMA. 1996;276(24):1957-63.

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Lipodystrophy at Unusual Site Due to Unusual Cause

BV NAGABHUSHANA RAO

CASE PRESENTATION

A 58-year-old female patient consulted us for her diabetes control. She was a known diabetic for the last 18 years and had been on insulin injection the last 10 years. She was on 30 units of Human Mixtard before breakfast and 25 units before dinner. In addition, she was also taking teneligliptin 20 mg and metformin 500 mg sustained release before lunch. Her blood sugars were erratic. She was frequently hyperglycemic and even a small increase in insulin dose landed her in hypoglycemia.

Physical examination did not reveal significant abnormality except for a soft tissue swelling on the ventral aspect of her left forearm (Fig. 1). The swelling was 6 × 8 cm in size mobile and had no erythema or tenderness. Laboratory investigations were within normal limits and glycated hemoglobin (HbA1c) was 8%.

We discussed further with her regarding the methodology of storing, loading, measuring and injecting insulin. We found that she was always injecting insulin on the ventral aspect of her left forearm. She lived alone in a place where medical facilities were scarce. She was afraid to take insulin on the abdomen as she thought she might go deeper and hurt her intestines. She could find none in her village who could inject insulin. Due to financial constraint and nonavailability, she would not changing the needles frequently.

As she had been injecting insulin subcutaneously at the same site, she developed lipohypertrophy (LH) over her left forearm. Absorption of insulin at the site of LH is erratic, predisposing her to fluctuations in blood sugar. She was given a live demonstration of administration of insulin over various sites in her body and she developed confidence to inject insulin in her abdominal skin. She stopped injecting to her left forearm and the swelling regressed gradually.

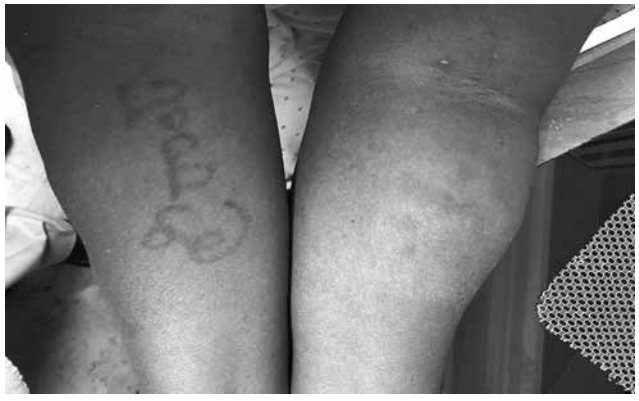

Figure 1. Soft tissue swelling on the ventral aspect of left forearm.

DISCUSSION

Lipohypertrophy (LH) and lipoatrophy (LA) are frequent problems in clinical practice in patients on subcutaneous insulin. LH is a lump under the skin caused by an accumulation of fat at the site of many subcutaneous injections of insulin. As high as 69.8% of patients with type 1 diabetes in India were found to have LH at one time or another during their lifetime, illustrating the frequency of this problem.[1] A systematic review and meta analysis reveal that 38% of the people who take insulin had LH.[2] The incidence of LH has come down drastically with the discovery and utilization of newer insulins, which are less antigenic.

LH can delay the absorption of insulin and jeopardize diabetes control. There were reports in literature where poor absorption of insulin through LH was the culprit of inducing diabetic ketoacidosis.[3]

In contrast, it was reported that erratic absorption may precipitate hypoglycemia. Recurrent hypoglycemia due

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to held up insulin in LH lesion had been reported.[4] In a study of LH in type 1 diabetes, it was found that injection at the same site recurrently is a major factor inducing LH rather than the size of the needle or its reuse.[5] It is very interesting to learn that organized LH interventions with clinical, biological and economical parameters could help to regress LH early and prevent new lesions.[6] Though clinical examination is essential to diagnose LH, an ultrasound examination may give an early clue, especially in those who are markedly obese.[7]

CONCLUSIONS

It is important to educate the patient the need of rotating the site of insulin injection. Healthcare workers should check the injection sites frequently.

REFERENCES

1. Gupta SS, Gupta KS, Gathe SS, Bamrah P, Gupta SS. Clinical implications of lipohypertrophy among people with type 1 diabetes in India. Diabetes Technol Ther. 2018;20(7):483-91.
2. Deng N, Zhang X, Zhao F, Wang Y, He H. Prevalence of lipohypertrophy in insulin-treated diabetes patients: A systematic review and meta-analysis. J Diabetes Investig. 2017;9(3):536-43.
3. Barola A, Tiwari P, Bhansali A. Insulin-mediated lipohypertrophy: an uncommon cause of diabetic ketoacidosis. BMJ Case Rep. 2017;2017:bcr2017220387.
4. Gentile S, Strollo F, Corte TD, Marino G, Guarino G; Italian Study Group on Injection Techniques. Skin complications of insulin injections: A case presentation and a possible explanation of hypoglycaemia. Diabetes Res Clin Pract. 2018;138:284-7.
5. Barola A, Tiwari P, Bhansali A, Grover S, Dayal D. Insulin-related lipohypertrophy: Lipogenic action or tissue trauma? Front Endocrinol (Lausanne). 2018;9:638.
6. Smith M, Clapham L, Strauss K. UK lipohypertrophy interventional study. Diabetes Res Clin Pract. 2017;126:248-53.
7. Kapeluto JE, Paty BW, Chang SD, Meneilly GS. Ultrasound detection of insulin-induced lipohypertrophy in Type 1 and Type 2 diabetes. Diabet Med. 2018;35(10):1383-90.

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Redefine Cardiac Injury Marker Cut-offs to Predict 28 Days Mortality in COVID-19 Inpatients

The abnormal cardiac biomarker pattern seen in patients with COVID-19 is significantly associated with a higher risk of death, and the cut-offs of those markers for effective prognosis of 28-day mortality of COVID-19 appear to be much lower than for regular heart disease, at 49% of currently recommended thresholds, according to a study in *Hypertension*.

The biomarkers are high-sensitivity cardiac troponin I (hs-cTnI), creatine kinase-MB (CK-MB), NT-proB-type natriuretic peptide (NT-proBNP), creatine phosphokinase (CK) and myoglobin (MYO).

Their retrospective cohort study enrolled patients diagnosed as COVID-19 and admitted to 9 hospitals in Hubei Province, China, from December 31, 2019, to March 4, 2020. The study included 3219 patients with myocardial biomarker measurement, and 2814 without. The primary endpoint was 28-day all-cause mortality.

Compared to patients without cardiac injury biomarker measurement, patients with biomarker values were older (median age at 57) and had higher percentages of pre-existing comorbidities and more severe symptoms.

All five myocardial biomarkers were significantly associated with 28-day all-cause death of COVID-19.

After adjusting for age, gender and comorbidities such as hypertension, diabetes, coronary heart disease and cerebrovascular disease, the 28-day mortality hazard ratio for hs-cTnI was 7.12, NT-proBNP was 5.11, CK-MB was 4.86, MYO was 4.50, and CK, a much less specific cardiac biomarker, was 3.56.

In patients showing heart injury during the entire hospitalization, neutrophil percentage and CRP were rapidly and simultaneously increased after disease onset, immediately followed by the increases of CK-MB, MYO and hs-cTnI.

The significant elevation of IL-6 occurred only after the increases of these myocardial markers and was highly elevated mainly in patients with evidence of cardiac injury.

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Is the Doctor Required to Obtain Consent of the Patient in Case of Accident?

KK AGGARWAL*, IRA GUPTA†

The Indian Medical Council (Professional Conduct, Etiquette & Ethics) Regulations, 2002 casts a duty on all medical practitioners, i.e., all medical practitioners must attend to sick and injured immediately and it is the duty of the medical practitioners to make immediate and timely medical care available to every injured person whether he is injured in accident or otherwise. The relevant provisions of Indian Medical Council (Professional Conduct, Etiquette & Ethics) Regulations, 2002 is reproduced hereunder:

"2. DUTIES OF PHYSICIANS TO THEIR PATIENTS

2.1 Obligations to the Sick

2.1.1 Though a physician is not bound to treat each and every person asking his services, he should not only be ever ready to respond to the calls of the sick and the injured, but should be mindful of the high character of his mission and the responsibility he discharges in the course of his professional duties. In his treatment, he should never forget that the health and the lives of those entrusted to his care depend on his skill and attention. A physician should endeavor to add to the comfort of the sick by making his visits at the hour indicated to the patients. A physician advising a patient to seek service of another physician is acceptable, however, in case of emergency a physician must treat the patient. No physician shall arbitrarily refuse treatment to a patient. However for good reason, when a patient is suffering from an ailment which is not within the range of experience of the treating physician, the physician may refuse treatment and refer the patient to another physician.

2.1.2 Medical practitioner having any incapacity detrimental to the patient or which can affect his performance vis-à-vis the patient is not permitted to practice his profession.

2.4 The Patient Must Not be Neglected

A physician is free to choose whom he will serve. He should, however, respond to any request for his assistance in an emergency. Once having undertaken a case, the physician should not neglect the patient, nor should he withdraw from the case without giving adequate notice to the patient and his family. Provisionally or fully registered medical practitioner shall not wilfully commit an act of negligence that may deprive his patient or patients from necessary medical care.

3.5 Treatment After Consultation

No decision should restrain the attending physician from making such subsequent variations in the treatment if any unexpected change occurs, but at the next consultation, reasons for the variations should be discussed/explained. The same privilege, with its obligations, belongs to the consultant when sent for in an emergency during the absence of attending physician. The attending physician may prescribe medicine at any time for the patient, whereas the consultant may prescribe only in case of emergency or as an expert when called for."

The Hon'ble Supreme Court of India, in the matter titled as **"Parmanand Katara versus Union of India, AIR 1989 SC 2039"** has held that:

"There can be no second opinion that preservation of human life is of paramount importance. That is so on account of the fact that once life is lost, the status quo ante cannot be restored as resurrection is beyond the capacity of man. The patient whether he be an innocent person or be a criminal liable to punishment under the laws of the society, it is the obligation of those who are in-charge of the health of the community to preserve life so that the innocent may be protected and the guilty may be punished. Social laws do not contemplate death by negligence to tantamount to legal punishment.

Article 21 of the Constitution casts the obligation on the State to preserve life. The provision as explained by this Court in scores of decisions has emphasized and reiterated with gradually increasing emphasis that position. A doctor at the Government hospital positioned to meet this State obligation is, therefore, duty-bound to extend medical assistance for preserving life. Every doctor whether at a Government hospital or otherwise has the professional obligation to extend

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his services with due expertise for protecting life. No law or State action can intervene to avoid/delay the discharge of the paramount obligation cast upon members of the medical profession. The obligation being total, absolute and paramount, laws of procedure whether in statutes or otherwise which would interfere with the discharge of this obligation cannot be sustained and must, therefore, give way. On this basis, we have not issued notices to the States and Union Territories for affording them an opportunity of being heard before we accepted the statement made in the affidavit of the Union of India that there is no impediment in the law. The matter is extremely urgent and in our view, brooks no delay to remind every doctor of his total obligation and assure him of the position that he does not contravene the law of the land by proceeding to treat the injured victim on his appearance before him either by himself or being carried by others. We must make it clear that zonal regulations and classifications cannot also operate as fetters in the process of discharge of the obligation and irrespective of the fact whether under instructions or rules, the victim has to be sent elsewhere or how the police shall be contacted, the guideline indicated in the 1985 decision of the Committee, as extracted above, is to become operative. We order accordingly."

The Hon'ble National Consumer Dispute Redressal Commission in the matter titled as **"Pravat Kumar Mukherjee versus Ruby General Hospital & Ors., 2005 (2) CPJ 35"** has held that:

"Considering the aforesaid law, it is apparent that: emergency treatment was required to be given to the deceased who was brought in a seriously injured condition; there was no question of waiting for the consent of the patient or a passerby who brought the patient to the hospital, and was not necessary to wait for consent to be given for treatment.

There is nothing on record to suggest that the Doctor has informed the patient or the relatives or the person who has brought him to the hospital with regard to dangers ahead or the risk involved by going without the operation/treatment at the earliest. Consent is implicit in such cases when patient is brought to the hospital for treatment, and a surgeon who fails to perform an emergency operation must prove that the patient refused to undergo the operation not only at the initial stage but even after the patient was informed about the dangerous consequences of not undergoing the operation."

Thus, the patient's consent is not necessary in case of accident/emergency as in such cases, the consent is implied when the patient is brought to the hospital. Further, it is an obligation on the doctor to treat his patient without any delay.

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Young, Healthy Adults with Mild COVID-19 can Take Weeks to Recover, Says CDC

It can take weeks for even young, previously healthy adults to recover completely from even a mild COVID-19 infection, reports the Centers for Disease Control and Prevention (CDC).

As per CDC, nearly one-fifth of the patients aged below 35 years reported that they had not returned to their usual state of health up to 21 days after testing positive. As reported in the *Morbidity and Mortality Weekly Report*, a telephone survey was conducted across 13 states of symptomatic adults with mild COVID-19 infection. The survey revealed that 35% of the subjects had not returned to their usual state of health 2-3 weeks following testing. The report thus stated that recovery could be prolonged even in young adults who do not have any chronic medical conditions… (*Reuters*)

First Cell-based Gene Therapy for Adult Patients with Relapsed or Refractory MCL Receives FDA Approval

Brexucabtagene autoleucel, a cell-based gene therapy for the treatment of adults with mantle cell lymphoma (MCL) who do not respond to or relapse after other treatments, has been approved by the US Food and Drug Administration (FDA).

This chimeric antigen receptor (CAR) T-cell therapy is the first cell-based gene therapy that has received the FDA approval for the treatment of MCL. The safety and efficacy of the treatment were confirmed in a multicenter trial including 60 adults with refractory or relapsed MCL followed for about 6 months after their first objective disease response. There was a complete remission rate of 62%, and an objective response rate of 87%... (*FDA*)

Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Medtalks with Dr KK Aggarwal

CMAAO Coronavirus Facts and Myth Buster

Round Table Expert Zoom Meeting on "Recovery is the Rule in COVID-19 and Death is an Exception"

4th July, 2020 (11 am-12 noon)

Participants: Dr KK Aggarwal, Dr Shashank Joshi, Prof Mahesh Verma, Dr Ashok Gupta, Dr Suneela Garg, Dr JA Jayalal, Dr Jayakrishnan AV, Dr Alex Thomas, Dr Shiv K Harti, Vaidya Sushil Dubey, Mrs Upasana Arora, Dr K Kalra, Ms Ira Gupta, Dr S Sharma

Key Points from the Discussion

- Timely action can save lives as most cases are mild; few are moderate and less than 5% are serious.
- Death rate is reducing as we are now able to better manage cases.
- In all patients who have loss of smell/taste, recovery is the rule and mortality is an exception. Analysis of 100 patients with loss of smell/taste showed that none needed oxygen or ventilator or hospitalization. It occurred more often in males, at any age and recovery is the rule within 4 weeks.
- Recovery is the rule means that the disease is salvageable at every step. It does not mean that mortality is zero.
- After 9 days, the virus becomes nonreplicative and after 9 days, the illness is a post-COVID (coronavirus disease) complication.
- Day 1 is the day when any of the symptom/s recognized by the Centers for Disease Control and Prevention/Ministry of Health and Family Welfare (CDC/MoHFW) guidelines such as fever, throat irritation, subconjuctival hemorrhage, rash, diarrhea, headache, calf pain, etc., develop; test may or may not be positive.
- Post-COVID inflammation is very common. It can be in the form of persistent fever/sore throat/bronchitis/diarrhea/cystitis/exertional tachycardia.
- Doctors have high viral load because of repeated exposure and they have more hypercoagulable state. So, if all healthcare workers (HCWs) are given anticoagulant + short course of steroids, even in mild cases, recovery is the rule.
- In non-HCW group of patients, if there are signs of chest congestion on Day 3-4, do an immediate chest CT scan and give 10-day course of steroids, antiviral and anticoagulant; then recovery should be the rule and death an exception.
- Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) may be positive for up to 40 days; this does not mean that the virus is culturable. The virus is culturable for only 9 days; after 9 days, the virus is present but is non-culturable. This data is available for patients who are not on ventilator.
- If any illness is developed during the 9 days, then the post-COVID illness (post-COVID inflammatory state) may last for up to 6 weeks.
- A delayed cytokine storm, which occurs between Day 14 and 18, has been observed in Mumbai. A 6-minute walk test is now mandatory at the time of discharge to look for drop in oxygen saturation. This is a valid marker for delayed cytokine storm. Give 5-10 days of low-molecular-weight heparin (LMWH)/oral anticoagulant and small dose of statin at the time of discharge, especially to those who have been in hospital for >28 days and are >55 years of age. This can reduce mortality.
- Initially, steroids were given only in serious cases, but now their indication has also shifted to moderately severe cases. And the time may well come when steroids may become mandatory in all patients starting from Day 3. Timely steroids can prevent secondary cytokine crisis.
- Capacity building, not just of HCWs but also RWAs, etc., as many patients are in home care; issues like stigma and discrimination also need to be addressed. The word "contact" needs to be eliminated as it is a type of stigma.
- Indian vaccine is a live attenuated vaccine (Bharat Biotech); Moderna vaccine is mRNA vaccine; all vaccines have different technologies. Three things to be detected when a vaccine is given: Cellular antibodies, humoral protection and non-specific immunity building (innate immunity). By 15th August, we may only be able to tell whether

antibodies are produced or not. Since this is a live attenuated virus, will there be a delayed response (cytokine crisis), we do not know.

- Isolate for 9 days, quarantine for 5 days and then monitoring with rest for next 2 weeks. Monitoring means that the person is not contagious, but is still likely to get secondary complications.
- Plasma therapy is effective if given within first 7 days of illness; plasma should be donated between 28 and 40 days.

Healthcare Workers with Appropriate PPE Don't Get COVID-19

- Healthcare workers (HCWs) with appropriate PPE (protective suits, masks, gloves, goggles, face shields and gowns) don't develop COVID-19 symptoms or test positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as per a Chinese study.
- The study examined data on 116 doctors and 304 nurses who were deployed to Wuhan, China, for 6-8 weeks from January 24, 2020 to April 7, 2020. They were all involved in aerosol-generating procedures, and were provided with appropriate PPE to care for patients with COVID-19.
- Participants worked 4- to 6-hour shifts over an average of 5.4 days a week, and spent an average of 16.2 hours weekly working in intensive care units (ICU).
- None of them reported COVID-19 symptoms when they were deployed to hospitals in Wuhan. After they returned home, all tested negative for SARS-CoV-2 specific nucleic acids and IgG or IgM antibodies.
- In Wuhan, most of the affected health professionals became infected in the early phase of the outbreak due to a lack of appropriate PPE.
- More than 80% of patients required critical care and 10-15% received mechanical ventilation.
- All participants received similar PPE and proper training to work in the ICU, regular wards and for cases involving aerosol-generating procedures (N95 respirator masks, medical suits, isolation gowns, aprons, gloves, eye protection and hair coverings. In areas with no COVID-19 contact, workers wore surgical masks).
- All of the study participants performed at least one procedure generating aerosols, including tracheal intubation, noninvasive mechanical ventilation, gastric intubation, sputum aspiration, aerosol inhalation, tracheostomy and throat swab collection.
- Out of hospital, they wore masks in public, followed strict social distancing rules and stayed in designated hotels.

(Source: The BMJ, online June 10, 2020.)

Predicting Factors for Pulmonary Embolism in Non-critically Ill COVID-19 Patients – D-dimer >5,000

A Spanish study published in the *Journal of Thrombosis and Thrombolysis* has reported a high rate of pulmonary embolism (PE) in non-critically ill hospitalized patients with COVID-19 despite the use of standard thromboprophylaxis. B Mestre-Gómez, Internal Medicine Department, Infanta Leonor University Hospital, Madrid, Spain and colleagues stated that they had found 29 patients with established PE and COVID-19 pneumonia out of 91 CTPA (computed tomography pulmonary angiography) tests performed among 452 patients admitted over the study period. This points to an incidence of 6.4% in a medical ward and one-third of positive CTPA despite prophylactic doses of LMWH.

Investigators further stated that an increase in D-dimer levels is a potential predictor of PE, with a best cut-off point of >5,000 μg/dL.

The single cohort, longitudinal study assessed patients admitted with COVID-19 diagnosis to the Internal Medicine Department of a secondary hospital in Madrid from March 30 through April 12, 2020. A retrospective review of 452 electronic medical records was done, to assess the cumulative incidence of PE, and associated risk factors. Ninety-one patients who underwent a multidetector CTPA during conventional hospitalization were included in the study.

Of the 91 CT scans, 29 patients (31.9%) were diagnosed with acute PE, while the cumulative incidence over the entire cohort was 6.4% (29/452 patients). Among the PE patients, 23 were found to have COVID-19 infection via RT-PCR positive tests, and 6 had positive CT scans and negative RT-PCR.

Among the PE patients, 72% (21/29) were male and the median age was 65 years (IQ 1-3: 56-73), while median body mass index was 28.8 kg/m^2 (IQ 1-3: 26.8-31.8). Median plasma D-dimer peak was 14,480 μg/dL (IQ 1-3: 5,540-33,170 μg/dL), median platelet counts 137×10^3 (IQ 1-3: 248-260 $\times 10^3$), median C-reactive protein 110.6 mg/dL (Q1-3: 40-193) and median ferritin 829 ng/mL (Q1-3: 387-1272). There appeared to be no associated

coagulopathy, with a prothrombin time of 12.5 seconds (Q1-Q3: 11.9-13.5). Most of the PE patients were given LMWH (79.3%; 23/29) at prophylactic doses at the time of diagnosis of PE.

Nearly 51.7% of PE cases were bilateral (15/29 patients) and 48.3% unilateral. Most PEs were noted in a peripheral location in segmental and subsegmental arteries (68.9%, 20/29 patients) and 31.0% (9/29 patients) in a central location (main and lobar arteries).

It was noted that D-dimer peak was significantly elevated in the PE patients (median 14,480 μg/dL, IQR 5,540-33,170) compared to patients without PE (7,230 μg/dL, IQR 2,100-16,415; p = 0.03).

A multivariate analysis of patients subjected to a CTPA suggested that plasma D-dimer peak independently predicted PE with a best cut-off point of >5,000 μg/dL (OR 3.77; IC95% (1.18-12.16), p = 0.03).

There were statistically significant differences between the two groups for history of dyslipidemia (10.7%, [3/29] in PE patients vs. 40.3% (25/62) in non-PE patients, p = 0.003), and for history of autoimmune disease (10.7% [3/29] vs. 0% [0/62], p = 0.03).

Investigators stated that the history of dyslipidemia appeared to be a protector factor for PE in the multivariate analysis. Patients who did not have this cardiovascular risk in their records, were found to have a nine times increased risk for PE compared to those with dyslipidemia (OR 9.06; IC95% (1.88-43.60). It seems possible that patients previously treated with statins had a potential benefit either by their immunomodulatory action or by preventing cardiovascular damage.

No statistical differences were noted in either mortality or admission to the ICU between the PE and non-PE groups in this cohort of non-critically ill COVID-19 patients.

The absence of classic risk factor for venous thromboembolism - advanced age, history of thrombosis, thrombophilia, cancer and ICU admission - and the peripherical localization of PE suggest microthrombosis *in situ*. Wells index does not seem to be accurate to predict PE in such a challenging context, according to the authors.

Additionally, there was no difference in severity of pneumonia by CURB-65 score. Furthermore, no statistical difference was evident in inflammation parameters (high in both groups), treatment or need of noninvasive ventilation; however, the figures are higher for non-PE group.

The actual presence of PE on CT was not found to be linked with mortality in this small sample.

(Source: DG Alerts; Journal of Thrombosis and Thrombolysis)

Minutes of Virtual Meeting of CMAAO NMAs on "Managing Fever"

4th July, 2020, Saturday (9:30 am-10:30 am)

Participants

***Member NMAs*:** Dr KK Aggarwal, President-CMAAO; Dr Yeh Woei Chong, Singapore Chair CMAAO; Dr Thirunavukarasu Rajoo, Hon. General Secretary-Malaysian Medical Association; Dr Alvin Yee-Shing Chan, Hong Kong; Dr Marie Uzawa Urabe, Japan; Dr Md Jamaluddin Chowdhury, Bangladesh; Dr Qaisar Sajjad, Pakistan; Prof Ashraf Nizami, Pakistan; Dr Prakash Budhathoky, Nepal

***Invitees*:** Dr Russell D'Souza, UNESCO Chair in Bioethics, Australia; Dr Sanchita Sharma, Editor-IJCP Group

Key Points from the Discussion

Dr KK Aggarwal shared his observations of about 100 patients with loss of taste and/or smell: They did not need hospitalization, none developed pneumonia, recovered in less than 4 weeks, more in men, none needed oxygen, about 50% recovered without treatment. It was the only presentation in many patients. Bitter and sour tastes and sour (lime) smell are retained.

After 9 days, the virus becomes non-replicative; there is no evidence that the virus is culturable after 9 days except for cases who were on ventilator. Antigen can remain positive for up to 40 days. There is also no evidence to date that a culturable virus is positive again.

India is now doing rapid antigen test. If antigen test is negative, do RT-PCR. If antigen test is positive, then this is considered positive. Antibody test (COVID-specific IgG) is done after 14 days.

If antigen is positive and COVID-specific IgG antibody is negative, this is resurgence of old infection. If COVID-specific IgG antibodies are present and RT-PCR is positive, look for other causes of fever.

The patient who comes after 9 days presents with post-COVID sequelae. These patients have persistent systemic inflammation. The commonest presentation is post-COVID fever (low grade <100.4, does not respond to paracetamol, responds to anti-inflammatory drugs like mefenamic acid, naproxen, nimesulide and indomethacin). Other presentations may be post-COVID bronchitis/sore throat/diarrhea/cystitis/exertional tachycardia.

If less than 9 days, critical days are Day 3, 4 and 5; if patient has chest congestion during these days, this is suggestive of pneumonia. A CT scan will show the pneumonia.

If at the onset of pneumonia, patient is given dexamethasone 6 mg × 10 days, statin and oral anticoagulant (rivaroxaban) × 40 days and antiviral, mortality may be reduced.

Secondary sudden death (after Day 14) may occur even after a month of recovery. Hypercoagulable state can last for up to 40 days.

Pakistan Update

- Patients have post-COVID problems, but not too much. Patients usually have fever, weakness lasting up to 2-3 weeks, loss of smell/taste × 4-5 days.
- Patients are advised to avoid exertion and take rest, hydration, multivitamins, vitamin D and balanced diet.
- If post-COVID patients complain of body pain or throat pain, ibuprofen or diclofenac has good response.

Bangladesh Update

- The number of cases are increasing; the number of deaths also increasing.
- Many hospital beds are vacant; this may be due to people taking oxygen at home. So, such cases are probably not coming to the hospital.

Malaysia Update

- Less than 100 patients in hospital; death rate <1.4%.
- All travelers coming into Malaysia are tested (antigen test) at the airport, they are required to download an App on their phones and undergo 14-day home quarantine. On the 13th day, they can go to GP clinic and undergo antibody test. On Day 14, they go to district health officer and report.
- No post-COVID fever reported so far.

Nepal Update

- Post-COVID fever is rare; there are 2 cases who recovered and were discharged and then presented with fever. They tested positive (RT-PCR).

Japan Update

- There are post-COVID fever cases, but the number is not so high.

Hong Kong Update

- There are about 1,200 cases, mostly imported cases; local community cases are only a small minority.
- Number of daily tests is around 3,000 and trying to increase number of testing.
- Relaxation of regulations of limiting public gatherings.

Australia Update

- A judicial inquiry is being held in the state of Victoria (Melbourne) following protocol breach by some of the security looking after international quarantined persons lodged in hotel.
- Rest of Australia is opened up; lockdown (phase 3) only in Victoria. In 10 days, cases have increased to more than 500. Only 5 are in intensive care. Army has been called in.
- Saliva test for coronavirus has been started in Melbourne in hotspots; it is not as specific as nasopharyngeal swab.

COVID Vaccine

Various parts of the virus are being used to manufacture the vaccine. Also, there are different ways to produce vaccine: Killed virus, live attenuated virus (India, phase 1 trial), mRNA vaccine (Moderna), spike protein (Oxford), VLP platform, conjugate vaccine, membrane and envelope vaccine. We have no idea which vaccine will succeed. We have to be guardedly optimistic about the vaccine. There are many unanswered questions such as:

- Will the vaccine produce cellular or humoral antibody? Vaccine may produce cellular reaction, but may not prevent cytokine crisis.
- Will they produce antibodies which are safe?
- Will they be able to prevent thromboinflammation?
- Will the effect of the vaccine be long-lasting or not?
- The mRNA can go into every cell of the body; this may be a cause for concern.

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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

News and Views

FDA Approves New Therapy for Myelodysplastic Syndromes That can be Taken at Home

The US Food and Drug Administration (FDA) has granted approval to decitabine and cedazuridine tablets for the treatment of adult patients with myelodysplastic syndromes (MDS) and chronic myelomonocytic leukemia (CMML).

This is an important advancement in the treatment options for patients with MDS who previously needed to visit a healthcare facility to receive intravenous therapy. This drug is taken as one tablet orally once daily for 5 consecutive days of each 28-day cycle… *(FDA)*

Weight Loss, Not Fiber Intake, Linked with Better A1c in Diabetes

A small study of overweight patients with type 2 diabetes revealed that consuming fewer calories resulting in weight loss of around 2 kg was tied to better glycemic control than consuming more fiber.

Investigators recruited 78 patients with type 2 diabetes who received monthly nutrition counseling about a guideline-recommended lower-calorie, healthy diet. Patients were randomized to three groups: high-fiber diet, fiber supplement or control. At 3 months, all three groups lost a similar amount of weight and had similar decline in A1c levels. However, fiber intake was not found to be associated with improved A1c levels, but weight loss was. The findings were presented recently during the virtual American Diabetes Association (ADA) 80th Scientific Sessions… *(Medscape)*

COVID-19 Lungs may be More Likely to Leak

Pneumothorax and other barotrauma was found to be more common in coronavirus disease (COVID-19) patients on invasive mechanical ventilation compared to other patients on ventilators, revealed a retrospective study.

Among invasive mechanical ventilation (IMV) patients at NYU Langone Health in New York City from March 1 to April 6, barotrauma was noted in 15% of those with COVID-19 and 0.5% of those without it ($p < 0.001$), reported researchers in *Radiology*. Barotrauma in COVID-19 independently predicted death (odds ratio [OR] 2.2, $p = 0.03$) and longer length of hospital stay (OR 1.03, $p < 0.001$)… *(Medpage Today)*

Image-guidance Tied to Improved Resection in Recurrent Colorectal Cancer

In comparison with historical controls, use of image-guidance during surgery resulted in improved rates of complete resection in locally advanced rectal cancer patients with recurrent disease, reported a single-center Dutch study.

Among patients with recurrent cancers, 78.9% achieved complete R0 resections when an image-guided navigation system was used, compared to a historical rate of 48.8% ($p = 0.047$), reported researchers in *JAMA Network Open*. No significant difference was evident among a group of patients undergoing primary surgical resection (92.9% vs. 84.2%, respectively, $p = 0.69$)… *(Medpage Today)*

Wheat could be the Most Common Food Allergen in Children

Globally, food allergies are widespread with an incidence up to 10% in Western countries in infants and a growing occurrence in developing countries. Food allergies are very common in children as compared to adults. Certain foods include more than 80% of the reaction in food allergies such as milk, egg, wheat, soy, peanut and tree nuts.

In pediatric patients, gluten-related disorders are very common. Wheat (*Triticum aestivum*) is the most extensively consumed food grain in the whole world due to its capability to grow in different climatic areas. Wheat can be responsible for a varied range of disorders that depends on allergen exposure and the underlying immunological mechanisms. Wheat is the most common food allergen seen in children and can be accountable for a number of clinical manifestations such as food-dependent exercise-induced anaphylaxis (FDEIA), contact urticaria, occupational asthma (or Baker's asthma) or rhinitis.

Wheat allergy is triggered by an immunoglobulin E (IgE)-dependent mechanism and its incidence differs as per the age and region. Several studies have explored the potential role of various external factors, which can influence the risk of developing wheat allergy, but results are still inadequate.

In children, the prognosis of IgE-mediated wheat allergy is usually favorable, as the majority of children

become tolerant by school age. Patients who had experienced an anaphylactic reaction earlier to 3 years of age and patients with higher levels of wheat- or ω-5 gliadin-specific IgE antibodies could be at higher risk of persistent wheat allergy. The present management of such patients is dietary avoidance. Currently, oral immunotherapy has been suggested for wheat allergy with promising results. Further studies are needed to create the best protocol for promoting tolerance in wheat-allergic children.

Source: Ricci G, Andreozzi L, Cipriani F, et al. Medicina (Kaunas). 2019;55(7):400.

WHO to Issue New Brief on Airborne Transmission

The World Health Organization (WHO) will issue a brief on the modes of transmission of the new coronavirus, stated a senior official.

Epidemiologist Dr Maria van Kerkhove, WHO technical lead on COVID-19, while responding to a question on an open letter by scientists calling for updating the recommendations on airborne transmission, stated that WHO welcomes interaction with the scientific community. She added that the group first wrote to the agency on 1st April and there has been 'active engagement' since. WHO is developing a scientific brief that includes the growing knowledge around this subject and it will be issued in the coming days… *(UN)*

A Favorable Lifestyle may Reduce Breast Cancer Risk Irrespective of Genetics

A favorable lifestyle was found to be associated with a reduced risk of breast cancer even among women with high genetic risk for the disease in a study of over 90,000 women.

According to the study, irrespective of genetic risk, women may reduce their risk of developing breast cancer by getting adequate levels of exercise; maintaining a healthy weight and limiting or avoiding the use of alcohol, oral contraceptives and hormone replacement therapy. The findings were published in *JAMA Network Open*… *(Medscape)*

Polymer-free Stents: 10-year ISAR-TEST-5 Results

Long-term adverse outcomes were shown to be similar for polymer-free and durable-polymer drug-eluting stents (DES) in the ISAR-TEST-5 study.

Patients randomized to the polymer-free, sirolimus- and probucol-eluting Isar DES had similar outcomes over 10 years as their peers given durable-polymer, zotarolimus-eluting Endeavor Resolute DES, reported researchers in the *Journal of the American College of Cardiology… (Medpage Today)*

WHO Reviewing Report Urging Updated Guidance Over Airborne Spread of Coronavirus

The WHO is reviewing a report calling for updated guidance on the novel coronavirus after over 200 scientists outlined evidence that the virus can spread in tiny airborne particles in a letter to the health agency.

In an open letter to the WHO, 239 scientists in 32 countries laid out evidence showing that floating virus particles can infect people who inhale them. As these smaller particles can stay in the air, the scientists urged WHO to update its guidance. WHO spokesman Tarik Jasarevic said, "We are aware of the article and are reviewing its contents with our technical experts." *(Reuters)*

More Outbreaks if Exploitation of Wildlife Continues: UN

Zoonotic diseases are on the rise and will continue to increase in the absence action to protect wildlife and preserve the environment, warned UN experts.

They blame the rise in diseases such as COVID-19 on high demand for animal protein, unsustainable agricultural practices and climate change. They stated that neglected zoonotic diseases are responsible for the death of 2 million people a year. The jump of zoonotic diseases from animals to humans is driven by the degradation of the natural environment, for instance through land degradation, wildlife exploitation, resource extraction and climate change, suggested a report by the United Nations Environment Programme and the International Livestock Research Institute… *(BBC)*

REM Sleep Duration Linked with Mid-Term Mortality Risk

Less rapid eye movement (REM) sleep was found to be associated with greater mortality risk in middle-age and older adults, according to a new research.

Every 5% reduction in REM sleep was linked to a 13% higher mortality rate in older men (age-adjusted hazard ratio [HR] 1.12; fully adjusted HR 1.13, 95% confidence interval [CI] 1.08-1.19) over about 12 years, reported researchers. In a parallel analysis, middle-age women and men exhibited similar results (HR 1.13, 95% CI 1.08-1.19) over about 21 years, reported researchers in *JAMA Neurology*. According to a random forest

model, REM sleep was the most important sleep stage associated with survival… *(Medpage Today)*

Antihypertensives Tied to Reduced Risk of Colorectal Cancer

Use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) for treatment of hypertension was associated with a reduced risk for colorectal cancer, suggested a large retrospective study.

According to the study, published online in the journal *Hypertension*, the use of ACE inhibitors/ARBs was linked with a 22% lower risk for colorectal cancer developing within 3 years after a negative baseline colonoscopy… *(Medscape)*

WHO Discontinues Hydroxychloroquine and Lopinavir/Ritonavir Treatment Arms for COVID-19

The WHO has accepted the recommendation from the Solidarity Trial International Steering Committee to terminate the hydroxychloroquine and lopinavir/ritonavir arms in the trial.

The recommendation was based on the evidence for hydroxychloroquine vs. standard-of-care and for lopinavir/ritonavir vs. standard-of-care from the Solidarity trial interim results, as well as a review of the evidence from all trials presented at the WHO Summit on COVID-19 research and innovation. The interim results suggest that hydroxychloroquine and lopinavir/ritonavir yield little or no reduction in the mortality among hospitalized COVID-19 patients, compared to standard of care… *(WHO)*

Hundreds of Scientists Say Coronavirus is Airborne

Hundreds of scientists have said that there is evidence to show that the novel coronavirus in smaller particles in the air can infect people. The scientists have called for the WHO to revise its recommendations, *The New York Times* reported.

In an open letter to the agency, 239 scientists in 32 countries laid out the evidence showing that smaller particles can infect people. Whether carried by large droplets, or by smaller exhaled droplets that may drift through a room, the coronavirus is borne through air and can infect people when inhaled, said the scientists, as per the *NYT*… *(Reuters)*

Epilepsy After TBI Tied to Worse 12-month Outcomes

The severity of head injury in traumatic brain injury (TBI) has a significant association with the risk of developing post-traumatic epilepsy (PTE) and seizures, and PTE itself further impairs outcomes at 12 months, suggests an analysis of a large, prospective database.

Of the 1,493 patients with TBI, 2.7% were determined to have PTE. Presenting Glasgow Coma Scale (GCS) score was a major risk factor for the development of PTE. Among those with scores of <8, indicating severe injury, the rate of PTE was 6% at 6 months and 12.5% at 12 months. Those with TBI presenting with GCS scores between 13 and 15, suggesting minor injury, had an incidence of PTE of 0.9% at 6 months and 1.4% at 12 months. The findings were presented at the virtual edition of the *American Association of Neurological Surgeons Annual Meeting*… *(Medscape)*

Apgar Score Provides Prognostic Information for Neonatal Survival

Preterm infants with lower Apgar scores had an increased risk of neonatal death, suggested a population study in Sweden.

Among babies born at 36 weeks or earlier, there was a higher risk of mortality among those born at lower gestational age and as Apgar scores decreased, with scores at 5 and 10 minutes predicting neonatal outcomes, reported researchers in the *New England Journal of Medicine*… *(Medpage Today)*

Pooled Data Favor Short-course HCV Treatment

Eight weeks of glecaprevir-pibrentasvir was found to be efficacious and well-tolerated in treatment-naive patients with all hepatitis C virus (HCV) genotype infections, with or without cirrhosis, reported researchers online in *Clinical Gastroenterology and Hepatology*.

A post-hoc analysis from eight pooled trials involving over 2,300 patients revealed that 8-week treatment with glecaprevir-pibrentasvir was associated with sustained viral response rates of 97.6% at 12 weeks in an intent-to-treat (ITT) population and 99.3% in a modified ITT population, irrespective of cirrhotic status… *(Medpage Today)*

Sleep Troubles in Infancy Linked to Later BPD, Psychosis

Some sleep patterns in infancy were found to be associated with psychotic experiences and borderline personality disorder (BPD) symptoms in adolescence, reported a cohort study from England.

Among 7,155 mother-child pairs, children whose mothers reported that they had irregular sleep routines in childhood, and frequent night awakenings at 18 months, appeared to be significantly more likely

to have psychotic symptoms by 12-13 years of age compared to children who did not wake up frequently at night (OR 1.13, 95% CI 1.01-1.26, p = 0.03), reported researchers in *JAMA Psychiatry*. In comparison with children with regular sleep patterns, children who slept less at night (OR 0.78, 95% CI 0.66-0.92, p = 0.004) and had later bedtimes at 3.5 years (OR 1.32, 95% CI 1.09-1.60, p = 0.005) exhibited associations with BPD symptoms in adolescence… *(Medpage Today)*

Better Pregnancy Spacing would Help Those with Gestational Diabetes

Women with a history of gestational diabetes had a 50% higher likelihood of having a short interval between pregnancies (18 months or less) compared with women without gestational diabetes, reported a new study.

The findings point to a possible modifiable risk factor to improve outcomes, said lead researcher Ronald Anguzu, MBChB, MPH, Medical College of Wisconsin, Milwaukee, presenting the results during the virtual American Diabetes Association (ADA) 80th Scientific Sessions… *(Medscape)*

Stretching Regimen Tied to Vascular Benefits

Leg stretching exercises were found to be associated with improved vascular function in a small study published in the *Journal of Physiology*.

Signs of local and systemic vascular improvement were observed after study participants were subjected to 12 weeks of training in passive stretching. There was a 30% increase in femoral change in blood flow, 25% rise in popliteal artery flow-mediated dilatation, 8% increase in brachial artery flow-mediated dilatation, 25% reduction in central arterial stiffness, 17% decrease in peripheral arterial stiffness, 4% decrease in systolic blood pressure (BP) and an 8% fall in diastolic BP. Controls randomized to no stretching had no significant changes in these measures… *(Medpage Today)*

Transfats from Processed Foods may Increase Ovarian Cancer Risk

UN scientists have identified a possible link between processed and fried foods containing so-called 'transfats' and ovarian cancer.

The International Agency for Research on Cancer (IARC) issued the announcement following a study of around 1,500 patients suffering from the disease. "This is the first Europe-wide prospective study showing a relationship between intake of industrial trans fatty acids and development of ovarian cancer," added the scientist from IARC, a part of the *WHO… (UN)*

FDA Approves New HIV Treatment for Patients with Limited Options

The US FDA has granted approval to fostemsavir to treat adult patients who have run out of treatment options.

The oral drug has been approved for adults whose human immunodeficiency virus (HIV) infection could not be successfully treated with other therapies owing to resistance, intolerance or safety considerations… *(Reuters)*

Subclinical Hypothyroidism Seems Common in Women with Miscarriage

Among women with a history of miscarriage or subfertility, the prevalence of subclinical hypothyroidism (SCH) appears to be about 20% using a thyrotropin (TSH) cut-off of 2.5 mIU/L, suggested a prospective observational study.

Using accepted reference ranges, undiagnosed overt hypothyroidism was identified in 0.2%, overt hyperthyroidism in 0.3%, severe SCH (TSH >10 mIU/L) in 0.2% and SCH (TSH >4.5 mIU/L) in 2.4%. Reducing the upper limit of TSH to 2.5 mIU/L, as recommended by international societies for 'high-risk' women, such as those with recurrent pregnancy loss or those undergoing assisted reproductive technology, would categorize 16-20% of women as having SCH, reported researchers. The findings were published in the *Journal of Clinical Endocrinology & Metabolism… (Medscape)*

Parental Behavior Linked with Greater Disability in Persistent Pediatric Headache

Parental attitudes and behavior predict outcomes in children with new daily persistent headache (NDPH), suggests new research.

Researchers at Boston Children's Hospital in Waltham, Massachusetts, noted that the degree of disability experienced by these children had a direct link with the levels of parental catastrophizing, fear of pain and protective behavior. Parents' rating of their own distress was also independently associated with their level of protective behavior. The findings were presented at the virtual American Headache Society (AHS) Annual Meeting 2020… *(Medscape)*

CDC Adds Three New Symptoms of COVID-19 to Existing List

The US Centers for Disease Control and Prevention (CDC) has added three new symptoms of the COVID-19 to the existing list.

Congestion or runny nose, nausea and diarrhea have been added to the list of 12 symptoms now. Symptoms that are already there in CDC's list include fever or chills, cough, shortness of breath or difficulty in breathing, fatigue, muscle or body aches, headaches, loss of smell or taste and sore throat. The agency stated, "This list does not include all possible symptoms. CDC will continue to update this list as we learn more about COVID-19." *(HT)*

Risk Factors for Depression in Postmenopausal Women

A considerable proportion of postmenopausal women experience depression, and the risk is increased by factors including physical disabilities and having many children, suggests new research.

In a cross-sectional study of 485 postmenopausal women surveyed with questionnaires, about 41% were found to have depression. Factors that significantly increased the risk included alcohol consumption (OR 11.772, p = 0.003), history of illness requiring continuous medication (OR 3.579, p = 0.001), presence of physical disability (OR 2.242, p = 0.001), history of any mental disorder with a physician's diagnosis (OR 4.213, p = 0.001), having four or more living children (OR 4.174, p = 0.001). The findings were published online in *Menopause… (Medpage Today)*

Fish Oil and Vitamin D not Helpful in Knee OA

Dietary supplementation with vitamin D or fish oil failed to relieve chronic knee pain in older adults, suggested a secondary analysis of data from the large randomized VITAL trial.

Baseline pain scores on the 100-point Western Ontario and McMaster Universities (WOMAC) Arthritis Index were 35.4 among patients receiving vitamin D and 36.5 for those given placebo. At the time of last follow-up, after over 5 years, mean WOMAC pain scores in the two groups were 32.7 and 34.6, respectively. There was no statistically significant difference in pain scores between the vitamin D and placebo groups at any time during the trial, reported researchers in *Arthritis & Rheumatology*. Among patients receiving marine ω-3 fatty acids or placebo, WOMAC pain scores at baseline were 36.5 and 35.4, and at the final follow-up visit, the scores were 33.6 in the fish oil group and 33.7 in the placebo group. There appeared to be no significant differences in pain scores between the two groups at any time point… *(Medpage Today)*

Major Breakthrough in Attempts to Control Diseases Spread by Mosquitos

The UN nuclear agency (International Atomic Energy Agency [IAEA]) announced a key development in the efforts to boost technology aimed at curbing disease-carrying mosquitos, and control dengue, yellow fever and Zika.

A study revealed that the use of a specialized drone, developed by IAEA and partners, to release thousands of male mosquitoes, sterilized using radiation, seems effective. Several of the sterilized males mate with females, who then produce no offspring, thus reducing the mosquito population over time. The drones are cheaper compared to manual ground releases, and cover a much wider area… *(UN)*

DPP1 Inhibitor Shows Promise in Noncystic Fibrosis Bronchiectasis

Treatment with the investigational anti-inflammatory drug brensocatib led to significant delay in the time to exacerbation in patients with noncystic fibrosis bronchiectasis, suggested new research.

Phase II results from the multicenter WILLOW trial, including 256 adults with at least two documented bronchiectasis exacerbations over the past year, revealed that both doses of the oral drug tested (10 and 25 mg/day) delayed the time to first pulmonary exacerbation over the 24-week treatment period compared with placebo. The findings were presented at an American Thoracic Society (ATS) 2020 virtual session… *(Medpage Today)*

IL-7 may Help Severe COVID-19 Patients

Administration of interleukin 7 (IL-7) immunotherapy to critically ill COVID-19 patients was shown to be associated with significantly restored lymphocyte counts in a case series in Belgium.

In all, 12 critically ill COVID-19 patients with low lymphocyte levels were administered IL-7, and were compared with a control group of 13 patients who were provided usual care. Patients given IL-7 had over twofold greater lymphocyte levels compared to controls at Day 30, reported researchers in *JAMA Network Open*. The mortality rate was similar in the two groups; however, those given the IL-7 therapy had a lower proportion of infections at Day 30 compared with controls (50% vs. 85%, respectively)… (*Medpage Today*)

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The Science of Power

KK AGGARWAL

Power is the ability to influence others to get a work done the way you want it. We have seen evolution in the way power works. There was a time when Brahmins ruled using the power of knowledge; then came the era of Kshatriyas, who ruled using the physical power. This was followed by the era of Vaishya ruling the world with the power of money and a time will come when Shudras will rule with the power of their work.

In one of his lectures, Deepak Jain from Kellogg's said that the world has seen eras of physical power, economic power and the time has come that it will now be ruled by the power of human resources.

Former Governor of Mizoram, AR Kohli, in one of his talks, said that there are four types of powers which govern the universe and these are – physical power, economic power, the power of the chair (ego) and the power of the human resource, which is based on consciousness.

Everyone has these four inherent powers. The physical power is based on fear, tamas and rajas. The economic and the power of chair are linked to one's ego and rajas. It is the power of human resource which is linked to the soul, consciousness and Satva.

The physical power is at the level of body, economic power is at the level of mind, the power of chair is at the level of intellect and ego and the power of human resources is at the level of soul. It is the power of human resource which is based on Dharma and is universally accepted by all religions.

As per Mahabharata, the powers are the power of human resource (righteousness or Yudhishthir), power to remained focused (Arjun), power to fight injustice (Bheem), power to help others (Sahdev) and power to remain neutral during any adversity (Nakul).

In Vedic sciences, these powers are also defined as Ichha shakti (the power of desires to be with the consciousness), Kriya shakti (the power to do selfless work), Gyan shakti (the power to learn about consciousness), Chitta shakti (the power to take consciousness-based decisions) and Anand shakti (the power for inner happiness).

The power of human resources talks about cultivating relationships. It is not based on the principles of survival of the fittest, which is an animal behavior. The power of human resource believes in training and developing everyone to survive and become the fittest of the fit.

Group Editor-in-Chief, IJCP Group

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Self-Swab COVID-19 Home Testing Appears Comparable

According to a new study, symptomatic people who seek COVID-19 testing can effectively swab themselves at home.

The study noted that the results of such testing were comparable to that with traditional nasopharyngeal swabbing by clinicians. Home swab testing was shown to be 80% sensitive and 98% specific for detecting SARS-CoV-2 compared with testing administered by clinicians, suggest investigators at the University of Washington School of Medicine in Seattle. The study was published online in *JAMA Network Open*… (*Medscape*)

Don't Sweat the Small Stuff

An expert in time management was once addressing a group of students and to make a strong point, used an illustration that the students will never forget.

He stood in front of the group of overachievers, and said, "Time for a quiz." He pulled out a one-gallon, wide mouthed Mason jar and set it on a table. He brought out a dozen fist-sized rocks and carefully placed them into the jar. When the jar was filled to the top with the rocks, he asked, "Is the jar full?"

Everyone in the class said, "Yes." He asked, "Really?"

He then pulled out a bucket of gravel, dumped some gravel in the jar and shook it. The pieces of gravel worked themselves down into the space between the big rocks.

He again asked the group, "Is the jar full?"

"Probably not," one of them answered. "Good!" he replied. Now he pulled out a bucket of sand and started dumping the sand in the jar. The sand now went into all the spaces left between the rocks and the gravel. Once again he asked the group, "Is the jar full?" "No!" the class shouted. Once again he said, "Good!"

Now he grabbed a pitcher of water and started pouring it in until the jar was filled to the brim. Then he asked, "What is the point of this illustration?" One student said, "No matter how full our schedule is, if we try really hard we can fit some more things in!"

"No," the speaker said, "That's not the point. The truth this illustration teaches us is: If we don't put the big rocks in first, we will never be able to get them in at all." "What are the 'big rocks' in your life?", he asked.

"Children, loved ones, education, dreams, a worthy cause, doing things that you love, time for yourself, your health, your significant other."

"Put the BIG ROCKS in first or you'll never be able to get them in at all. If you sweat the little stuff, like the gravel, the sand, you'll fill your life with little things to worry about that don't really matter, and you'll never have the real quality time that you need to spend on the big, significant stuff."

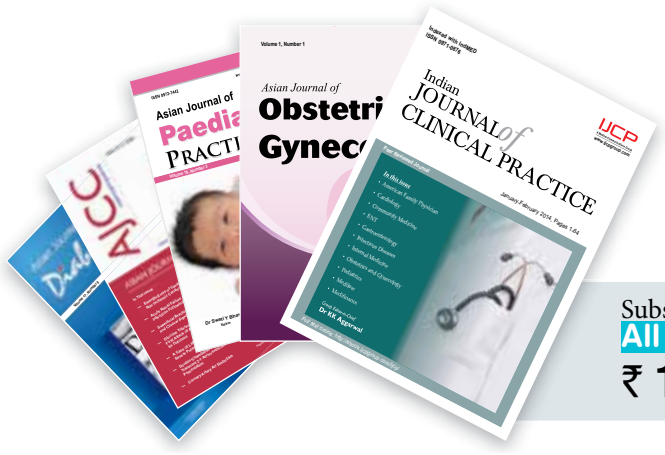
Ask yourself: What are the 'big rocks' in my life? Then, put those in the jar first.

■■■■

Postmenopausal Estrogen Alone Reduces Breast Cancer Cases and Deaths

A follow-up study of menopausal hormone therapy has revealed that prior use of conjugated equine estrogen (CEE) led to a reduction in both breast cancer incidence as well as mortality, while prior use of CEE plus medroxyprogesterone acetate (MPA) was tied to an increase in incidence.

To explore the outcomes of the Womens Health Initiative for hormone therapy and breast cancer risk, investigators assessed the long-term follow-up of two randomized trials involving 27,347 postmenopausal women with no prior breast cancer and negative mammograms at baseline. An analysis done in 2015 revealed that CEE alone was associated with lower risk of breast cancer while CEE plus MPA was associated with increased risk. The present analysis confirmed that following a median follow-up of 20.3 years, and with mortality data available for over 98% of participants, CEE alone was linked with fewer cases of breast cancer compared with placebo. Additionally, CEE alone was also associated with lower mortality compared with placebo. Contrary to that, CEE plus MPA was associated with more cases of breast cancer than placebo and no statistically significant difference could be seen between CEE plus MPA and placebo for mortality. The study is published in *JAMA*… (*Medscape*)



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Indian Journal of Clinical Practice, Vol. 31, No. 2, July 2020

Lighter Side of Medicine

HUMOR

PRICE YOU PAY FOR BEING GOOD

Three men were waiting to go to heaven. St Peter was at the gate and said, "However, good you were to your wife that is the vehicle you will get in heaven".

The first guy comes up to the gate and says, "I never, ever cheated on my wife and I love her". So, St Peter gives him a Rolls Royce.

The next man comes up and says, "I cheated on my wife a little but I still love her." He gets a mustang and drives off into heaven.

The next guy came up and said, "I cheated on my wife a lot". He gets a scooter.

Next day the guy that got the scooter was riding along and he saw the guy who owned the Rolls Royce crying.

He asked, "Why are you crying you have such a nice car?!" and the man sobbed, "My wife just went by on roller skates".

I COULD USE A LITTLE MONEY

Dear Father, $chool i$ really great. I am making lot$ of friend$ and $tudying very hard. With all my $tuff, I $imply can't think of anything I need, $o if you would like, you can ju$t $end me a card, a$ I would love to hear from you. Love, Your $on.

After receiving his son's letter, the father immediately replies by sending a letter back.

Dear Son, I kNOw that astroNOmy, ecoNOmics and oceaNOgraphy are eNOugh to keep even an hoNOr student busy. Do NOt forget that the pursuit of kNOwledge is a NOble task, and you can never study eNOugh. Love, Dad.

DAUGHTER IN COLLEGE

Did you hear about the banker who was recently arrested for embezzling $100,000 to pay for his daughter's college education?

As the policeman, who also had a daughter in college, was leading him away in handcuffs, he said to the banker, "I have just one question for you. Where were you going to get the rest of the money?"

THE LEAVE APPLICATION

From an employee who was performing the "mundan" ceremony of his 10-year-old son: "as I want to shave my son's head, please leave me for 2 days..."

KNOCK ON WOOD

Three sisters, ages 92, 94 and 96 live in a house together. One night the 96-year-old draws water for a bath. She puts her foot in and pauses. She yells to the other sisters: "Was I getting in or out of the bath?"

The 94-year-old yells back: "I don't know. I'll come up and see." She starts up the stairs and pauses.

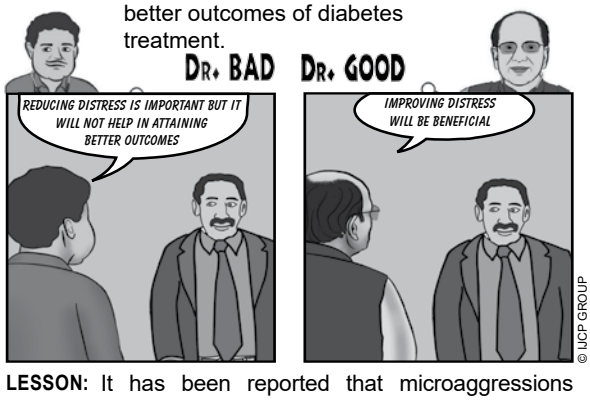
"Was I going up the stairs or down?"

The 92-year-old is sitting at the kitchen table having a cup of tea listening to her sisters.

She shakes her head and says" "I sure hope I never get that forgetful, knock on wood." She then yells: "I'll come up and help both of you as soon as I see who's at the door."

Dr. Good and Dr. Bad

SITUATION: A 54-year-old male with type 2 diabetes was advised to reduce distress in order to achieve better outcomes of diabetes treatment.



LESSON: It has been reported that microaggressions display a positive link with diabetes distress and an indirect association with selfcare via diabetes distress. Ameliorating diabetes distress plays a vital role in managing the disease successfully, reducing the complications and improving self-care even in the presence of chronic social stressors such as microaggressions.

J Behav Med. 2017;41(1):122-9.

Indian JOURNAL of CLINICAL PRACTICE

Indian Citation Index (ICI),

IndMed (http://indmed.nic.in/)

MedIND (http://medind.nic.in/)

University Grants Commission (20737/15554).

ISSN number 0971-0876

RNI number 50798/1990.

The Medical Council of India (UGC, ICI)

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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.

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R.N.I. No. 50798/1990
Date of Publication 13th of Same Month
Date of Posting 13-14 Same Month

POSTAL REGISTRATION NO. DL (S)-01/3200/2018-2020
Posted in N.D. PSO New Delhi