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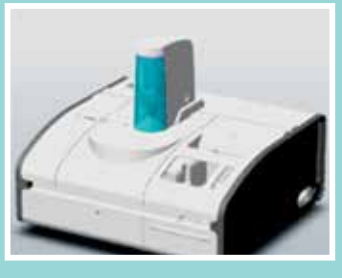

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CMAAO Coronavirus Facts and Myth Buster: Around the Globe

National Comprehensive Cancer Network (NCCN) – Preliminary Recommendations for COVID-19 Vaccination in Patients with Cancer

Patients receiving hematopoietic cell transplantation or cellular therapy: Coronavirus disease 2019 (COVID-19) vaccination should be done ≥3 months after hematopoietic cell transplantation (allogeneic or autologous) or cellular therapy (e.g., chimeric antigen receptor [CAR] T-cell therapy).

Patients with hematologic malignancies: For patients receiving intensive cytotoxic chemotherapy, vaccination against COVID-19 must be delayed until the absolute neutrophil count has recovered. For patients with marrow failure due to disease or treatment who are likely to have limited or no recovery, and for those on long-term maintenance therapy, vaccination should be done when the vaccine becomes available.

Patients with solid-tumor malignancies: For patients who are receiving cytotoxic chemotherapy, targeted therapy, checkpoint inhibitor therapy or other immunotherapy, or radiation therapy, vaccination should be done when the vaccine becomes available.

For patients who have to undergo a major surgery, COVID-19 vaccination must be postponed until at least a few days after surgery.

Involve Private Practitioners in the National Program to Give the Vaccine

- Private practitioners can meet patients where they are. The most vulnerable patients do not have to stand in a queue or travel several kilometers to be vaccinated. They are present within the communities, are easily accessible, and can shift people away from gatherings of large groups of people who may be sick.
- One can avoid wasting time and resources.
- Vaccines are being distributed only to hospitals that are already overwhelmed with COVID-19 patients.
- Practicing doctors can identify the most vulnerable patients and contact them to get them vaccinated first.
- Their knowledge of their patients is current and deep, while hospital systems know comparatively lesser about people's chronic conditions, recent health problems, lifestyles and other risk factors.
- Physician practices can fight the myths and misconceptions.

The US Food and Drug Administration (FDA) issued emergency use authorization (EUA) for the first molecular COVID-19 test for home and over the counter use - the Cue COVID-19 Test. This will be the first

molecular diagnostic test that will be available without a prescription.

Individuals who have been fully vaccinated against COVID-19 can safely gather without mask and inside with nonvulnerable people who are not yet vaccinated, suggest guidance issued by the Centers for Disease Control and Prevention (CDC).

The new guidance states that people for whom it has been at least 2 weeks since their last required dose can:

- Meet other fully vaccinated people indoors without wearing masks or physical distancing
- Visit with unvaccinated people from one other household who have a low risk for severe COVID-19 indoors without wearing masks or practicing physical distancing
- Avoid quarantine and testing after exposure to someone infected with COVID-19, if they remain asymptomatic.

However, some restrictions continue to be there until further data is obtained. Those who are fully vaccinated must:

- Wear masks and practice physical distancing in public settings and around people at high risk for severe disease
- Wear masks and practice physical distancing when visiting unvaccinated people from more than one household.
- Avoid medium- and large-sized gatherings
- Avoid traveling.

Individuals who are considered to have a high risk for severe disease include cancer patients, those with chronic kidney disease, chronic obstructive pulmonary disease (COPD), Down syndrome, heart disease, heart failure, a weak immune system, obesity, sickle cell disease and type 2 diabetes. It also includes pregnant women and smokers.

In public places, fully vaccinated people are required to follow guidance to protect themselves and others, which includes wearing a well-fitted mask, physical distancing (at least 6 feet), avoiding crowds, avoiding spaces that are not well-ventilated, covering coughs and sneezes, washing hands frequently, and following any applicable workplace or school guidance. Fully vaccinated people should also be vigilant of symptoms of COVID-19, especially after exposure to someone with suspected or confirmed COVID-19.

Vaccinated grandparents can visit children and grandchildren who are healthy and local.

Studies from Spain and Israel have shown that the amount of viral load appears to be significantly lower if someone gets infected after receiving vaccination, compared to people who get infected and have not received the vaccine.

(*Excerpts from Medscape*)

With input from Dr Monica Vasudev

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Travel Restrictions for Countries Affected by Ebola Announced by CDC

The US CDC has stated that travel restrictions are going to be imposed for people coming from Guinea and the Democratic Republic of Congo (DRC) to the US. These two countries have seen recent outbreaks of the Ebola virus. The US government will direct travelers from Guinea and the DRC to six US airports, reported the CDC. Airlines will be required to obtain information from all passengers boarding flights to the US who have been in either of the two countries within the previous 21 days. The data has to be shared with the CDC and local health departments for monitoring. Similar travel precautions were imposed during the 2014 Ebola outbreak as well… (*CNN*)

MS Disability, Age Linked to Worse COVID Outcomes

According to registry data, disability and age have been reported to be linked with poorer COVID-19 outcomes in patients with multiple sclerosis (MS). Out of nearly 2,000 people with MS and COVID-19 in North America, 17.8% of the nonambulatory patients died, compared to 4.3% patients who walked with assistance and 0.6% patients who were ambulatory. Death was more common among MS patients aged 75 years and older, who had COVID-19. The findings come from 2,059 MS patients reported by more than 150 healthcare providers in North America between April 1, 2020 and January 29, 2021. About 85.4% of the patients had laboratory-confirmed COVID-19. The data were presented at ACTRIMS Forum 2021, the annual meeting of the Americas Committee for Treatment and Research in Multiple Sclerosis… (*Medpage Today*)

Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

Rehabilitation of Patients After COVID-19 Pandemic

YATIN MEHTA

ABSTRACT

After severe coronavirus disease 2019 (COVID-19), many patients will encounter a variety of issues with their normal functioning routine and will require rehabilitation services to overcome these issues. Rehabilitation will be needed for survivors of COVID-19, those who have become deconditioned as a result of movement restrictions or limited movement, social isolation and inability to access healthcare and many of whom are older, with underlying health problems. The principles of rehabilitation include a simple screening process, use of a multidisciplinary expert team and evidence-based classes of intervention. The purpose of rehabilitation in COVID-19 patients is to relieve anxiety, depression, reduce complications, minimize disability, preserve function, provide psychological support and improve quality of life. This article reviews the likely rehabilitation needs of people with moderate to acute COVID-19 and discusses strategies to deliver effective rehabilitation and implementation in a world with COVID-19.

Keywords: COVID-19, coronavirus, rehabilitation

In March 2020, World Health Organization (WHO) declared the outbreak of a novel coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and it has evolved into a pandemic.[1] Coronavirus causes a highly infectious respiratory sickness that prompts respiratory, physical and psychological dysfunction in patients. In most patients, COVID-19 infection confers mild illness with fever (88.7%), sore throat (57.6%) and dyspnea (45.6%). However, for a considerable number of patients, those aged >65 years with comorbidities such as hypertension and diabetes, the infection can have intense sequelae. Among patients requiring hospitalization, a relatively high percentage (20.3%) requires admission in the intensive care unit (ICU), often for acute respiratory distress syndrome (ARDS); these patients can likewise encounter multiorgan failure.[2]

Early intricacies of COVID-19 include ARDS, sepsis or septic shock, multiorgan failure, acute kidney injury and cardiac injury. In many cases, patients stay bedridden in the ICU for extended time periods in an inclined situation, which can cause post-ICU dysphagia, muscle weakness, myopathy and neuropathy leading to critical illness, as well as reduced joint mobility, pain in the neck and shoulders, trouble standing and hindered balance and step, with consequent limitations in activities of daily living (ADL).[3,4] In addition, persistent mental health impairment is commonly manifested, with pooled estimates demonstrating a high prevalence of depression (29%).[4] The longer a patient remains in the ICU, the greater the risk of long-term physical, cognitive and emotional problems.[5]

Patients who were seriously ill with COVID-19 and have passed the critical phase of lung infection, and are discharged but have symptoms of pulmonary dysfunction, should be prescribed a rehabilitation program to restore wellness and reduce anxiety and depression.[5,6]

Rehabilitation is like medical aid, to make sure that patients do not deteriorate after discharge and need readmission. It begins with an assessment aiming to discover the patient's primary problems and concerns, and to understand how did it arise and how can it be ameliorated. Effective rehabilitation interventions fall into five categories that are the same across all conditions:[7]

- Everyday exercise to increase cardiorespiratory work

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- Performing basic functional activities
- Psychosocial treatments
- Education with an emphasis upon self-management
- Set of specific actions custom-made to the patient's priorities, requirements and goals, covering all domains of the biopsychosocial model of illness, and being assessed routinely for their benefits and to decide if they should be continued, changed or relinquished (Fig. 1).

PHYSIOTHERAPY AND POST-ACUTE COVID-19 REHABILITATION PHASE

Physiotherapists are instrumental in the rehabilitation of patients as they transition from the acute phase to the post-acute phase.[8] The outcomes of COVID-19 will be narrowed down in each individual and their rehabilitation needs will be specific to these consequences such as:

- Long-term ventilation
- Immobilization
- Deconditioning
- Related impairments – respiratory, neurological and musculoskeletal.

COVID-19 patients will often present with pre-existing comorbidities and this must be considered within the rehabilitation plan for the patient.

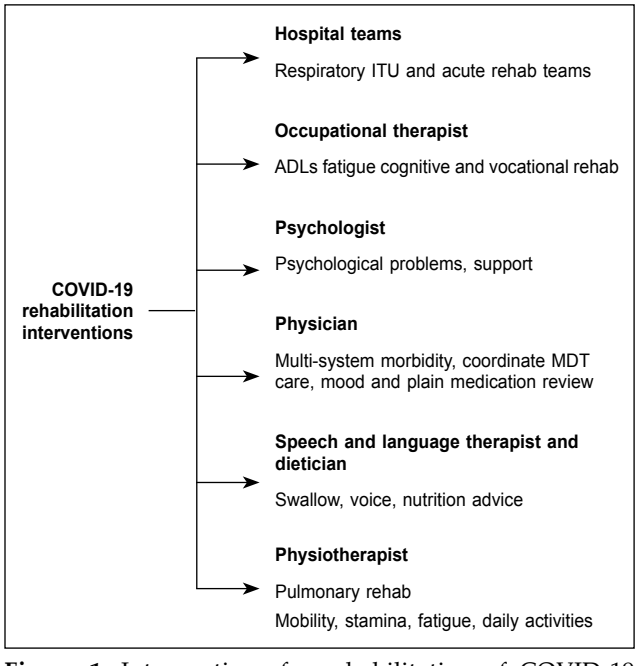

Figure 1. Interventions for rehabilitation of COVID-19 patients.

ITU = Intensive treatment unit; ADLs = Activities of daily living; MDT = Multidisciplinary team.

REHABILITATION FOR PATIENTS WITH MILD AND MODERATE COVID-19

Most patients with COVID-19 present with mild influenza like symptoms and may encounter fever, fatigue, cough, muscle pain and other indications. The principal interventions of respiratory rehabilitation include airway clearance, respiratory control, posture management, active work and exercise.[9,10] A diagnosis of COVID-19 may build a feeling of fear in patients[11] and psychological counseling is especially significant. Besides, these patients ought to zero in on making sure to do regular work and rest, have a balanced diet and stop smoking.[9] For patients with mild and moderate signs and symptoms of COVID-19, Traditional Chinese Medicine (TCM) and adjuvant therapy involving acupuncture, moxibustion, massage, cupping, acupoint application and aromatherapy are reported.[12]

REHABILITATION FOR SEVERE AND CRITICALLY ILL COVID-19 PATIENTS WITH UNDERLYING COMORBIDITIES OR WHO ARE ELDERLY

Severe and critically ill patients with COVID-19 often develop respiratory distress and/or hypoxemia 1 week after onset, progressing to ARDS, septic shock, metabolic acidosis and even death.[8,11,12] For severe and critically ill patients, specialists from different nations have proposed that respiratory rehabilitation should be undertaken once a patient's condition is steady, but not start too early, to abstain from intensifying respiratory failure or unnecessary spreading of the virus through droplets.[8,12] Therefore, determining an exact recovery time is significant. Timely rehabilitation can reduce or even eliminate the occurrence of these complications and the negative effects on patients' everyday life.[13,14]

Early rehabilitation should be performed within a patient's resilience level, including posture management, rollover, active/passive joint activity, respiratory muscle training, sputum training, basic exercises for patients confined to their beds, mobility training, stand on support, standing independently and ADL training.[8,15-18] For patients with ventilator dependence, progressive resistance training of inspiratory muscles has been observed to be a feasible and viable treatment to improve inspiratory muscle strength and improve quality of life (QoL) after weaning.[9,19] It should be noted that in the early stage of severe illness, aerobic exercise should be avoided as much as possible, as it may cause respiratory failure in some patients.[17]

REHABILITATION OF PATIENTS WITH COVID-19 WHO ENCOUNTER PSYCHOLOGICAL DISORDERS

Patients diagnosed with COVID-19 may experience outrage, fear, nervousness, depression, insomnia or hostility during the isolation treatment period, as well as psychological problems such as depression, loneliness, lack of cooperation or abandonment of treatment due to fear of the disease, which all negatively affect patient treatment and rehabilitation.[3,4,17,20] Patients in ICU have been found to have differing levels of nervousness, depression and post-traumatic stress disorder (PTSD),[21-23] and these conditions can prompt dyspnea, tachycardia, raised blood glucose levels, hyperlacticacidemia and low blood pressure, thus influencing the adequacy of treatment.[23]

Prevention or treatment of these clinical symptoms is likely to be of considerable benefit to patient recovery and ADL. Two studies detailed that clinical psychologists may assist patients to recover from their intense and unpleasant encounters. Clinical psychologists provide patients with interactive communication, stress management and personalized care. The findings of both studies showed that patient's vital signs improved and pain scores decreased and that anxiety, complication rates and sleep patterns all improved; notwithstanding, barely any examinations have straightforwardly measured the impacts of early mediations by clinical therapists for patients who are severely or critically ill.[24,25] Each patient's degree of capacity to convey may vary; therefore, psychological treatment should be personalized. Patient education can improve understanding and reduce anxiety levels. This methodology has been shown to improve recuperation times and reduce pain, psychological stress and length of hospital stay.[25]

Relaxation exercises (e.g., progressive muscle relaxation, meditation and breathing exercises) have been reported to improve patient mood and vital signs. Moreover, these exercises have been found to reduce the incidence of complications, pain levels, fatigue, fear, use of sedatives and length of hospital stay and improve sleep quality.[12] Distraction methods (such as reading, engaging in dialogue and listening to music) have been found to improve patients' pain symptoms.[12] Similarly, hypnotic interventions can effectively relieve pain and reduce the use of analgesics.[25] One study demonstrated that acupuncture, massage and other TCM treatments can also reduce patient stress.[26] Music therapy is a widely used nonpharmaceutical intervention, which has been accounted to reduce stress, anxiety, pain, depression and feelings of isolation for patients.[23,25]

In spite of the fact that drug therapy is currently the main intervention to alleviate patients' anxiety and psychological distress, nonpharmacological interventions have gradually become widely acknowledged and implemented, benefiting many patients and reducing the risk of drug-related adverse reactions.[23,27]

Rehabilitation Interventions at Different Phases of Care During COVID-19

Acute phase of care

Rehabilitation intervention:

- While patients with severe COVID-19 are receiving ventilator support, rehabilitation professionals may be engaged in supporting acute respiratory management,[14] and the maintenance and improvement of functioning to encourage early recovery.
- Specialized rehabilitation experts can provide interventions that help with improving oxygenation, airway secretion clearance and ventilation weaning,[28,29] and can likewise assume a function in promoting nutrition and preventing aspiration pneumonia, especially post-intubation and/or in patients with a tracheostomy.[30]

Typical delivery setting:

- Intensive and/or critical care units
- High dependency units (including in SARS centers).

Subacute phase of care

Rehabilitation intervention:

- In the early recuperation time frame, once patients have returned to a hospital ward or step-down facility, or for patients where illness severity did not warrant admission to an ICU, rehabilitation interventions may zero in on addressing ongoing impairments in mobility, respiratory capacity, cognition, swallow and nutrition, and communication.[31,32]
- Interventions during this period further aim to promote independence with activities of everyday living, and to give psychosocial support.[33]

Typical delivery setting:

- Hospital wards
- Step-down facilities (including in SARS centers).

Long-term phase of care

Rehabilitation intervention:

- Following discharge, rehabilitation experts can provide evaluated exercise, instruction on energy conservation and behavior modification, as well as rehabilitation for any specific individual impairment.
- During the long-term recovery of severe COVID-19, patients may benefit from pulmonary rehabilitative interventions, which target physical and respiratory impairments, and incorporate a combination of evaluated exercise, education, ADL and psychosocial support.
- In numerous specific situations, pandemic related constraints (physical distancing, limited human resources and limited public transport) and infection risks imply that telehealth is likely to be required following discharge.
- This could be reached out to incorporate remote exercise (e.g., virtual education and exercise) and peer-to-peer support from COVID-19 patients who have received the suitable training.[34]

Typical delivery setting:

- Rehabilitation centers
- Outpatient programs
- In-home services
- Mobile services
- Telehealth.

Recommendation for Discharging Patients[35]

Rationale	Recommendation
Exclusion criteria	• Heart rate >100 beats/min • Blood pressure <90/60 mmHg or >140/90 mmHg • Blood oxygen saturation ≤95% • Other diseases where exercise is not suitable
Exercise termination criteria	• Fluctuations in body temperature >37.2°C • Respiratory symptoms and fatigue deteriorate; not relieved after rest • Stop exercises promptly and counsel a specialist if the accompanying side effects happen: chest tightness/pain, breathing difficulty, severe cough, dizziness, headache, blurred vision, palpitations, sweating, trouble standing
Rehabilitation evaluation	Clinical assessment: Physical examination, imaging, laboratory, lung function, etc. Evaluation of activity and respiratory capacity: • Respiratory muscle strength: Maximum inspiratory pressure/maximum expiratory pressure • Muscle strength: Isokinetic muscle testing • Joint range of motion evaluation • Balance function evaluation using Berg Balance Scale • Aerobic exercise capacity evaluation: 6-minute walk test • Physical activity assessment: International Physical Activity Questionnaire, physical activity scale for the elderly, etc. ADL ability
Respiratory rehabilitation interventions	Patient education: • Manuals or videos to explain the significance of respiratory restoration • Healthy and sound lifestyle education • Motivate patients to participate in family and social activities Proposals for respiratory recovery: • Aerobic exercise: Walking, jogging, swimming, etc., starting from low intensity and gradually increasing the intensity and duration: 3-5 times/week for 20-30 minutes each time. Discontinuous exercise can be utilized in patients who are prone to fatigue. • Strength training: Progressive resistance training 2-3 times/week, with a training period of 1.5 months and a weekly increase of 5-10%.

- Balance training: Patients with balance dysfunction ought to go through balance training, including hands-free training and balance training using a device, under the direction of a physiotherapist.
- Breathing training: In case of shortness of breath, wheezing, difficulty with sputum discharge, patient should start breathing and sputum training, adjusting breathing rhythm, thorax activity training and activating breathing muscle group participation.
- Sputum training: First, breathing techniques can be used to help reduce sputum and energy consumption in coughing. Then, patients should be assisted with positive expiratory pressure (PEP)/oscillatory PEP and other gear.

ADL guidance:

- Basic ADL: Evaluate the patient's ability to perform day-to-day activities such as training transfer, grooming, toileting, bathing and provide rehabilitation guidance for daily life impediments.
- Instrumental ADL: Assess the ability of instrumental daily activities, distinguish obstacles in task participation, and conduct targeted intervention under the guidance of an occupational therapist.

CONCLUSION

COVID-19 created an unprecedented situation in the entire world. It has tested all medical services, including rehabilitation, and will continue to do so for the next coming years. During hospitalization, patients with COVID-19 are basically affected by respiratory dysfunction. Rehabilitation intervention (including positioning and respiratory management, traditional herbal medicine, physiotherapy and psychological support) should be given along with routine treatment, which can decrease hospital length of stay and improve patient status and QoL. Ideal arrangement and insightful planning can assist with restricting any effect that emerges from this pandemic.

REFERENCES

1. Demeco A, Marotta N, Barletta M, Pino I, Marinaro C, Petraroli A, et al. Rehabilitation of patients post-COVID-19 infection: a literature review. J Int Med Res. 2020;48(8):300060520948382.
2. Brugliera L, Spina A, Castellazzi P, Cimino P, Tettamanti A, Houdayer E, et al. Rehabilitation of COVID-19 patients. J Rehabil Med. 2020;52(4):jrm00046.
3. Kiekens C, Boldrini P, Andreoli A, Avesani R, Gamna F, Grandi M, et al. Rehabilitation and respiratory management in the acute and early post-acute phase. "Instant paper from the field" on rehabilitation answers to the COVID-19 emergency. Eur J PhysRehabil Med. 2020;56(3):323-6.
4. Simpson R, Robinson L. Rehabilitation after critical illness in people with COVID-19 infection. Am J Phys Med Rehabil. 2020;99(6):470-4.
5. Stam HJ, Stucki G, Bickenbach J; European Academy of Rehabilitation Medicine. Covid-19 and post intensive care syndrome: a call for action. J Rehabil Med. 2020;52(4):jrm00044.
6. Chinese Association of Rehabilitation Medicine; Respiratory Rehabilitation Committee of Chinese Association of Rehabilitation Medicine; Cardiopulmonary Rehabilitation Group of Chinese Society of Physical Medicine and Rehabilitation. [Recommendations for respiratory rehabilitation of coronavirus disease 2019 in adult]. Zhonghua Jie He He Hu Xi Za Zhi. 2020;43(4):308-14.
7. Wade DT. Rehabilitation after COVID-19: an evidence-based approach. Clin Med (Lond). 2020;20(4):359-65.
8. World Confederation for Physical Therapy (WCPT). WCPT response to COVID-19 Briefing paper 2. Rehabilitation and the vital role of Physiotherapy. May 2020. Last accessed June 24, 2020.
9. Zhao HM, Xie YX, Wang C; Chinese Association of Rehabilitation Medicine; Respiratory Rehabilitation Committee of Chinese Association of Rehabilitation Medicine; Cardiopulmonary Rehabilitation Group of Chinese Society of Physical Medicine and Rehabilitation. Recommendations for respiratory rehabilitation in adults with coronavirus disease 2019. Chin Med J (Engl). 2020;133(13):1595-602.
10. Rayegani SM, Raeissadat SA, Fakharian A, Babaee M, Nezamabadi M, Boland Nazar NS, et al. Role of rehabilitation medicine in the COVID-19 pandemic: an Iranian consensus. Eur J Phys Rehabil Med. 2020 Jun 19.
11. Wang C, Pan R, Wan X, Tan Y, Xu L, Ho CS, et al. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in china. Int J Environ Res Public Health. 2020;17(5):1729.
12. Sun T, Guo L, Tian F, Dai T, Xing X, Zhao J, et al. Rehabilitation of patients with COVID-19. Expert Rev Respir Med. 2020;14(12):1249-56.
13. Sheehy LM. Considerations for postacute rehabilitation for survivors of COVID-19. JMIR Public Health Surveill. 2020;6(2):e19462.
14. Borg K, Stam H. Editorial: Covid-19 and physical and rehabilitation medicine. J Rehabil Med. 2020;52(4): jrm00045.
15. Thomas P, Baldwin C, Bissett B, Boden I, Gosselink R, Granger CL, et al. Physiotherapy management for

COVID-19 in the acute hospital setting: clinical practice recommendations. J Physiother. 2020;66(2):73-82.

16. de Sire A, Andrenelli E, Negrini F, Negrini S, Ceravolo MG. Systematic rapid living review on rehabilitation needs due to COVID-19: update as of April 30th, 2020. Eur J Phys Rehabil Med. 2020;56(3):354-60.
17. Sommers J, Engelbert RH, Dettling-Ihnenfeldt D, Gosselink R, Spronk PE, Nollet F, et al. Physiotherapy in the intensive care unit: an evidence-based, expert driven, practical statement and rehabilitation recommendations. Clin Rehabil. 2015;29(11):1051-63.
18. Curci C, Pisano F, Bonacci E, Camozzi DM, Ceravolo C, Bergonzi R, et al. Early rehabilitation in post-acute COVID-19 patients: data from an Italian COVID-19 Rehabilitation Unit and proposal of a treatment protocol. Eur J Phys Rehabil Med. 2020;56(5): 633-41.
19. Goemé L, Biebouw S, Linden P, Mortelé P. The impact of COVID-19 on rehabilitation: The Belgian experience. Eur J Phys Rehabil Med. 2020;56(3):371-2.
20. Yohannes AM. COPD patients in a COVID-19 society: depression and anxiety. Expert Rev Respir Med. 2020;15(1):5-7.
21. Coraci D, Fusco A, Frizziero A, Giovannini S, Biscotti L, Padua L. Global approaches for global challenges: the possible support of rehabilitation in the management of COVID-19. J Med Virol. 2020;92(10):1739-40.
22. Neufeld KJ, Leoutsakos JS, Yan H, Lin S, Zabinski JS, Dinglas VD, et al. Fatigue symptoms during the first year following ARDS. Chest. 2020;158(3):999-1007.
23. Golino AJ, Leone R, Gollenberg A, Christopher C, Stanger D, Davis TM, et al. Impact of an active music therapy intervention on intensive care patients. Am J Crit Care. 2019;28(1):48-55.
24. Peris A, Bonizzoli M, Iozzelli D, Migliaccio ML, Zagli G, Bacchereti A, et al. Early intra-intensive care unit psychological intervention promotes recovery from post traumatic stress disorders, anxiety and depression symptoms in critically ill patients. Crit Care. 2011;15(1):R41.
25. Meraner V, Sperner-Unterweger B. Patienten, Ärzte und Pflegepersonal auf Intensivstationen: Psychologische und psychotherapeutischeInterventionen [Patients, physicians and nursing personnel in intensive care units: Psychological and psychotherapeutic interventions]. Nervenarzt. 2016;87(3):264-8.
26. Liu ML, Liu M, Zhong H, Yu J, Luo J, Ai K, et al. Significance and operation mode of moxibustion intervention for the group under quarantine after close contact with COVID-19. Zhongguo Zhen Jiu. 2020;40(5):457-61.
27. Gélinas C, Arbour C, Michaud C, Robar L, Côté J. Patients and ICU nurses'perspectives of non-pharmacological interventions for pain management. Nurs Crit Care. 2013;18(6):307-18.
28. file:///F:/REHABILITATION/NMHMHCOVID19200010_eng.pdf.
29. Pathmanathan N, Beaumont N, Gratrix A. Respiratory physiotherapy in the critical care unit. Contin Educ Anaesth Crit Care Pain. 2014;15(1):20-5.
30. McRae J, Montgomery E, Garstang Z, Celary E. The role of speech and language therapists in the intensive care unit. J Inten Care Soc. 2020;21(4):344-8.
31. Held N, Moss M. Optimizing post-intensive care unit rehabilitation. Turkish Thoracic J. 2019;20(2):147-52.
32. Griffiths RD, Jones C. Seven lessons from 20 years of follow-up of intensive care unit survivors. Curr Opin Crit Care. 2007;13(5):508-13.
33. Holm SE, Mu K. Discharge planning for the elderly in acute care: the perceptions of experienced occupational therapists. Physical Occup Ther Geriatr. 2012;30(3):214-28.
34. Bolton CE, Bevan-Smith EF, Blakey JD, Crowe P, Elkin SL, Garrod R, et al; British Thoracic Society Pulmonary Rehabilitation Guideline Development Group; British Thoracic Society Standards of Care Committee. British Thoracic Society guideline on pulmonary rehabilitation in adults. Thorax. 2013;68 Suppl2:ii1-30.
35. Demeco A, Marotta N, Barletta M, Pino I, Marinaro C, Petraroli A, et al. Rehabilitation of patients post-COVID-19 infection: a literature review. J Int Med Res. 2020;48(8):300060520948382.

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Over 20 Million People in the UK Receive First COVID-19 Vaccine Dose

Over 20 million individuals in Britain have been administered the first COVID-19 vaccine dose, reported recently.

Prime Minister Boris Johnson stated that this was a big national achievement and urged all people to get the vaccination when called. "Every jab makes a difference in our battle against COVID," he said.

The United Kingdom has reported the highest death toll due to COVID-19 in Europe, which is currently at 1,22,849 deaths, and has suffered the greatest economic setback among rich countries. However, the speed with which the nationwide vaccination rollout is proceeding, it is expected that the current lockdown restrictions will gradually be lifted from now till June-end… (*Reuters*)

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Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

Negative Pressure Wound Therapy in Infected Wounds – Indian Public Hospital Observational Study

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ABSTRACT

Introduction: Negative pressure wound therapy (NPWT) is a procedure in which vacuum is used to enhance wound healing. Vacuum-assisted closure (VAC) refers to wound dressing that uses pressure below normal continuously or intermittently to the surface of a wound. The negative pressure is maintained by an apparatus; this promotes healing in various kinds of wounds and also helps in wound debridement. **Aims:** This study was carried out with an aim to find out the rate of wound contraction, compare infection clearance, granulation tissue formation and to study postoperative pain after using NPWT. **Material and methods:** All types of infected wounds with slough were selected. Patients irrespective of sex between 18 and 70 years of age were included. The wounds included were traumatic, diabetic foot, varicose ulcer, infected wounds, carbuncle, etc. The procedure included surgical debridement as a preliminary procedure, followed by application of NPWT. The wound criteria: 1) size, 2) shape, 3) wound margin and floor, 4) edge and contraction were studied. **Results and Discussion:** Infected wounds can be treated by specific modalities like daily wound dressing, surgical debridement, hyperbaric oxygen therapy and NPWT. NPWT seems more efficient than standard wound care for infected wounds. In our study, the mean size of ulcer in diabetic patients before NPWT was found to be 6.33 × 4.52 cm; after application of NPWT, it was 4.7 × 2.95 cm. The mean size of ulcer in traumatic patients before NPWT was found to be 7.1 × 5.1 cm, while after application of NPWT, it was 5 × 3.63 cm. The mean size of ulcer in vascular patients was found to be 5.71 × 3.85 cm before NPWT, and after application of NPWT, it was 4 × 2.42 cm. NPWT dressings have been proven to be beneficial as a variant method of dressing, mainly by negative pressure which sucks out serous fluid and helps in the formation of granulation tissue. Used in various wounds, continuous suction over period of time and later intermittent suction depending on wound status enhance wound healing process and lead to faster recovery compared to conventional methods of dressing. **Conclusion:** The wound healing period for large traumatic wounds and chronic diabetic wounds is 123 days as per published data. In our study, where NPWT was used, the average wound healing period was 35 days, ranging between 10 and 62, which is statistically significant ($p < 0.005$). NPWT is cost-effective, reduces hospital stay of patient with minimal chances of limb amputation with better results than standard wound care.

Keywords: Vacuum-assisted closure, hyperbaric oxygen therapy, negative pressure wound therapy

Negative pressure wound therapy (NPWT) is a relatively novel method used for managing wounds, both acute and chronic.[1] Vacuum-assisted closure (VAC), or NPWT, uses vacuum to improve wound healing. VAC involves wound dressing that applies pressure below normal, continuously or intermittently, to the surface of a wound.[2-4] The negative pressure promotes healing in different types of wounds.[5-7] It also assists with wound debridement. Wound healing is best at negative pressure of 85-125 mmHg. Application of negative pressure removes fluid, decreases edema and enhances blood flow, and decreases bacterial counts. It is less costly than traditional management of infected wounds.[8-13]

A negative pressure of 50-125 mmHg lowers the interstitial pressure, and fluid and debris from the wound gets sucked into a collection chamber.[14-18] In the beginning, the vacuum is continuous, but as the drainage is reduced, the vacuum is applied intermittently. The vacuum dressing is usually changed at approximately 2- to 6-dayinterval.[19-25]

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AIMS AND OBJECTIVES

This study was carried out with an aim to find out rate of wound contraction, compare infection clearance, granulation tissue formation and to study postoperative pain after using NPWT. The study also aimed to determine the length of hospital stay and to evaluate the cost-effectiveness of the procedure and effect on amputation prevention.

MATERIAL AND METHODS

Source of Data

- Patients of Grant Government Medical College and JJ Hospital, Mumbai, Maharashtra.
- A total of 50 cases clinically presenting as ulcer between June 2017 and December 2019 were included in the study.

Inclusion Criteria

- Both male and female
- Patients between 18 years and 70 years.
- Patients who signed informed written valid consent to be included in the study.
- Patients having acute or chronic wounds, including traumatic wounds, varicose ulcer, bed sore, diabetic wounds.

Exclusion Criteria

- Age less than 18 or above 70 years.
- Patients on chemotherapy or suffering from malignancy.
- Suspected poor compliance.
- If the patient did not sign the consent form.
- Peripheral vascular disease wound with acute or chronic osteomyelitis.

Procedure

Preparation of the wound

After cleaning the wound, foam dressing was cut to shape and kept into the wound cavity. The wound was then sealed with an adhesive dressing ensuring that the drapes covered the foam and tubing and 3 cm of healthy skin.

Negative pressure application

Negative pressure was applied to the wound using vacuum pump (Fig. 1), which delivered continuous or intermittent pressures, ranging from 50 to 125 mmHg. The foam dressing squeezed to the negative pressure. The pressure was applied continuously for the first 48 hours and then changed.

RESULTS AND DISCUSSION

The study was done on 50 patients in Dept. of Surgery, JJ Hospital Mumbai, Maharashtra.

In our study, as shown in Table 1, the mean size of ulcer in diabetic patients before VAC was found to be 6.33 × 4.52 cm, while after the application of VAC, it appeared to be 4.75 × 2.9 cm; the mean size of ulcer in traumatic patients before VAC was found to be 7.1 × 5.1 cm, and after application of VAC, it appeared to be 5 × 3.63 cm; the mean size of ulcer in vascular patients was found to be 5.71 × 3.85 cm before VAC, and after application of VAC, it appeared to be 4 × 2.42 cm. The p value was <0.05 and it was statistically significant. Figure 2 shows diabetic foot infection and Figure 3 depicts necrotizing fasciitis before and after treatment.

VAC therapy is an alternative to routine wound management.

In our study, average age of wounds was 35 days. In a study by Caniano et al,[26] average age of wounds was

Figure 1. VAC instrument.

Table 1. Mean Ulcer Size (cm) Before and After VAC Therapy in Wounds of Different Etiology

Etiology	Before VAC		After VAC	
	Length (cm)	Breadth (cm)	Length (cm)	Breadth (cm)
Diabetic	6.33	4.52	4.75	2.95
Traumatic	7.1	5.1	5	3.63
Vascular	5.71	3.85	4	2.42

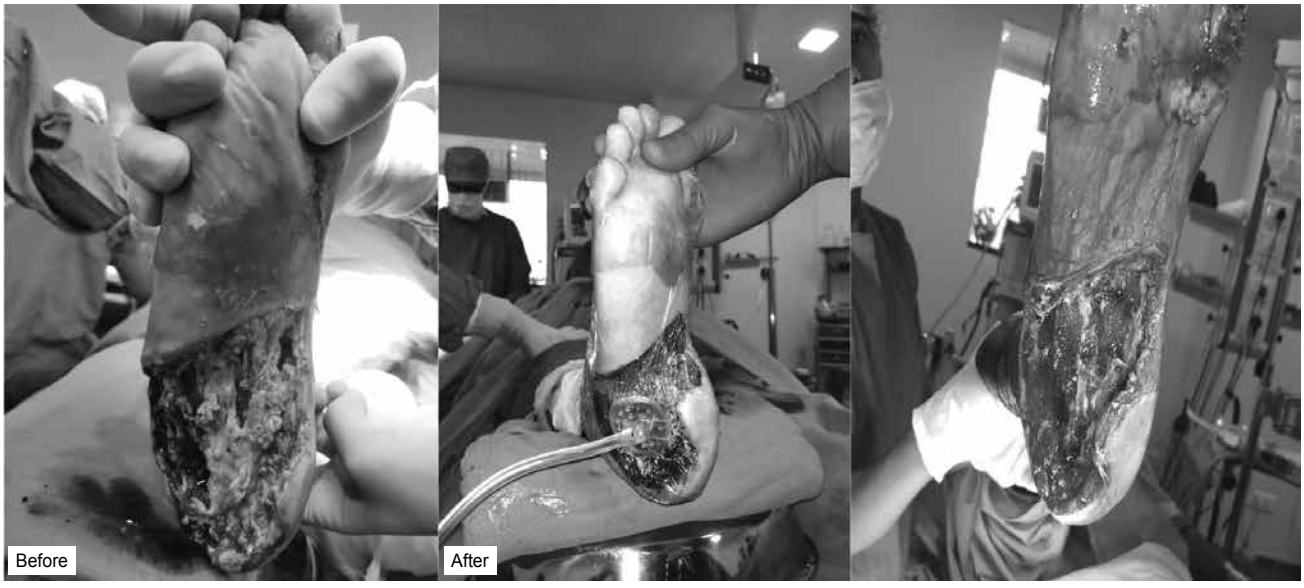

Figure 2. Diabetic foot infection (biofilm).

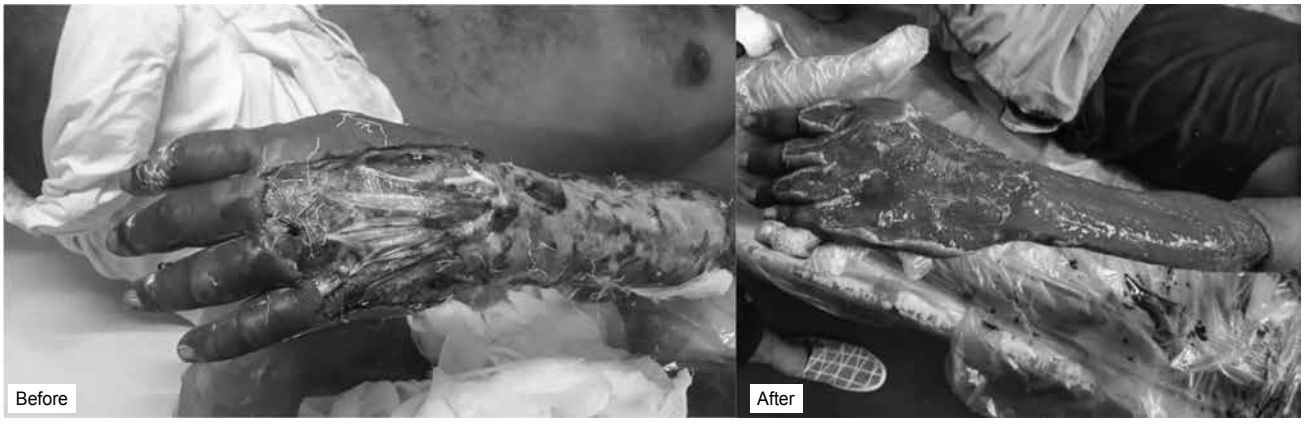

Figure 3. Necrotizing fasciitis.

37 days and in that by Ulusal et al,[27] it was 32 days, as compared to 59 days with standard dressing. In our study, the mean duration of wound healing was found to be 35.2 days with standard deviation (SD) of 12.03 days. In a study by Zimny et al,[28] the mean duration of wound healing was found to be 123.4 days with SD of 10.5 days. On statistical analysis, the p value was calculated to be <0.00001, which is statistically significant with 95% confidence interval (CI).

The wound healing period for large traumatic wounds and chronic diabetic wounds is 123 days as per published data.[28] In our study, where NPWT was used, the average wound healing period was 35 days.

Many mechanisms are suggested. VAC works by increasing the local blood flow and diminishes the edema fluid and colonization rates. The procedure promotes wound closure as it accelerates the formation of granulation tissue and also via mechanical effects on the wound.[29] It provides a clean moist wound and removes excess wound fluid, thus giving way to an ideal wound healing environment.

In our study, out of 50 patients, 36 patients had wound over foot region, 12 patients had wound over back region.

NPWT provides a moist wound environment, favoring granulation of edge of ulcer. A moist wound bed promotes re-epithelialization, action of growth factors, angiogenesis.

A moist wound environment also limits local pain, protecting the nerve endings and enhancing quality of life. Decrease in edema limits interstitial pressure and has a positive impact on microvascular occlusion and lymphatic drainage, thus enhancing the availability of nutrients, oxygen and antibiotics in the wound area.[30]

CONCLUSION

From our study, it can be concluded that NPWT is useful in wound healing in various types of wounds; therefore, NPWT should be the modality of choice in management of infected wounds. Vacuum-assisted dressing is more effective than traditional wound dressing. NPWT, in combination with surgical debridement and antibiotic therapy, is effective in managing infected wounds.

The wound healing period for large traumatic wounds and chronic diabetic wounds is 123 days as per published data. In our study, where NPWT was used, the average wound healing period was 35 days, ranging between 10 and 62 days, which was statistically significant ($p < 0.005$).

NPWT is cost-effective, reduces hospital stay of patient with minimal chances of limb amputation with better results than standard wound care.

REFERENCES

1. Eginton MT, Brown KR, Seabrook GR, Towne JB, Cambria RA. A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds. Ann Vasc Surg. 2003;17(6):645-9.
2. Banwell PE, Teot L. Topical negative pressure (TNP): the evolution of a novel wound therapy. J Wound Care. 2003;12(1):22-8.
3. Morykwas MJ, Argenta LC, Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice. First South-East Asia Edition, Philadelphia, PA: Elsevier Saunders; 2012. p. 152.
4. Sabiston DC, Townsend CM. Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice. First South-East Asia Edition, Philadelphia, PA: Elsevier Saunders; 2012. p. 152.
5. Schwartz SI, Brunicardi FC. Schwartz's Principles of Surgery: Self-assessment and Board Review. 10th Edition, New York, London; 2009. p. 266.
6. Greenfield LJ, Mulholland MW. Surgery: Scientific Principles and Practice. 6th Edition, Philadelphia: Lippincott Williams & Wilkins; 2001. p. 3211.
7. Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005;366(9498):1704-10.
8. Lazarus GS, Cooper DM, Knighton DR, Percoraro RE, Rodeheaver G, Robson MC. Definitions and guidelines for assessment of wounds and evaluation of healing. Wound Repair Regen. 1994;2(3):165-70.
9. Joseph E. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic nonhealing wounds. Wounds. 2000;12:60-7.
10. Lionelli GT, Lawrence WT. Wound dressings. Surg Clin North Am. 2003;83(3):617-38.
11. Bowler PG. Wound pathophysiology, infection and therapeutic options. Ann Med. 2002;34(6):419-27.
12. Williams NS, Bullstrode CJK, O'Connell PR. Bailey & Love's Short Practice of Surgery, 25th edn. Ann R Coll Surg Engl. 2010;92(2):178.
13. Webb LX, Schmidt U. Wound management with vacuum therapy. Unfallchirurg. 2001;104(10):918-26.
14. Lee HJ, Kim JW, Oh CW, Min WK, Shon OJ, Oh JK, et al. Negative pressure wound therapy for soft tissue injuries around the foot and ankle. J Orthop Surg Res. 2009;4:14.
15. Gammal S, Popp R, Schäfer M, el Gammal C, Altmeyer P. A color CD-ROM image analysis system to quantify débridement and healing of ulcers. In: Abatangelo G, Donati L, Vanscheidt W (Eds.). Proteolysis in Wound Repair. Berlin, Heidelberg: Springer Berlin Heidelberg; 1996. pp. 71-86.
16. Cohen IK. An overview of wound healing biology. In: Ziegler TR, Pierce GF, Herndon DN (Eds.). Growth Factors and Wound Healing: Basic Science and Potential Clinical Applications. New York, NY: Springer; 1997. pp. 3-7.
17. Jones SM, Banwell PE, Shakespeare PG. Advances in wound healing: topical negative pressure therapy. Postgrad Med J. 2005;81(956):353-7.
18. Erba P, Ogawa R, Ackermann M, Adini A, Miele LF, Dastouri P, et al. Angiogenesis in wounds treated by microdeformational wound therapy. Ann Surg. 2011;253(2):402-9.
19. Sato K, Yokota T, Ichioka S, Shibata M, Takeda S. Vasodilation of intramuscular arterioles under shear stress in dystrophin-deficient skeletal muscle is impaired through decreased nNOS expression. Acta Myol. 2008; 27(1):30-6.
20. Roseborough IE, Grevious MA, Lee RC. Prevention and treatment of excessive dermal scarring. J Natl Med Assoc. 2004;96(1):108-16.
21. Ryan TJ. Cellular responses to tissue distortion. In: Bader DL (Ed.). Pressure Sores - Clinical Practice and Scientific Approach. London: Macmillan Education UK; 1990. pp. 141-52.
22. Hasegawa S, Sato S, Saito S, Suzuki Y, Brunette DM. Mechanical stretching increases the number of cultured bone cells synthesizing DNA and alters their pattern of protein synthesis. Calcif Tissue Int. 1985;37(4): 431-6.
23. Fabian TS, Kaufman HJ, Lett ED, Thomas JB, Rawl DK, Lewis PL, et al. The evaluation of subatmospheric pressure and hyperbaric oxygen in ischemic full-thickness wound healing. Am Surg. 2000;66(12):1136-43.
24. Joseph E, Hamori CA, Sb B, Roaf E, Swann N, Anastasi G. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic nonhealing wounds. Wounds. 2000;12:60-7.

25. Mullner T, Mrkonjic L, Kwasny O, Vecsei V. The use of negative pressure to promote the healing of tissue defects: a clinical trial using the vacuum sealing technique. Br J Plast Surg. 1997;50(3):194-9.
26. Caniano DA, Ruth B, Teich S. Wound management with vacuum-assisted closure: experience in 51 pediatric patients. J Pediatr Surg. 2005;40(1):128-32.
27. Ulusal AE, Sahin MS, Ulusal B, Cakmak G, Tuncay C. Negative pressure wound therapy in patients with diabetic foot. Acta Orthop Traumatol Turc. 2011;45(4):254-60.
28. Zimny S, Schatz H, Pfohl M. Determinants and estimation of healing times in diabetic foot ulcers. J Diabetes Complications. 2002;16(5):327-32.
29. Mendez-Eastman S. Guidelines for using negative pressure wound therapy. Adv Skin Wound Care. 2001; 14(6):314-22.
30. Meloni M, Izzo V, Vainieri E, Giurato L, Ruotolo V, Uccioli L. Management of negative pressure wound therapy in the treatment of diabetic foot ulcers. World J Orthop. 2015;6(4):387-93.

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Persistent or New Obesity Tied to Gout

People who were obese all through their adult life had an increased risk for developing gout. Individuals who gained weight between early adulthood and midlife also had an increased risk, reported a large retrospective study.

In comparison with people who had a stable weight in the normal range during adulthood, the HR for incident gout was 1.84 (95% CI 1.08-3.14) for those who had obesity as young adults and also at midlife, reported researchers online in *Arthritis Research & Therapy*. People who gained weight during adult life were found to have 1.65-times greater risk for developing gout (95% CI 1.19-2.29)… (*Medpage Today*)

New Mutations in Novel Coronavirus Revealed by Indian Scientists

Multiple mutations and unique proteins in isolates of SARS-CoV-2 have been identified by the scientists from the Indian Institute of Sciences. The study which is published in the 'Journal of Proteome Research,' has shown that the host produces many proteins of their own as immunological response to the viral attack. The team analysis has suggested that the virus is now mutating at a faster rate compared with the earlier three isolates from Bengaluru with 27 mutations in their genomes with over 11 mutations per sample. The study showed that the isolates in India have multiple origins and did not evolve from a single ancestral variant. The study has concluded that proteins act as reliable markers of infections like COVID-19 as they are more ample and steady as compared to RNA molecules on which the prevalent reverse transcription polymerase chain reaction (RT-PCR) tests are dependent. (*ET Healthworld*)

Germany has Recommended AstraZeneca Vaccine for Individuals Over 65 Years

The Standing Committee on Vaccination in Germany has now recommended the COVID-19 vaccine form AstraZeneca for all age groups, including people older than 65 years. The recommendation is that for a complete vaccination, two AstraZeneca vaccine doses are needed, with the time between the two vaccinations to be 12 weeks if possible.

The Standing Committee had previously recommended the vaccine only for individuals under 65 years. However, now in addition to the AstraZeneca vaccine, vaccines from BioNTech and Pfizer as well as Moderna are officially approved in Germany. After over 2 months of the start of the coronavirus vaccination program in Germany, more than 2.27 million people have received the second vaccination bringing the country's vaccination rate to 2.7%. (*IANS*)

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Reasons for Default among Patients Receiving Antitubercular Treatment in Eastern Uttar Pradesh

PRAVEEN B GAUTAM*, HN CHAUDHARY†

ABSTRACT

Objective: To study the reasons for nonadherence to antituberculosis treatment (ATT) in Eastern Uttar Pradesh. **Methods:** This retrospective analysis was done among a cohort of 670 patients attending BRD Medical College, Gorakhpur, Uttar Pradesh during 2014. Defaulters were interviewed using semi-structured questionnaire to elicit reasons of treatment default. Statistical analysis was done by using Chi-square test. **Results:** Out of the total 670 patients enrolled in the study, 87 (16.35%) pulmonary, 7 (6.08%) extrapulmonary and 2 (8.69%) both pulmonary as well as extrapulmonary, defaulted ATT. Overall default rate was 14.32%. Major reasons for treatment interruption were early improvement (24.19%), high cost of treatment (16.12%) and ATT-induced side effects (11.29%). Maximum treatment interruption occurred between second and third month of ATT. More than one reason was often reported for discontinuation of treatment. **Conclusion:** Noncompliance was found to be mainly due to early improvement, high cost of treatment and side effects of medicine. So, information on disease and treatment should be intensified and appropriate to the level of education of population, in order to promote adherence to treatment and counter the spread of multidrug-resistant tuberculosis.

Keywords: Noncompliance, antituberculosis treatment

Tuberculosis (TB) is a major public health concern in the South-East Asia region, with the region accounting for 39% of the global TB burden in terms of incidence. India alone accounts for 26% of the global TB burden. India is the second-most populous country in the world and is home to a quarter of the global TB cases annually. Of the estimated global annual incidence of 8.6 million TB cases in the year 2012, 2.3 million cases were estimated to have occurred in India.

World Health Organization (WHO) has recommended Directly Observed Treatment, Short-course (DOTS) strategy for global TB control, which is accepted worldwide. Direct observation and regular home visit by treatment providers are provisions to increase treatment completion under DOTS. Based on DOTS strategy, India's Revised National Tuberculosis Control Programme (RNTCP) was launched in 1997. Though treatment completion rate reported by RNTCP is satisfactory, recently there is growing concern of emergence of drug-resistant strains of TB bacillus. Incomplete antituberculosis treatment (ATT) is the reason for emergence of multidrug-resistant (MDR) strains of TB bacillus that emerged in the early 1990s. Extensively drug-resistant (XDR) strains emerged in 2006 and totally drug-resistant strains emerged in 2011 in India.

Further poor adherence to treatment leads to emergence of MDR bacilli. So, ensuring compliance is of utmost importance to control TB and halt the MDR-TB epidemic at its beginning. There is continuing need to sustain and further intensify the action being undertaken to reduce default. The focus must remain on dealing with important reasons of default and timely retrieval of patients who interrupt treatment. The aim of this study was to determine the reasons for nonadherence to ATT in Eastern Uttar Pradesh.

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METHOD

The present study was conducted over a 6-month period from March to August 2014 and consists of an analysis of the data of pulmonary as well as extrapulmonary TB patients, indoor and outdoor, of BRD Medical College, Gorakhpur, Uttar Pradesh. After obtaining consent, patients were interviewed using a semi-structured questionnaire. Information recorded in the questionnaire included personal data, socio-demographic data, past and present history of ATT and reasons for discontinuation of ATT.

Definition – *Defaulter*: As per RNTCP guidelines, defaulter is defined as a patient who has not taken antitubercular drugs for 2 or more consecutive months, any time after registration.

Patients who gave a history of treatment interruption as defined above were enrolled for the study. All these patients were then interviewed in detail using a pre-tested semi-structured questionnaire. In addition to the personal and socio-demographic data, treatment history was recorded in detail.

Statistical analysis was performed by using the Chi-square test and a 'P' value of <0.05 was considered as significant.

RESULT

The study was conducted among patients of BRD Medical College, Gorakhpur, Uttar Pradesh, who were admitted and attended OPD in the Dept. of TB and Chest. A total 670 patients suffered from TB. Among the 670 TB patients, 96 (14.32%) were found to have history of ATT interruption and were included in study. Biosocial characteristics of the patients were studied and the effect of various factors on patients' compliance to treatment was observed.

In the present study, 78 (16.95%) males and 18 (8.5%) females defaulted. The highest number of defaulter were in the age group of 25-45 years [69 (18.15%)] while 15 (11.71%) defaulted in the age group of >45 years. In all, 12 (7.4%) defaulted in age group of below 25 years (Table 1).

On analyzing the religion, 76 (14.84%) Hindus and 16 (12.30%) Muslims defaulted, while among others (i.e., Christian, Sikh), 4 (14.28%) defaulted. Analysis of marital status revealed that 34 (12.97%) married patients had history of treatment interruption while among others (unmarried, widow, divorced), 62 (15.19%) patients defaulted.

Table 1. Factors Associated with Noncompliance to Treatment

Factors	Total no. of patients (n = 670)	Non-compliance (%) n = 96	P value
Age (years)			
<25	162	12 (7.40)	<0.05
25-45	380	69 (18.15)	
>45	128	15 (11.71)	
Sex			
Male	460	78 (16.95)	<0.05
Female	210	18 (8.5)	
Religion			
Hindu	512	76 (14.84)	NS
Muslim	130	16 (12.30)	
Others	28	4 (14.28)	
Marital status			
Married	262	34 (12.97)	NS
Others	408	62 (15.19)	
Education level			
Illiterate	260	59 (22.69)	<0.05
Literate	410	37 (9.0)	
Smoking			
Smokers	215	35 (16.27)	NS
Ex- or nonsmokers	455	61 (13.40)	
Occupation			
Employed	68	5 (7.35)	<0.01
Laborer	276	58 (21.01)	
House wives	180	15 (8.33)	
Unemployed	146	18 (12.32)	
Type of disease			
Pulmonary	532	87 (16.35)	<0.05
Extrapulmonary	115	7 (6.08)	
Both	23	2 (8.69)	

On analyzing the effect of education and occupation level, 59 (22.69%) illiterate and 37 (9.0%) literate patients had history of noncompliance to treatment, while 58 (21%) laborers, 18 (12.32%) unemployed, 15 (8.33%) house wives and 5 (7.3%) employed defaulted.

On analyzing the effect of smoking, 35 (16.27%) patients defaulted who were smokers while 61 (13.4%) patients defaulted, who were nonsmokers.

Among 670 patients, 87 (16.35%) pulmonary, 7 (6.08%) extrapulmonary and 2 (8.69%) both pulmonary as well as extrapulmonary patients defaulted. Eighty-one of the

Table 2. Reasons for Default (186)

Reasons	No. of patients who interrupted treatment (n = 186)	Percentage (%)
Early improvement	45	24.19
High cost of treatment	30	16.12
ATT-induced side effect	21	11.29
Alcoholism	20	10.75
No improvement or deterioration	16	8.6
Advised to stop treatment by physician	13	6.98
Unaware about long duration of treatment	12	6.45
Long distance travel to center	11	5.91
Lack of faith in treatment	8	4.30
Personal reasons	10	5.37
a. Family problem	6	3.22
b. Went to village	4	2.15
Total	**186**	

patients interviewed had no comorbidities and among the remaining 15 patients had history of comorbidities (e.g., diabetes mellitus, hypertension).

Among the 96 patients interviewed, 51 (53.12%) had defaulted treatment only once and 32 (33.3%) had interrupted treatment twice, while rest of patients had interrupted treatment more than two times (i.e., three or four). Thus, the 96 patients included in the study had interrupted treatment 157 times. Among 157 treatment interruption episodes, 102 (64.96%) occurred when the prescribing source of ATT was private practitioner, 50 (31.84%) took place while on treatment under DOTS therapy and remaining 5 (3.18%) interruptions took place while on non-DOTS treatment from a Government source.

Among the 96 patients interviewed, 38 (39.58%) stated only one reason for defaulting their treatment, 34 (35.4%) patients stated two reasons and 16 (16.66%) and 8 (8.33%) gave three and four reasons, respectively. Thus, 186 reasons for treatment interruption were obtained from 96 patients.

Maximum interruptions were found to occur between second and third month of ATT and 61 (64%) had defaulted treatment by the end of second month.

On analyzing the reasons of default among defaulters (Table 2), early improvements following medications were found to be the most common reason 45 (24.19%). Next important reasons were high cost of treatment and ATT-induced side effects (16.12% and 11.29%, respectively).

Alcoholism, no relief of symptoms and advised to stop by physician were other important reasons behind the default (10.75%, 8.6% and 6.98%, respectively). Some other reasons such as unaware about long duration of treatment, long distance travel to center, lack of faith and personal problem were also found to be important reasons for treatment interruption (6.45%, 5.91%, 4.30% and 5.37%, respectively).

DISCUSSION

Among the 670 TB patients, indoor and outdoor, during the study period, 96 (14.32%) had history of treatment interruption, of which 90.62% patients had pulmonary TB while 7.29% extrapulmonary and 2.08% had both pulmonary as well as extrapulmonary TB.

In the present study, out of 157 treatment interruptions, 102 (64.96%) interruptions occurred on private treatment, while 50 (31.84%) interruptions took place on DOTS and remaining 3.18% treatment interruptions occurred on non-DOTS government treatment. This emphasizes the need to provide DOTS to all as it is the only path to minimize treatment interruption.

In our study, default to treatment was found to be more in the 25-45 years age group of patients (18.15%), while good compliance to treatment was observed among less than 25 years (7.40% default). Similar results were

also observed in a study conducted by Chandrasekaran et al where the odds of default were higher in those aged >45 years. In another study, Kumar et al observed maximum default in 35-44 years age group (25.4%), followed by the patients aged above 45 years (18.1%). Further, comparatively more default in the 25-45 years of age group is mainly due to the subjects being economically productive members of the family, which led them to the skip treatment rather than to leave their earning of the day.

Another risk factor for default is sex. Males defaulted more (16.95%) as compared to female (8.5%). More default among males is supposed to be due to being on job frequently; while in contrast, DOTS centers are present in most of the localities, so females can visit the center regularly. Similar results were also found in a study by Jaggarajamma et al in which male and female defaulters were 24% and 8%, respectively.

Another risk factor for default is education. Illiterate defaulted more as compared to literate (22.69% vs. 9.0%). Similar results were also found in the study by Jaggarajmma et al.

Persons involved in various occupations, especially the laborer (21%), defaulted more as compared to housewives, unemployed (students, retired) and employed. Mittal et al observed that more people defaulted among businessman (30.6%), unemployed/ retired (25%) and laborer (18.2%) groups. While few others did not find any association between patient's occupation and response to treatment. The main reason behind the difference in compliance among persons with occupation seems to be loss of wages and lack of time.

In our study, 64% patients had interrupted treatment by the end of second month and other studies have also reported that maximum number of patients interrupted their treatment by the end of second or third month. Kaona et al reported up to 29.8% patients stopped taking their medication within the first 2 months of commencing treatment. Oliveira et al from Brazil found 43.3% of the defaulters in the first 2 months of treatment.

The present study identified early improvement following medication as the most common reason of default. So, the most common reason was a feeling of early improvement as stated by 45 patients (24.19%). Kaona et al also found that 29.8% of TB patients interrupted treatment once they start feeling better. In another survey by Tissera at Colombo Chest Clinic, relief from symptoms emerged as the most common reason for treatment interruption (13%).

The next most common reason for default was high cost of treatment cited by 30 (16.12%) patients in our study. This was exclusively reported by patients who took ATT from outside the government sources, i.e., purchased their medicine from the market. It is thus necessary that all TB patients should be registered under DOTS for treatment, so as to reduce the number of interruption occurring due to high cost of treatment.

Third common reason for default was ATT-induced side effects, in the present study, stated by 21 (11.29%) patients. Wares et al found the most common reason for stopping treatment being the adverse effects of ATT. A study from Bihar and West Bengal reported that improvement in symptoms (40% and 56%), intolerance to drugs (20% and 9%) and other illness causes in some patients. O'Boyle et al have also reported similar finding.

In the present study, 20 (10.75%) patients blamed alcoholism as the reason for their treatment interruption and 35 (16.27%) patients who smoked defaulted. Jakubowiak et al found alcohol use among the commonest reasons (30%) for treatment default. Sophia et al stated in their study that alcoholism can also predict poor treatment adherence.

Sixteen (8.6%) patients stopped treatment due to no improvement and 12 (6.45%) patients defaulted because they were unaware about long duration of treatment. Mittal et al have found similar finding.

Eleven (5.91%) patients had defaulted treatment due to long distance of travel to their DOTS center and 5.37% patients interrupted treatment due to personal reasons. In a study by Chatterjee et al, an important reason for default was distance from the treatment center. Mishra et al reported that the risk of nonadherence to treatment was significantly associated with cost of travel to the TB treatment facility.

CONCLUSION

There were many reasons reported for discontinuation of treatment and maximum interruption was found in the end of second and third month. The default could be a result of inadequate pre-treatment health education and counseling and poor defaulter tracing mechanism resulting from overworked healthcare personnel, feeling better after medication for a while and socioeconomic factors, including inadequate food and opportunity costs. Multiple factors influence default.

Keeping in mind all the important reasons of default, initial counseling by the health personnel explaining the

treatment plan before starting of the treatment, periodic motivation of patient, increased number of DOTS centers and prompt action to tackle any problem will enhance compliance. Adequate health education and information about TB has been demonstrated to be most effective when given as one to one counseling. Such measures are likely to increase the therapeutic success rate, impacting on global disease burden attributable to TB and thus MDR-TB can be decreased.

SUGGESTED READING

1. World Health Organization. Tuberculosis control in the South-East Asia region, Annual Report. 2014. Available from: https://reliefweb.int/sites/reliefweb.int/files/resources/annual_tb_report_2014.pdf.
2. RNTCP Annual Status Report TB India, 2014.
3. World Health Organization. The origin of DOTS. Research for action: Understanding and controlling tuberculosis in India. WHO, 2000.
4. Coghlan A. Totally drug-resistant TB at large in India. New Scientist Health. January 12, 2012.
5. Chandrasekaran V, Gopi PG, Subramani R, Thomas A, Jaggarajamma K, Narayanan PR. Default during the intensive phase of treatment under DOTS programme. Indian J Tuberc. 2005;52:197-202.
6. Kumar M, Singh JV, Srivastava AK, Verma SK. Factors affecting the non-compliance in directly observed short course chemotherapy in Lucknow District. Indian J Community Med. 2002;27(3):114-7.
7. Jaggarajamma K, Sudha G, Chandrasekaran V, Nirupa C, Thomas A, Santha T, et al. Reasons for non-compliance among patients treated under Revised National Tuberculosis Control Programme (RNTCP), Tiruvallur district, south India. Indian J Tuberc. 2007;54(3):130-5.
8. Mittal C, Gupta S. Noncompliance to DOTS: How it can be decreased. Indian J Community Med. 2011;36(1):27-30.
9. Kaona FA, Tuba M, Siziya S, Sikaona L. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. BMC Public Health. 2004;4:68.
10. Oliveira VL, da Cunha AJ, Alves R. Tuberculosis treatment default among Brazilian children. Int J Tuberc Lung Dis. 2006;10(8):864-9.
11. Tissera WAA. Non-compliance with anti-tuberculosis treatment at Colombo Chest Clinic. NTI Bulletin. 2003;39(1&2):5-9.
12. Wares DF, Singh S, Acharya AK, Dangi R. Non-adherence to tuberculosis treatment in the eastern Tarai of Nepal. Int J Tuberc Lung Dis. 2003;7(4):327-35.
13. Chatterjee P, Benerjee B, Dutt D, Pati RR, Mullick A. A comparative evaluation of factors and reasons for defaulting in tuberculosis treatment in the states of West Bengal, Jharkhand and Arunachal Pradesh. Indian J Tuberc. 2003;50:17-21.
14. O'Boyle SJ, Power JJ, Ibrahim MY, Watson JP. Factors affecting patient compliance with anti-tuberculosis chemotherapy using the directly observed treatment, short-course strategy (DOTS). Int J Tuberc Lung Dis. 2002;6(4):307-12.
15. Jakubowiak WM, Bogorodskaya EM, Borisov SE, Danilova ID, Lomakina OB, Kourbatova EV. Social support and incentives programme for patients with tuberculosis: experience from the Russian Federation. Int J Tuberc Lung Dis. 2007;11(11):1210-5.
16. Sophia V, Balasangameswara VH, Jagannatha PS, Saroj VN, Kumar P. Defaults among tuberculosis patients treated under DOTS in Bangalore city: A research for solution. Indian J Tuberc. 2003;50:185-95.
17. Mishra P, Hansen EH, Sabroe S, Kafle KK. Adherence is associated with quality of professional-patient interaction in Directly Observed Treatment Short-course, DOTS. Patient Educ Couns 2006;63(1-2):29-37.

■■■■

CDC Director Urges People to Wear Masks and Observe Distancing Irrespective of What States Decide

The director of the US CDC hoped that people will decide to do what is right when it comes to distancing and wearing masks, even in states that move to remove restrictions against the CDC's recommendations.

Dr Rochelle Walensky, during a White House COVID-19 Response Team briefing, said that the CDC has been clear that this is not the time to release restrictions. Her comments came after governors of Texas and Mississippi announced that they were lifting mask mandates and were going to allow businesses to open at full capacity. President Joe Biden also condemned states lifting COVID restrictions, calling it a big mistake and stated that masks make a difference… (*CNN*)

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Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

ALBI and Child-Pugh Score in Predicting Mortality in Chronic Liver Disease Patients Secondary to Alcohol: A Retrospective Comparative Study

NAGARAJA BS*, MADHUMATHI R*, SANJEET SB†

ABSTRACT

Background/Aims: The severity of liver dysfunction in chronic liver disease (CLD) is often estimated with Child-Pugh (CTP) classification or model for end-stage liver disease (MELD) score. The albumin-to-bilirubin (ALBI) score is a new model for assessing the severity of liver dysfunction, which is simple and more objective. In the present study, we aimed to retrospectively compare the performance of ALBI score with Child-Pugh score for predicting the mortality in patients with CLD. **Material and methods:** Data of patients with CLD, irrespective of etiology, were retrospectively reviewed. Child-Pugh score and ALBI score were calculated for the patients and results from receiver operating characteristic (ROC) curves were analyzed. **Results:** The study was conducted on 299 patients of CLD; age distribution was between 20 and 85 years with mean age of patients being 45.7 ± 10.94 years, sex ratio male: female 265:34 with mortality rate of 19.73%. The area under the curve (AUC) of ROC of ALBI and Child-Pugh were 0.586 and 0.549, respectively. **Conclusion:** Ability of ALBI score for predicting mortality was comparable with that of Child-Pugh score but Child-Pugh score of >10 had better performance of predicting mortality as compared to ALBI score.

Keywords: Chronic liver disease, liver cirrhosis, alcoholic liver disease, Child-Pugh score, MELD score, ALBI score

The World Health Organization (WHO) estimates 2 billion people as consuming alcohol and 76.3 million as having alcohol use disorders. Thirty percent of Indian adults use alcohol, among which 4-13% are daily consumers. The alcohol consumption rose by 30% in 2015. An estimate of 14 million has been made as heavy consumers. Looking at this data, the burden of alcoholic liver disease on the community is obvious. Alcohol abuse leads to a spectrum of liver diseases, ranging from fatty liver, alcoholic hepatitis to cirrhosis and hepatocellular carcinoma. Liver cirrhosis is a common cause of death worldwide.[1,2] The accurate prognostification of liver cirrhosis is important in our daily practice. The most commonly used tool to predict the prognosis of liver cirrhosis is Child-Pugh score.[3] However, it has been established for a long time, and its components are selected primarily based on the surgeons' experiences. Model for end-stage liver disease (MELD) score is another tool for prognostic assessment of liver cirrhosis.[4,5] Until now, there is a lot of controversy regarding the comparison of Child-Pugh versus MELD scores.[6-8] Of late, albumin-to-bilirubin (ALBI) score has been proposed as a novel, simple and readily available model calculated using mathematical formula $-0.085 \times (\text{alb g/L}) + 0.66 \times \log (\text{bil } \mu\text{mol/L})$.

The ALBI score, by combining serum albumin and bilirubin, is a new model for assessing the severity of liver dysfunction. Johnson and colleagues reported that the ALBI score more accurately predicts patients' mortality without requiring subjective determinants of liver failure, including ascites and encephalopathy, in patients with hepatocellular carcinoma.[9]

A retrospective study also investigated the prognostic significance of the ALBI score among patients with primary biliary cirrhosis.[10] It was found that the ALBI score seems to outperform other scores (such as Child-Pugh and MELD score) for predicting the occurrence of hepatic events in such patients. Furthermore, Chen et al[11] demonstrated that ALBI score had a significantly better performance for long-term survival prediction in patients with hepatitis B virus (HBV)-related cirrhosis than the Child-Pugh or MELD

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scores. Herein, we attempted to study the ALBI score for in-hospital death in alcoholic cirrhosis patients.

AIMS AND OBJECTIVES

- To calculate ALBI and Child-Pugh score in chronic liver disease (CLD) patients secondary to alcohol.
- To assess the utility of ALBI in predicting the mortality in CLD patients secondary to alcohol.
- To evaluate the discriminative abilities of ALBI and Child-Pugh score in predicting the in-hospital mortality in CLD patients secondary to alcohol.

MATERIAL AND METHODS

Study Design

The study was conducted at Bowring and Lady Curzon Hospital (Attached to Bangalore Medical College and Research Institute). Cirrhotic patients secondary to alcohol admitted in the hospital between January 2017 and December 2017 were retrospectively reviewed and the data of the patients were collected. Approval was obtained from the Institutional Ethical Committee.

Inclusion Criteria

- Age >18 years.
- Liver cirrhosis patients secondary to alcohol.

Exclusion Criteria

- CLD due to HBV, hepatitis C virus (HCV), malignancy, metabolic causes and autoimmune hepatitis.

Method of Collection of Data

Detailed history and clinical examination was done for all patients. Routine investigations like complete hemogram, renal function test, liver function test, serum electrolytes, human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), HCV, prothrombin time/International Normalized Ratio (PT/INR), activated partial thromboplastin time (APTT), ultrasonography (USG) abdomen and other relevant investigations were noted. Diagnosis of liver cirrhosis was established by USG abdomen with shrunken liver with altered echo texture.

ALBI score and Child-Pugh score (Table 1) were calculated and compared.

ALBI score = $(-0.085 \times [\text{alb g/L}] + 0.66 \times \log [\text{bil } \mu\text{mol/L}])$

Table 1. Calculation and Comparison of ALBI and Child-Pugh Score

Parameter	Numerical score		
	1	2	3
Ascites	None	Slight	Moderate-to-severe
Encephalopathy	None	Slight-to-moderate	Moderate-to-severe
Bilirubin (mg/dL)	<2.0	2-3	>3.0
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
Prothrombin time (Prolonged in seconds)	1-3 s	4-6 s	>6.0

Child-Pugh Class A = 5-6 points; Child-Pugh Class B = 7-9 points; Child-Pugh Class C = 10-15 points.

Method of Statistical Analysis

All statistical analyses were performed using Medcalc software. Continuous data were expressed as the mean ± SD (standard deviation) and median with minimum and maximum. Categorical data were expressed as the frequency. The receiver operating characteristic (ROC) curve were performed to identify the discriminative ability of ALBI and Child-Pugh score in predicting in-hospital mortality. The area under the curve (AUC) were calculated and compared. The best cut-off value was selected as the sum of sensitivity and specificity was maximal. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) were reported.

RESULTS AND ANALYSIS

The sample size in our study was 299 patients. The age distribution was between 20 and 85 years with mean age of patients being 45.7 ± 10.94 years. Two hundred sixty-five were males and 34 were females. Among 299 patients, 59 patients had in-hospital mortality and 240 were discharged with mortality percentage of 19.73%.

Comparison of In-Hospital Mortality with ALBI and Child-Pugh Scores

The in-hospital morality was 19.73%. The AUC of the ALBI score for predicting the in-hospital mortality was 0.586 (confidence interval [CI]: 95%; 0.528-0.642). The best cut-off value was –1.01, with sensitivity of 94.92%, a specificity of 32.5%, PLR of 1.406 and NLR 0.156 (Fig. 1).

The AUC of the Child-Pugh score for predicting the in-hospital mortality was 0.549 (CI 95%; 0.490-0.606). The best cut-off value of the Child-Pugh score was 10, with a sensitivity of 76.27%, a specificity of 34.58%, PLR of 1.165 and NLR of 0.686 (Fig. 2).

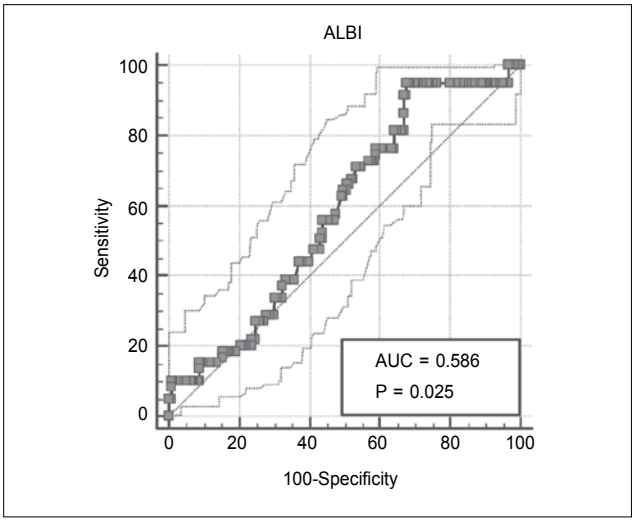


Figure 1. ROC curve of ALBI score for predicting in-hospital mortality.

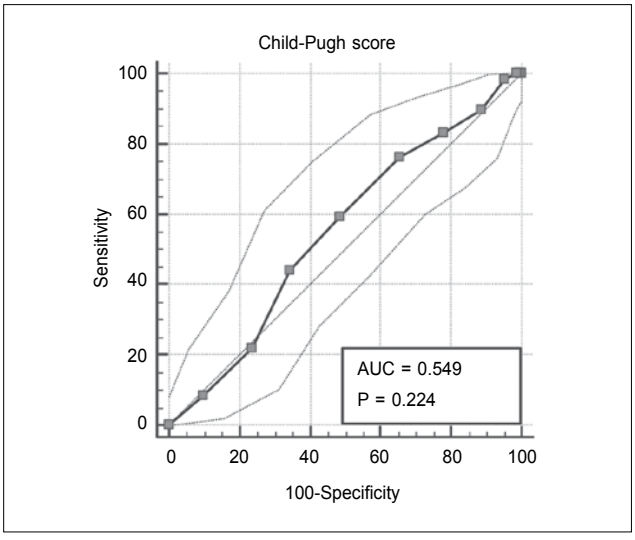


Figure 2. ROC curve of Child-Pugh score for predicting in-hospital mortality.

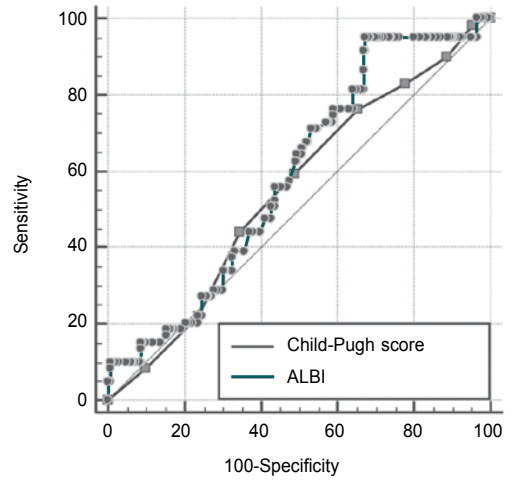
The AUC for predicting the in-hospital mortality was not significantly different between the Child-Pugh and ALBI scores. (Child-Pugh and ALBI: p = 0.4461) (Fig. 3).

The performance of Child-Pugh score is higher than ALBI score.

DISCUSSION

Child-Pugh score and MELD score have been studied extensively for their prognostic abilities and have shown good performance in predicting the mortality of cirrhotic patients. But, the cumbersome calculation of scores and the variables included in them have subjective variability that has led to the development of ALBI score.

Variable	AUC	SE	95% CI
Child-Pugh score	0.549	0.0401	0.490-0.606
ALBI	0.586	0.0382	0.528-0.642



Child-Pugh score ~ ALBI	
Difference between areas	0.0370
SE	0.0486
95% CI	–0.0582 to 0.132
Z statistic	0.762
Significance level	P = 0.4461

Figure 3. Comparison of ROC curves.

ALBI score involves only two variables and has already been studied in various liver disorders such as HBV, hepatocellular carcinoma, primary biliary cirrhosis and has shown to perform well and is comparable with the Child-Pugh and MELD scores. In our study, an attempt has been made to compare the discriminative ability of ALBI score with that of the Child-Pugh score in predicting the in-hospital mortality in alcoholic cirrhosis patients. ALBI score showed better performance compared to Child-Pugh score in predicting mortality, but there was no statistical difference between them.

In a study by Shao et al, ALBI score demonstrated similar ability as that of Child-Pugh and MELD score in predicting in-hospital mortality in cirrhosis. It also suggested that ALBI score can be readily used as prognostic model.[3]

Another study by Chen et al showed that the ALBI score determined on admission indicates the likelihood of survival of acute-on-chronic liver failure patients.[12]

In a study conducted by Zou et al, in patients with alcohol-related liver cirrhosis, ALBI score had the largest AUC, followed by the Child-Pugh and MELD scores, so they concluded that ALBI score has moderate-to-high prognostic performance.[13]

A study conducted by Peng et al showed that there was no significant difference among the three scores in predicting in-hospital mortality in cirrhotic patients.[14]

A retrospective study done by Xavier et al on 111 patients between January 2011 and November 2015, came out with the conclusion that ALBI score is particularly useful in the evaluation of short-term outcomes, with a better performance than the most commonly used scores.[15]

The limitations of our study were that it was a retrospective study, the late mortality was not considered and follow-up was not done.

CONCLUSION

AUC of the ALBI score and the Child-Pugh score were comparable and there was no statistical difference between them. ALBI can be used in place of Child-Pugh score in peripheral centers to assess the prognosis of CLD patients secondary to alcohol in view of simple calculation, only two variables and no subjective variation of the score.

REFERENCES

1. Blachier M, Leleu H, Peck-Radosavljevic M, Valla DC, Roudot-Thoraval F. The burden of liver disease in Europe: a review of available epidemiological data. J Hepatol. 2013;58(3):593-608.
2. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2095-128.
3. Shao L, Han B, An S, Ma J, Guo X, Romeiro FG, et al. Albumin-to-bilirubin score for assessing the in-hospital death in cirrhosis. Transl Gastroenterol Hepatol. 2017;2:88.
4. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, et al. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001;33(2):464-70.
5. Kamath PS, Kim WR; Advanced Liver Disease Study Group. The model for end-stage liver disease (MELD). Hepatology. 2007;45(3):797-805.
6. Gheorghe L, Iacob S, Simionov I, Vadan R, Gheorghe C, Iacob R, et al. Natural history of compensated viral B and D cirrhosis. Rom J Gastroenterol. 2005; 14(4):329-35.
7. Cholongitas E, Marelli L, Shusang V, Senzolo M, Rolles K, Patch D, et al. A systematic review of the performance of the model for end-stage liver disease (MELD) in the setting of liver transplantation. Liver Transpl. 2006;12(7):1049-61.
8. Peng Y, Qi X, Dai J, Li H, Guo X. Child-Pugh versus MELD score for predicting the in-hospital mortality of acute upper gastrointestinal bleeding in liver cirrhosis. Int J Clin Exp Med. 2015;8(1):751-7.
9. Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. J Clin Oncol. 2015;33(6):550-8.
10. Chan AW, Chan RC, Wong GL, Wong VW, Choi PC, Chan HL, et al. New simple prognostic score for primary biliary cirrhosis: Albumin-bilirubin score. J Gastroenterol Hepatol. 2015;30(9):1391-6.
11. Chen RC, Cai YJ, Wu JM, Wang XD, Song M, Wang YQ, et al. Usefulness of albumin-bilirubin grade for evaluation of long-term prognosis for hepatitis B-related cirrhosis. J Viral Hepat. 2017; 24(3):238-45.
12. Chen B, Lin S. Albumin-bilirubin (ALBI) score at admission predicts possible outcomes in patients with acute-on-chronic liver failure. Medicine (Baltimore). 2017;96(24):e7142.
13. Zou D, Qi X, Zhu C, Ning Z, Hou F, Zhao J, et al. Albumin-bilirubin score for predicting the in-hospital mortality of acute upper gastrointestinal bleeding in liver cirrhosis: A retrospective study. Turk J Gastroenterol. 2016;27(2):180-6.
14. Peng Y, Qi X, Tang S, Deng H, Li J, Ning Z, et al. Child-Pugh, MELD, and ALBI scores for predicting the in-hospital mortality in cirrhotic patients with acute-on-chronic liver failure. Expert Rev Gastroenterol Hepatol. 2016;10(8):971-80.
15. Xavier SA, Vilas-Boas R, Boal Carvalho P, Magalhães JT, Marinho CM, Cotter JBXavier SA, et al. Assessment of prognostic performance of Albumin-Bilirubin, Child-Pugh, and Model for End-stage Liver Disease scores in patients with liver cirrhosis complicated with acute upper gastrointestinal bleeding. Eur J Gastroenterol Hepatol. 2018;30(6):652-8.

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Comparative Study of Clinical Efficacy and Safety of Intravenous Iron Sucrose and Ferric Carboxymaltose in Treatment of Postpartum Iron Deficiency Anemia

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ABSTRACT

Background: Anemia, specifically iron deficiency anemia, is a major cause of postpartum morbidities. Oral iron is the most preferred treatment of iron deficiency. But its side effects require other modalities, including intravenous supplementation. Ferric carboxymaltose (FCM) is one such newer regime. The present study was conducted to compare clinical efficacy and safety of FCM with iron sucrose and oral ferrous sulfate. **Methods:** A prospective randomized controlled trial was conducted from December 2018 to May 2019 with 90 postpartum patients giving consent and satisfying inclusion criteria. The patients were divided into three groups to compare the clinical efficacy and safety of FCM with iron sucrose and oral iron. All the data was entered in MS-Excel and statistical analysis was done on SPSS 17.0. Student *t*-test was used to compare mean rise in hemoglobin of the patients in different groups. **Results:** Patients treated with FCM showed statistically significant highest rise in mean hemoglobin, followed by iron sucrose group, while oral iron group showed lowest rise. Maternal complications in FCM group were significantly lower as compared to other groups ($p < 0.0001$). Iron sucrose group patients also reported significantly less maternal complications as compared to oral iron supplementation. **Conclusion:** Intravenous FCM was found to be an effective treatment option for patients with iron deficiency anemia during postpartum period. It was also reported as the safest method when compared with intravenous ferrous sucrose and oral ferrous sulfate.

Keywords: Iron deficiency, postpartum, ferric carboxymaltose, ferrous sucrose, ferrous sulfate

Anemia (hemoglobin <12 g/dL in adult females and <11 g/dL in pregnancy) is considered to be a major cause of morbidity and mortality around the globe, specifically in the developing countries. During postpartum period, hemoglobin concentration <10 g/dL is considered as anemic. Major causes which may lead to postpartum anemia may include iron deficiency, hemodilution, anemia during pregnancy, antepartum and postpartum hemorrhages (PPH), etc.

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Iron deficiency may result either from inadequate dietary intake, diseases like malaria, excessive blood loss during childbirth, parasitic infection and flaring up of physiological anemia of pregnancy, among other causes. Many maternal morbidities are observed to be associated with postpartum anemia. A few to mention are lethargy, tiredness, headaches, dizziness, postpartum depression, lactation failure and mortality. These problems are aggravated in prevailing conditions, as seen in our country.

Iron supplementation is the mainstay of treatment for iron deficiency anemia. Anemia occurring because of heavy blood loss during childbirth may easily be reversed with iron replenishment. Oral iron therapy is the most preferred and an easy mode of treatment because of its safety, effectiveness and low cost. But this is associated with certain side effects, including nausea, gastritis, vomiting, constipation, etc., which affects compliance of patients towards treatment. Parenteral iron therapy (intravenous iron replenishment) is increasingly

recommended in cases where such side effects are observed. The older intravenous iron containing preparations like iron dextran have been found to be associated with episodes of anaphylaxis in 1-2% of the patients as reported by some authors. Iron sucrose and iron gluconate are free from any such reaction as they don't have dextran moiety. But their physical character and administration rate limit their use.

Ferric carboxymaltose (FCM), which is a type I polynuclear iron (III)-hydroxide carbohydrate complex, has shown promising results among patients of iron deficiency anemia. It delivers complexed iron slowly but in controlled manner to the endogenous binding sites. Few randomized controlled trials have also proved the efficacy of FCM in improving hemoglobin status among postpartum patients with anemia, as compared to their oral counterparts.

Owing to the scarcity of such studies among north Indian population of the country, a study was carried out with the objective to compare clinical efficacy and safety of intravenous FCM and iron sucrose for treatment of postpartum iron deficiency anemia.

MATERIAL AND METHODS

A prospective randomized controlled trial was conducted at Dept. of Obstetrics and Gynecology, ESIC Model Hospital & PGIMSR, Basaidarapur, New Delhi, from December 2018 to May 2019. All the women less than 10 days after delivery with hemoglobin between ≥6 g/dL and ≤9 g/dL requiring iron supplementation, and consenting to participate, were enrolled in the study. Patients having significant vaginal bleeding in past 24 hours, having asthma, bleeding disorders, any cardiac disease, received intravenous iron treatment or red blood cells transfusion and received erythropoietin within 3 months prior to the study were excluded from the study.

Sample Size Calculations

A total of 90 participants were enrolled in the study. They were divided into three groups. Each group had 30 participants and were randomized using random number generator.

Detailed history and clinical examination of all the patients was done. Diagnosis of anemia was confirmed on peripheral blood smear and related pathological investigations. All patients were dewormed. Group A patients were given intravenous FCM 1,000 mg single dose (carboxymaltose 1,000 mg diluted in 100 mL of 0.9% normal saline given in 20-30 minutes).

Group B received iron sucrose therapy in multiple doses; 200 mg/day on Day 0, 2, 4, 6, 8; total of 1,000 mg (iron sucrose 200 mg diluted in 100 mL of 0.9% normal saline and given over 20-30 minutes). Group C patients acted as control group and were given oral iron supplementation. In all groups, Hb% was done on 0 and Day 30 of last dose of parenteral/oral iron. Side effects like headache, myalgia, arthralgia, nausea, vomiting, epigastric discomfort and anaphylactoid reactions were assessed and managed accordingly. Patients were called after 1 month for follow-up and investigations were repeated.

Rise in hemoglobin was considered primary outcome measure while complications like headache, myalgia, arthralgia, nausea, vomiting, epigastric discomfort and anaphylactoid reactions were considered as secondary outcome.

Ethical Statement and Statistical Comments

Patients were informed in detail about the study and its benefits. Written consent was taken. They were free to withdraw at any stage of the study. The study protocol was approved from Institutional Ethics Committee (IEC) of ESI-PGIMSR, Basaidarapur, New Delhi.

All the data was entered in MS-Excel and statistical analysis was done on SPSS 17.0. Student *t*-test was used to compare mean rise in hemoglobin of the patients of different groups.

RESULTS

A total of 90 patients were enrolled in the study with 30 patients in each of the three groups as described earlier (FCM group [A], ferrous sucrose group [B] and ferrous sulfate group [C], out of which ferrous sulfate group acted as our control group). In this prospective study, we compared clinical efficacy and safety of intravenous FCM and iron sucrose for treatment of postpartum iron deficiency anemia. There was no lost to follow-up of patients in any of the groups.

Majority of patients belonged to age group of 20-30 years in all the three groups. Age distribution was comparable among the three groups, and no significant difference was present ($p > 0.05$). The mean age of the patients in Group A was 25.17 ± 4.01 years; in Group B was 25.38 ± 3.07 years and in Group C was 25.31 ± 4.06 years. The mean age of marriage in Group A was 21.13 ± 2.3 years, in Group B was 21.20 ± 2.5 years while in Group C it was 21.67 ± 1.9 years, and was comparable in the three groups. Majority of patients had parity of one in all the groups and was

comparable in the three groups. Majority of patients in all the groups had period of gestation in between 37 and 42 weeks at the time of delivery and there was no significant difference in relation to period of gestation among the three groups ($p > 0.05$). About one-third of patients had completed secondary school in all the three groups. Majority of patients belonged to middle class and there was no significant difference in relation to socioeconomic classes among the three groups ($p > 0.05$).

When study participants were assessed for modes of delivery, it was observed that majority (56.7% and 53.3%) of participants in Group A and B had normal vaginal delivery while Group C saw majority of participants with cesarean section as a mode of delivery (Table 1).

Only 6.7% of Group A patients had history of PPH, while in Group B it was 10% and in control group it was 3.3% only. The history of any medical or surgical illness in Group A was comparable to Group B ($p > 0.05$) and both the study groups had comparable comorbid conditions with the control Group C ($p > 0.05$).

Table 2 and Figure 1 shows that mean hemoglobin rise at zero day and at 30th day was highest in Group A followed by Group B and was lowest in Group C. This difference was statistically significant when compared among all the three groups ($p < 0.001$) as well as when groups were compared with each other.

Table 3 and Figure 2 shows that the maternal complications in Group A were significantly lower as compared to Group B and Group C ($p < 0.001$).

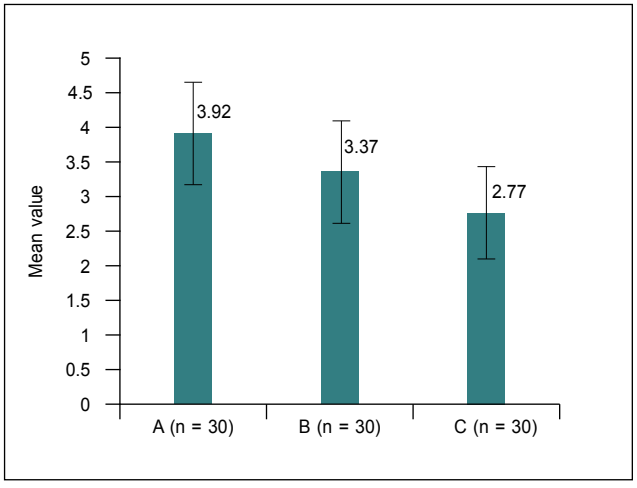

Figure 1. Comparison of mean hemoglobin rise among three groups.

Table 1. Distribution of Study Participants of Various Groups According to Mode of Delivery (n = 30 in Each Group)

Groups of patients	Mode of delivery			P value
	Vaginal delivery	Cesarean section	Total	
Group A	17 (56.7%)	13 (43.3%)	30 (100%)	0.732*
Group B	16 (53.3%)	14 (46.7%)	30 (100%)	
Group C	14 (46.7%)	16 (53.3%)	30 (100%)	

*Chi-square test.

Table 2. Comparison of Mean Hemoglobin Rise among the Groups

	Groups			P value	A vs. B	A vs. C	B vs. C
	A (n = 30)	B (n = 30)	C (n = 30)				
Mean hemoglobin rise (± SD)	3.92 ± 0.81	3.37 ± 0.87	2.77 ± 0.6	0.001	0.015	0.001	0.003

Table 3. Comparison of Maternal Complications among the Groups

Maternal complication	Groups			Total (n = 90)	P value	A vs. B	A vs. C	B vs. C
	A (n = 30)	B (n = 30)	C (n = 30)					
Yes	3 (10%)	10 (33.3%)	14 (46.6%)	27 (30.0%)	<0.007	<0.028	<0.001	<0.291
No	27 (90%)	20 (66.6%)	16 (53.3%)	63 (70.0%)				
Total	**30 (100%)**	**30 (100%)**	**30 (100%)**	**90 (100%)**				

Group B had lower maternal complication as compared to Group C but this difference was not statistically significant ($p > 0.05$).

Table 4 gives details of various complications experienced by participants of different groups. Headache was reported by 02 (6.6%) of them in Group A. Joint pain and tingling sensation was the most common complication reported by 08 (26.6%) participants of Group B and transient hypotonia (46.7%) and nausea and heartburn (40%) were among common complications experienced by participants of Group C.

DISCUSSION

A randomized controlled trial was conducted with a total of 90 patients (30 patients in each of three groups). In this study, we compared clinical efficacy and safety of intravenous FCM and iron sucrose for managing iron deficiency anemia during postpartum period.

When age groups of patients were assessed, it was observed that majority (72.2%) of patients belonged to age group 20-30 years and the mean age of the patients receiving FCM was 25.17 ± 4.01 years; those treated with ferrous sucrose was 25.38 ± 3.07 years and 25.31 ± 4.06 years for patients given ferrous sulfate. Similar results were reported by Rathod et al in their study in 2015 with mean age as 25.9 ± 3.57, 26.0 ± 3.66 and 25.4 ± 3.05, respectively, in the three groups. Shim et al, in their study in 2018, reported different mean age as 34.5 ± 4.8 years in the FCM group patients and 33.4 ± 4.9 in ferrous sulfate patients, in one group of their study population.

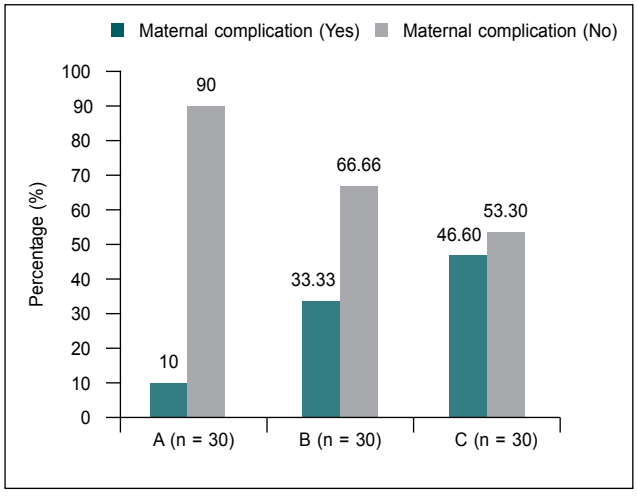

Figure 2. Comparison of maternal complications among three groups.

When period of gestation was assessed, majority of patients in all the three groups had it in between 37 and 42 weeks but no significant difference in relation to period of gestation among three groups was found ($p > 0.05$). Shim et al, in their study, reported differently with majority of the patients having gestational age 20-33 weeks across all study groups.

When study participants were assessed for modes of delivery, it was observed that majority (56.7% and 53.3%) of patients receiving FCM and iron sucrose, respectively, had normal vaginal delivery while the group receiving oral iron saw majority of participants with cesarean section as a mode of delivery. For FCM and iron sucrose group, similar results were reported by Rathod et al, but their results were different for patients receiving oral iron as there also majority of them had normal vaginal delivery.

Only 6.7% of Group A patients had history of PPH, in Group B it was 10% while in control group it was 3.3% only. These results are similar to the study by Khandale et al (2015) reporting 5.78% of the total patients reporting PPH and differed from the study conducted by Rathod el al in 2015, where PPH was reported among 24%, 21% and 27% of the patients of FCM, ferrous sucrose and ferrous sulfate groups, respectively.

Mean hemoglobin rise from baseline at 30th day of follow-up was highest in FCM group followed by patients receiving ferrous sucrose and patients having oral ferrous sulfate had lowest rise in mean hemoglobin. This difference of mean rise of hemoglobin among three groups was statistically significant ($p < 0.001$). Seid et al also reported in their study in 2017 significantly

Table 4. Distribution of Study Participants According to Complications Experienced by Them

Groups of patients	Complications*				
	Nausea and heartburn	Joint pain and tingling sensation	Headache	Constipation	Transient hypotonia
Group A	00	01 (3.3%)	02 (6.6%)	00	00
Group B	00	08 (26.6%)	00	00	03 (10%)
Group C	12 (40%)	00	00	06 (20%)	14 (46.7%)

*Multiple responses by single patient.

greater rise in mean hemoglobin levels among patients receiving FCM ($p < 0.001$), as also Rathod et al, in their study, who observed significantly highest rise in mean hemoglobin level at 2 and 6 weeks of follow-up ($p < 0.001$) in patients receiving FCM.

Maternal complications in patients receiving FCM were significantly lower as compared to ferrous sucrose and oral ferrous sulfate groups ($p < 0.0001$). Headache was reported by 6.6% of the patients in Group A. Joint pain and tingling sensation was the most common complication reported by 26.6% participants of Group B and transient hypotonia (46.7%) and nausea and heartburn (40%) were among common complications experienced by participants of Group C. Similar results were reported by Shim et al in their study in 2018, where FCM group had less adverse events as compared to ferrous sulfate group patients.

Patients receiving ferrous sucrose also had lower maternal complications as compared to those receiving oral ferrous sulfate, though this was not statistically significant ($p > 0.05$). Abhilashini et al in their study in 2014 also reported similar results with oral iron group patients having more side effects.

CONCLUSION

Intravenous FCM given as a 1,000 mg single dose was found to be an effective modality for treatment of postpartum anemia with patients showing significantly highest rise in mean hemoglobin in FCM group as compared to intravenous ferrous sucrose and oral ferrous sulfate (control) groups. Also, FCM was found to be safest across all three treatments with least number of adverse effects.

SUGGESTED READING

1. Jimenez K, Kulnigg-Dabsch S, Gasche C. Management of iron deficiency anemia. Gastroenterol Hepatol (N Y). 2015;11(4):241-50.
2. Kassebaum NJ, Jasrasaria R, Naghavi M, Wulf SK, Johns N, Lozano R, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-24.
3. Yefet E, Suleiman A, Garmi G, Hatokay A, Nachum Z. Evaluation of postpartum anaemia screening to improve anaemia diagnosis and patient care: A prospective non-randomized before-and-after anaemia screening protocol implementation study. Sci Rep. 2019;9(1):7810.
4. El Khouly NI. Comparison of intravenous ferrous sucrose and oral ferrous sulphate in treatment of postpartum iron deficiency anemia. J Matern Fetal Neonatal Med. 2017;30(8):967-71.
5. Froessler B, Collingwood J, Hodyl NA, Dekker G. Intravenous ferric carboxymaltose for anaemia in pregnancy. BMC Pregnancy Childbirth. 2014;14:115.
6. Jain G, Palaria U, Jha SK. Intravenous iron in postpartum anemia. J Obstet Gynecol India. 2013;63(1):45-8.
7. Kalra PA, Bhandari S. Efficacy and safety of iron isomaltoside (Monofer®) in the management of patients with iron deficiency anemia. Int J Nephrol Renovasc Dis. 2016;9:53-64.
8. Breymann C, Gliga F, Bejenariu C, Strizhova N. Comparative efficacy and safety of intravenous ferric carboxymaltose in the treatment of postpartum iron deficiency anemia. Int J Gynecol Obstet. 2008;101: 67–73.
9. Rathod S, Samal SK, Mahapatra PC, Samal S. Ferric carboxymaltose: A revolution in the treatment of postpartum anemia in Indian women. Int J Appl Basic Med Res. 2015;5(1):25-30.
10. Shim JY, Kim MY, Kim YJ, Lee Y, Lee JJ, Jun JK, et al. Efficacy and safety of ferric carboxymaltose versus ferrous sulfate for iron deficiency anemia during pregnancy: subgroup analysis of Korean women. BMC Pregnancy Childbirth. 2018;18(1):349.
11. Khandale SN, Kedar K. Managing postpartum anemia with ferric carboxymaltose at tertiary level hospital: a retrospective study. J Evolut Med Dent Sci. 2015;4(44):7580-6.
12. Seid MH, Butcher AD, Chatwani A. Ferric carboxymaltose as treatment in women with iron-deficiency anemia. Anemia. 2017;2017:9642027.
13. Abhilashini GD, Sagili H, Reddi R. Intravenous iron sucrose and oral iron for the treatment of iron deficiency anaemia in pregnancy. J Clin Diagn Res. 2014;8(5): OC04-OC7.

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Abbott

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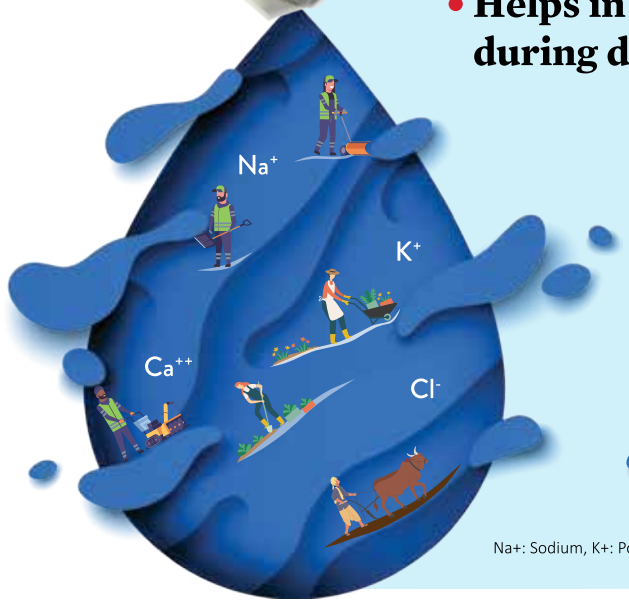

Dosage and Method of Administration%:

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References: 1. Popkin BM, et al. Water, hydration, and health. Nutr Rev. 2010;68(8):439-58. 2. Haemaccel Prescribing Information. 3. Minot AS, et al. Plasma loss in severe dehydration, shock and other conditions as affected by therapy. Ann Surg. 1940;112(4):557-567.

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Posology of Antidiabetic Drugs and Insulins: A Review of Standard Textbooks

GARIMA BHUTANI*, SANJAY KALRA†

ABSTRACT

Objectives: The aim of this bibliographic review is to assess whether standard pharmacology, endocrinology and diabetology textbooks adequately mention the details regarding timings of administration, frequency and dose of various oral and injectable antidiabetic drugs. **Material and methods:** Four standard textbooks of pharmacology, two of diabetology and three of endocrinology were assessed for the published information regarding dose, timing and frequency of antidiabetic drugs. **Results:** Various omissions and contraindications were found in the coverage of glucose-lowering drugs in standard textbooks. Proper timing and frequency of administration of sulfonylureas, thiazolidinediones, SGLT2 inhibitors, GLP receptor agonists and DPP-4 inhibitors have been omitted in majority of the textbooks. **Conclusions:** This article stresses upon the need of a uniform source of information for providing adequate and standardized knowledge regarding timing, frequency and dose of antidiabetic drugs.

Keywords: Posology, antidiabetic drugs, postprandial hyperglycemia

Correct timing of glucose-lowering therapy is an important aspect of diabetes pharmacotherapeutics. Matching the dose of a particular drug with meals depends upon its mechanism of action and pharmacokinetic profile. This timing varies from class-to-class and drug-to-drug. Each drug has a specific time action profile. This should match with food absorption. Inappropriate timing/frequency/dose of administration may lead to unwanted hyperglycemia or hypoglycemia leading onto poor glycemic control or complications in the patients.

This glycemic variability is easily avoidable with the better knowledge and understanding of appropriate dose, timing of administration and frequency of drug administration. Pharmacology, diabetology and endocrinology textbooks are an important and reliable source of such information, both for students and clinicians. This article aims at assessing the adequacy of the knowledge provided by these textbooks regarding posology (i.e., dose, frequency and timing of antidiabetic drugs).

MATERIAL AND METHODS

Some of the most popular and most commonly read textbooks of pharmacology, diabetology and endocrinology were included in the study. Four standard textbooks of pharmacology (2 by Indian authors and 2 by US authors) were analyzed. Two textbooks of diabetology were also studied, out of which 1 textbook is by Indian author and other is by US author. Three textbooks of endocrinology (2 US and 1 Indian in origin) were also assessed for the desired information. Latest available editions of the textbooks were taken for analysis.

RESULTS

The results of the analysis have been tabulated in Table 1, which shows the comparison of information about antidiabetic drugs available in different textbooks.

DISCUSSION

This bibliometric analysis highlights various omissions and contraindications in the coverage of glucose-lowering drugs in standard textbooks.

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Table 1. Comparison of Information in Pharmacology, Endocrinology and Diabetology Textbooks

Drug class	Drug	Goodman and Gilman's the Pharmaceutical Basis of Therapeutics[1]	Basic and Clinical Pharmacology[2]	Essentials of Medical Pharmacology[3]	Principles of Pharmacology[4]	Endocrino-logy[5]	Textbook of Diabetes[6,7]	RSSDI Text book of Diabetes Mellitus[8-10]	Manual of Clinical Endocrino-logy[11]	Williams Textbook of Endocrino-logy[12]
Biguanides	Metformin	0.5-2.5 g b.i.d., with meals	500 mg-2.55 g at bedtime for fasting hyperglycemia and before meals for postprandial hyperglycemia	0.5-2.5 mg, 1-2 doses per day	500 mg before breakfast and 500 mg with evening meal	Start with 500 mg o.d. Titrate up to 500-1,000 g b.i.d., given with meals	500 mg o.d.-2,550 mg (divided doses) with meals or immediately before meals[6]	-	500 mg o.d. to 2,500 mg in divided doses	At least b.i.d.
	Metformin SR	Max dose is 2 g o.d., with meals	-	-`	-	With evening meal	Once-daily in morning or b.i.d. (morning and evening)[6]	-	-	-
Thiazolidine-diones	Pioglitazone	15-45 mg o.d.	15-45 mg o.d.	15-45 mg o.d.	11-45 mg o.d.	15-45 mg daily	15-45 mg/day[6]	-	15-45 mg/ day o.d.	-
	Rosiglitazone	4-8 mg o.d.	2-8 mg o.d. or b.i.d.	-	4-8 mg o.d.	2-8 mg daily	4-8 mg[6]	-	-	-
Meglitinide analog	Repaglinide	0.5-16 mg preprandially	0.25-4 mg, just before each meal (max 16 mg/day)	1-8 mg, 3-4 doses/day, before each major meal	0.25-4 mg shortly before each meal	0.5-2 mg t.i.d. with each meal	0.5-4 mg, 15-30 min before each main meal[6]	0.5-4 mg in 3-4 doses, just before or soon after starting a meal[8]	Preprandial dosing	Max 4 mg with each meal
	Nateglinide	180-360 mg, 1-10 min before a meal	60-120 mg, just before meals	180-480 mg, 3-4 doses per day, 10 min before meal	60-120 mg, shortly before each meal	60-120 mg t.i.d. with each meal	60-180 mg t.d.s., preprandial use[6]	60-180 mg in 3-4 doses, just before or soon after starting a meal[8]	Preprandial dosing	120 mg with each meal
Sulfonylureas	Glipizide	5-40 mg o.d. or b.i.d.	5-30 mg, 30 min before breakfast	5-20 mg, o.d. or b.i.d.	5-20 mg o.d. or b.i.d.	2.5-5 mg initially. Max 40 mg divided b.i.d.	2.5-20 mg[6]	1.25-15 mg in 2-3 doses, 20-30 min before meals[8]	5-40 mg/day	Initial 5 mg, Max 40 mg, divided b.i.d.
	Glipizide extended release	5-20 mg daily	Once-daily morning dose, max 20 mg/day	-	-	2.5-5 mg initially. 20 mg o.d. max dose	Once-daily dose[6]	-	5-20 mg/day	Initial 5 mg. Max 20 mg o.d.
	Gliclazide	-	-	40-240 mg, o.d. or b.i.d.	40-250 mg o.d. or b.i.d.	-	40-320 mg[6]	40-240 mg in 1-3 doses, 20-30 min before meals[8]	-	-

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	Gliclazide MR	-	-	-	-	-	30-120 mg o.d.[6]	-	-	-
	Glyburide (glibenclamide)	1.25-20 mg o.d. or b.i.d.	1.25-20 mg, single morning dose	2.5-15 mg o.d. or b.i.d.	5-15 mg o.d. or b.i.d.	1.25-5 mg initially. Max dose 20 mg, divided b.i.d.	1.25- 15 mg[6]	1.25-20 mg in 1-3 doses/day, 20-30 min before meals[8]	1.25-20 mg/day	Initial dose 2.5 mg. Max dose 20 mg, divided b.i.d.
	Micronized glyburide	0.75-12 mg daily	-	-	-	1.5-3 mg initial dose. Max dose is 6 mg, b.i.d.	-	-	0.75-12 mg/day	Initial 3 mg. Max 6 mg b.i.d.
	Glimepiride	1-8 mg o.d.	1-8 mg o.d.	1-6 mg o.d. or b.i.d.	1-6 mg o.d.	1-2 mg initially. Maximum dose is 8 mg o.d.	1-6 mg[6]	1-8 mg o.d., 20-30 min before meals[8]	1-8 mg/day	1-8 mg o.d.
α-Glucosidase inhibitors	Acarbose	25-100 mg, before meals	25-100 mg, just before ingesting the final portion of each meal	50-100 mg t.d.s., at the beginning of each major meal	50-100 mg t.d.s. at the beginning of each major meal	25-100 mg t.i.d. with first bite of carbohydrate containing meal	50 mg o.d. to 200 mg t.d.s., with meals[6]	25 mg t.d.s. at the start of each main meal to max of 100 mg t.d.s.[9]	-	-
	Voglibose	-	-	200-300 mg t.d.s. just before meals	-	-	With meals[6]	0.2 mg t.d.s., just before each meal - max of 0.3 mg t.d.s.[9]	-	-
	Miglitol	25-100 mg before meals	25-100 mg just before ingesting the final portion of each meal	25-100 mg t.d.s. at the beginning of each major meal	-	25-100 mg t.i.d. with first bite of carbohydrate containing meal	With meals[6]	-	-	-
DPP-4 inhibitors	Vildagliptin	50-100 mg daily	-	50-100 mg o.d. or b.i.d.	50 mg o.d. before meals	-	50 mg b.i.d.[6]	50 mg o.d. or b.i.d., with or without food[10]	50 mg b.i.d.	-
	Linagliptin	-	-	-	-	-	-	-	5 mg/day	-
	Sitagliptin	100 mg daily	100 mg orally o.d.	100 mg o.d.	100 mg o.d. before meals	25-100 mg o.d.	100 mg o.d. in morning[6]	100 mg o.d.[10]	100 mg/day	-
	Saxagliptin	2.5-5 mg daily	2.5-5 mg daily	5 mg o.d.	-	25-100 mg daily	-	5 mg/day[10]	-	-
	Alogliptin	-	-	-	-	-	-	12.5-25 mg[10]	12.5-25 mg/day	-

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GLP receptor agonist	Exenatide	0.01-0.02 mg s/c inj, before meals	5-10 µg s/c b.i.d. inj, within 60 min before a meal	s/c inj	5-10 µg b.i.d., 30-60 min before meals	5-10 µg b.i.d. s/c up to 60 min before main meals	5-10 µg b.i.d. within 60 min of morning and evening meals[7]	-	5-10 µg b.i.d., s/c, 60 min prior to meals	-
	Exenatide QW	-	-	-	-	-	Once weekly[7]	Once weekly[10]	Once weekly	-
	Liraglutide	s/c inj o.d.	Started at 0.6 mg injectable dose	s/c inj once-daily	-	-	-	Once-daily[10]	0.6-1.8 mg/day	-
	Albiglutide	-	-	-	-	-	30 mg weekly[7]	-	-	-
	Dulaglutide	-	-	-	-	-	-	Once weekly[10]	-	-
	Semaglutide	-	-	-	-	-	-	-	Once weekly	-
	Lixisenatide	-	-	-	-	-	-	-	-	-
SGLT2 inhibitor	Dapaglifozin	-	-	o.d.	-	-	-	-	-	-
	Canagliflozin	-	-	-	-	-	-	-	-	-
	Ipragliflozin	-	-	-	-	-	-	-	-	-
Dopamine D2 receptor agonist	Bromocriptine	1.6-4.8 mg, with food in the morning within 2 h of awakening	-	0.8-4.8 mg o.d., early in the morning	-	-	-	1.6-4.8 mg o.d. within 2 h after waking in the morning, with food[9]	-	Within 2 h of rising in the morning
Amylin analog	Pramlintide	15-60 µg s/c inj in type 1 DM, 60-120 µg s/c inj in type 2 DM. Injected prior to meals	15-60 µg s/c inj in type 1 DM, 60-120 µg s/c inj in type 2 DM. Injected immediately before eating	s/c inj before meal	15-60 µg s/c inj before meals as an adjunct to insulin in DM type 1 cases and 60-120 µg s/c inj before meals with insulin in type 2 DM.	60-120 µg t.i.d. (for DM type 2), 15-30 µg (for DM type 1), s/c before meals	60-90 µg, 3-4 times/day s/c prior to meals (type 1 DM). Higher doses s/c b.i.d. in type 2 DM[7]	-	-	15-60 µg before meals in type 1 DM; max 120 µg before meals in type 2 DM
Bile acid binding resin	Colesevelam	3 tab (625 mg) b.i.d. before lunch and dinner or 6 tab prior to largest meal	1,875 mg b.i.d. or 3,750 mg o.d. orally	-	-	-	-	-	-	-

Metformin is covered well by 8 out of 9 textbooks, with 6 of them mentioning relatively concordant doses, and 2 describing only frequency of administration. Timing of administration was reported by 5 books. Metformin SR preparation was listed by only 3 textbooks, both American in origin, though its use is widespread across the world. Pioglitazone usage is covered in 7 textbooks, with similar dosages, but relationship with meal timings is not stated by any author.[6]

Rosiglitazone, which is used in a restricted subset of patients, is covered by 5 texts. But none of the textbooks mention timings of this drug. The omission of this molecule's details from majority of endocrinology and diabetology books reflects the decline in its popularity. Meglitinide analogs are discussed in uniform detail by all 9 textbooks surveyed. This is a pleasant (and perhaps superfluous) exercise, as nateglinide is rarely used in clinical practice and repaglinide is relatively less commonly prescribed than sulfonylureas.

Sulfonylureas are the oldest class of glucose-lowering drugs currently in use. A large number of drugs and preparations are available, and are well-covered by most textbooks. Micronized glyburide, glipizide ER and gliclazide, which are not available in all countries, are discussed by relatively less authors (5 and 4, respectively). While information related to glipizide and glibenclamide is uniform in most books, there is conflicting advice regarding the frequency of dosage of glimepiride. Timing of administration is not mentioned by many authors. A blanket recommendation to prescribe all sulfonylureas 20-30 minutes before meals is given by the leading Indian textbook of diabetes. The maximum dose of glimepiride is mentioned as 6 mg by three, and 8 mg by six authors. This may reflect the difference in maximum doses approved by various regulatory authorities. A similar lack of consensus is seen for gliclazide, where maximum doses vary from 240 to 320 mg and frequency of dosage ranges from 1 to 3 per day.

Alpha-glucosidase inhibitors are discussed in detail by seven (acarbose), four (miglitol) and two (voglibose) authors. Most of the advice contained in these texts is concordant with each other. The dipeptidyl peptidase-4 (DPP-4) inhibitors are relatively newer class of drugs, which may explain why their dose is not mentioned in many texts. The timing of administration; however, is written differently in various books. While some authors omit this aspect of posology, others recommend vildagliptin and sitagliptin before meals, and yet others advise no regard to meal times. The glucagon-like peptide-1 (GLP-1) receptor agonists are covered by some, but not all, books. While exenatide's timing of administration is discussed by six authors, no book makes mention of the timing of dosage of liraglutide. New once-weekly GLP-1 receptor agonists are discussed by one (dulaglutide, semaglutide) and three (exenatide QW) textbooks. Bromocriptine and colesevelam are nondiabetic drugs, which have recently been approved for use in type 2 diabetes. They are prescribed infrequently. While four books mention bromocriptine, in a uniform manner, only two US textbook covers colesevelam. This poor coverage reflects the poor availability of this molecule. Another molecule which has limited availability, relevance and usage, is pramlintide. Approved for the management of postprandial hyperglycemia in both type 1 and type 2 diabetes, this is well-described, in a similar manner, by five texts. Sodium glucose co-transporter 2 (SGLT2) inhibitors, which are the latest class of oral glucose-lowering drugs, have found mention in one current US pharmacology textbook.

CONCLUSION

This bibliometric analysis highlights the need to have standardized, uniform sources of information regarding posology of glucose-lowering drugs. Such information will be of importance to students and professionals of diabetology, and will benefit their patients as well.

LIMITATIONS

All textbooks of pharmacology, diabetology and endocrinology were not analyzed for the review. However, the textbooks analyzed here are the most commonly used ones.

REFERENCES

1. Powers AC, D'Alessio D. Endocrine pancreas and pharmacotherapy of diabetes mellitus and hypoglycaemia. In: Brunton LL, Chabner BA, Knollmann BC (Eds.). Goodman and Gilman's the Pharmaceutical Basis of Therapeutics. 12th Edition, New York: Tata McGraw Hill; 2011. pp. 1237-74.
2. Nolte MS. Pancreatic hormones and anti diabetic drugs. In: Katzung BG, Masters SB, Trevor AJ (Eds.). Basic and Clinical Pharmacology. 12th Edition, New York: Tata McGraw Hill; 2012. pp. 743-68.
3. Tripathi KD. Insulin, oral hypoglycaemic drugs and glucagon. In: Essentials of Medical Pharmacology. 7th Edition, New Delhi: Jaypee Brothers Medical Publishers; 2013. pp. 258-81.
4. Sharma HL, Sharma KK. Insulin and other anti diabetic drugs. In: Principles of Pharmacology. 2nd Edition, Hyderabad: Paras Medical Publisher; 2010. pp. 626-41.

5. Buse GB, Dungan KM. Management of type 2 diabetes mellitus. In: De Groot LJ, Jameson JL (Eds.). Endocrinology: Adult and Pediatric. 6th Edition, Philadelphia: Elsevier Saunders; 2010. pp. 897-915.
6. Bailey CJ, Krentz AJ. Oral antidiabetic agents. In: Holt RI, Cockram CS, Flyvbjerg A, Goldstein BJ (Eds.). Textbook of Diabetes. 4th Edition, Malden: Wiley-Blackwell; 2010. pp. 452-77.
7. Holst JJ, Madsbad S, Schmitz O. Non-insulin parenteral therapies. In: Holt RI, Cockram CS, Flyvbjerg A, Goldstein BJ (Eds.). Textbook of Diabetes. 4th Edition, Malden: Wiley-Blackwell; 2010. pp. 478-93.
8. Sahay RK. Insulin secretagogues. In: Chandalia HB (Eds.). RSSDI Textbook of Diabetes Mellitus. 3rd Edition, New Delhi: Jaypee Brothers Medical Publishers; 2014. pp. 527-37.
9. Singh J. Nutrient blockers and bromocriptine. In: Chandalia HB (Ed.). RSSDI Textbook of Diabetes Mellitus. 3rd Edition, New Delhi: Jaypee Brothers Medical Publishers; 2014. pp. 560-71.
10. Kumar A. Incretin based therapy. In: Chandalia HB (Ed.). RSSDI Textbook of Diabetes Mellitus. 3rd Edition, New Delhi: Jaypee Brothers Medical Publishers; 2014. pp. 546-59.
11. Bajaj S (Eds.). Manual of Clinical Endocrinology. 2nd Edition. New Delhi: Jaypee Brothers Medical Publishers; 2014. pp. 81-108.
12. Buse JB, Polonsky KS, Burant CF. Type 2 diabetes mellitus. In: Melmed S, Polonsky KS, Larsen PR, Kronenberg HM (Eds.). Williams Textbook of Endocrinology. 12th Edition, Philadelphia: Elsevier Saunders; 2011. pp. 1371-435.

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Some Type 2 Diabetes Patients have Major ECG Abnormalities

Investigators noted major ECG abnormalities in 13% of over 8,000 unselected patients with type 2 diabetes in a community-based Dutch cohort. There was a 9% prevalence of major abnormality in the subgroup of these patients without identified cardiovascular disease (CVD). It was noted that minor ECG abnormalities were even more common.

The study obtained data from 8,068 patients with type 2 diabetes, enrolled in the prospective Hoorn Diabetes Care System cohort. Major abnormality was noted in 13%, while 16% had a minor abnormality. The most common types of abnormalities included ventricular conduction defects (14%) and arrhythmias (11%). In the subgroup of patients with no history of CVD, 9% were found to have a major abnormality while 15% had a minor abnormality. The findings are published in the *Journal of Diabetes and Its Complications*… (*Medscape*)

COVID-19 Vaccines Reach Sudan and Rwanda Through COVAX

Through the COVAX vaccine facility, Sudan and Rwanda have become the latest countries to receive the COVID-19 vaccines, stated UN agencies.

Overall, 8,00,000 doses of the AstraZeneca vaccine arrived in Khartoum as Sudan became the first country in the Middle East and North Africa region to receive the vaccine through COVAX. Rwanda received 2,40,000 doses of the AstraZeneca vaccine and expects to receive 1,02,000 more doses from Pfizer-BioNTech. Both the countries will start the vaccine drive initially targeting essential health workers and vulnerable people.

Julianna Lindsey Children, UNICEF Representative in Rwanda, called it an historic moment, and stated that people across the country can now breathe a sigh of relief knowing that the nation is moving towards recovering from the COVID-19 pandemic… (*UN*)

Bharat Biotech Says Its COVID-19 Vaccine Shows 81% Efficacy

Bharat Biotech's COVID-19 vaccine has shown an interim efficacy of 81% in late-stage clinical trials, reported the company.

The interim analysis included 43 recorded cases of COVID-19 in a trial of 25,800 participants. Thirty-six of these 43 cases were noted in participants in the placebo group, while 7 cases were recorded in those who received the Bharat Biotech vaccine. This translated to an efficacy rate of 80.6%.

India had approved the Bharat Biotech vaccine, called COVAXIN, in January without late-stage efficacy data. The vaccination drive in the country includes COVAXIN as well as a vaccine developed by Oxford University and AstraZeneca. Earlier this week, Prime Minister Narendra Modi was also given the first dose of COVAXIN… (*ET Healthworld – Reuters*)

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Study of Thyroid Function Tests in Patients with Metabolic Syndrome

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ABSTRACT

Background: The metabolic syndrome is a constellation of clinical and metabolic abnormalities including abdominal obesity, hypertension, dyslipidemia and impaired fasting glucose or impaired glucose tolerance. Metabolic syndrome and thyroid dysfunction are independent risk factors for cardiovascular disease. **Aims and objectives:** To study the prevalence, symptomatology of thyroid dysfunction and fine needle aspiration cytology (FNAC) findings of thyroid in the patients having metabolic syndrome. **Material and methods:** The study was carried out in 60 cases of metabolic syndrome (according to NCEP ATP III criteria) selected from the medicine outdoor clinic (including diabetic clinics, thyroid clinics) and medicine indoor wards in Post Graduate Department of Medicine, SN Medical College and Hospital, Agra. Diagnosis of thyroid dysfunction was made by history, examination and serum FT4 and TSH. **Result and observations:** Out of 60 patients of metabolic syndrome, 30 patients (50%) were euthyroid, 13 patients (21.66%) had subclinical hypothyroid and 12 patients (20%) had overt hypothyroid. Five patients (8.33%) of metabolic syndrome had hyperthyroidism. Truncal obesity was most prevalent (80.0%) component of metabolic syndrome, followed by hypertriglyceridemia (70%). Diabetes mellitus was equally prevalent in both males as well as females and was present in about 40.0% patients and 53% of patients with metabolic syndrome were hypertensive. **Conclusion:** This study shows that 50% metabolic syndrome patients had thyroid dysfunction. About 21.66% had subclinical hypothyroidism, 20% had overt hypothyroidism and 8.33% were having hyperthyroidism. The most common symptom in metabolic syndrome patients with hypothyroidism was lethargy/sleepiness followed by dry and coarse skin. The most common symptom in hyperthyroid patients was nervousness (100%) followed by sweating, heat intolerance and palpitation in 80% of the patients.

Keywords: Metabolic syndrome, subclinical hypothyroid, hypothyroid, hyperthyroid

The metabolic syndrome is a constellation of clinical and metabolic abnormalities including abdominal obesity, hypertension, dyslipidemia and impaired fasting glucose or impaired glucose tolerance. All these manifestations are surrogate markers of insulin resistance which is the crux abnormality associated with metabolic syndrome. Thyroid hormones markedly stimulate the basic metabolic rate and the metabolism of carbohydrate, lipids and proteins. This hormone appears to serve as a general pacemaker accelerating metabolic process and may be associated with metabolic syndrome. It also plays an important role in the development of the reproductive system. As metabolic syndrome and thyroid dysfunction (subclinical or overt hypothyroidism and hyperthyroidism) are independent risk factors for cardiovascular disease, it is possible that patients suffering from both these disease entities may have a compounded risk.

AIMS AND OBJECTIVES

The aim of this study was to determine the prevalence, symptomatology of thyroid dysfunction and fine needle aspiration cytology (FNAC) findings of thyroid in the patients having metabolic syndrome.

MATERIAL AND METHODS

In our study, 60 patients of metabolic syndrome without liver disease (viral, alcoholic, drug, autoimmune, etc.), chronic renal disease, pancreatitis and pregnancy were studied. Their clinical (age, sex, family history and blood pressure), biochemical (thyroid-stimulating

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hormone [TSH], free thyroxine [FT4], lipid profile, blood sugar) and thyroid FNAC profiles were studied. According to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) at least three of the following criteria should be present to diagnose metabolic syndrome:

- Elevated waist circumference: Men - ≥90 cm for Indians, Women - ≥80 cm for Indians.
- Elevated triglycerides: ≥150 mg/dL.
- Reduced HDL ("good") cholesterol: Men - <40 mg/dL, Women - <50 mg/dL.
- Elevated blood pressure: ≥130/85 mmHg.
- Elevated fasting glucose: ≥110 mg/dL.

The thyroid hormone assays (FT4 and TSH) were done using enzyme-linked immunosorbent assay (ELISA), and fasting blood sugar, triglycerides and high-density lipoprotein cholesterol (HDL-C) were done enzymatically on Roche Automated Clinical Chemistry Analyzer.

Diagnosis of thyroid dysfunction was made by FT4 and TSH - *Euthyroid:* normal TSH and normal FT4; *Subclinical hypothyroidism:* high TSH and normal FT4; *Hypothyroidism:* high TSH and low FT4 and *Hyperthyroidism:* low TSH and high FT4.

OBSERVATIONS AND RESULTS

Our study group consisted of 24 male (40%) and 36 (60%) female patients. Male-to-female ratio was 2:3. Majority of patients (40.0%) belonged to age group 40-49 years. Mean age of all the patients was 47.6 ± 7.5 years. The mean age of males and females was 49.6 ± 8.0 and 46.2 ± 7.1, respectively.

The prevalence of components of metabolic syndrome (Fig. 1) in men and women were, central obesity in 18 (75%) and 30 (83.3%) patients, respectively; low HDL-C in 12 (50%) and 28 (77.8%) patients, respectively; high triglycerides in 18 (75%) and 24 (66.7%), respectively; impaired fasting glucose (>100 mg/dL) or diabetes in 12 (50.0%) and 12 (33.3%), respectively and elevated blood pressure in 18 (75%) men and 32 (88.9%) women.

Out of 60 patients of metabolic syndrome (Fig. 2), 30 patients (50%) were euthyroid, 13 patients (21.66%) had subclinical hypothyroid and 12 patients (20%) had overt hypothyroid while 5 patients (8.33%) had hyperthyroid.

The most common symptom (Table 1) in both subclinical and overt hypothyroid patients was (77.77%) lethargy (sleepiness) followed by dry and coarse skin (72.22%), cold intolerance (66.66%), puffiness of face (66.66%),

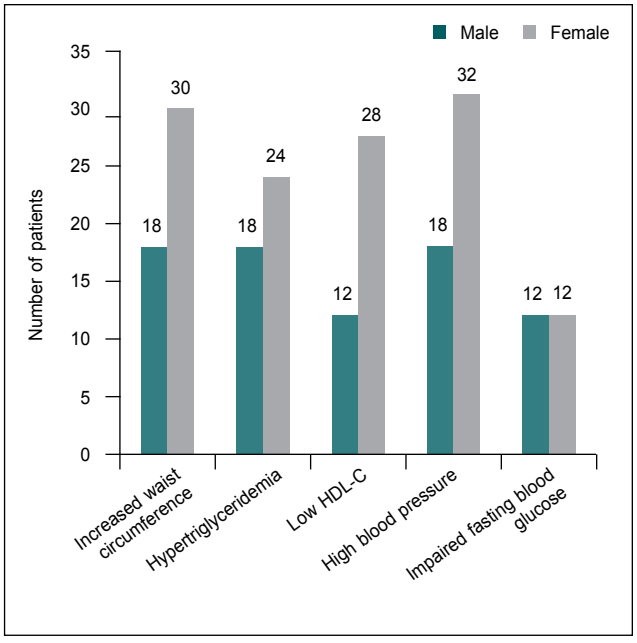

Figure 1. Different components of metabolic syndrome in the study group.

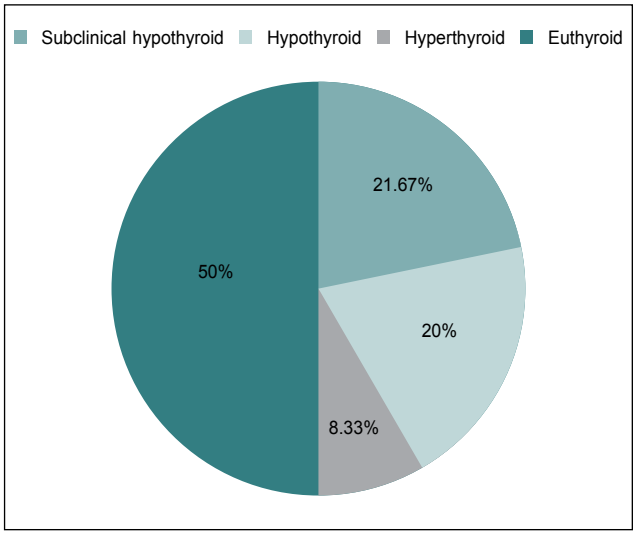

Figure 2. Thyroid dysfunction in study group.

constipation (61.11%), depression (55.55%) and body aches (55.55%). Weight gain was seen in 50% and paresthesia in 44.44% hypothyroid patients. Thyroid gland size was enlarged in (33.33%) 6 patients. Five hypothyroid females (35.71%) had menorrhagia. Hair loss was present in 5 patients (27.77%).

The total number of hyperthyroid patients was 5 in the study. The commonest symptom (Table 2) was nervousness (100%) in our patients. Other symptoms like sweating (80%), hypersensitivity to heat (80%) and palpitation (80%) were also common in these patients. Fatigue, weight loss and enlarged thyroid (goiter) were

Table 1. Prevalence of Symptomatology of Hypothyroidism in the Study Group

Symptoms	Male (n = 4)		Female (n = 14)		Total (n = 18)	
	No.	%	No.	%	No.	%
Lethargy/ Sleepiness	3	75	11	78.57	14	77.77
Dry and coarse skin	3	75	10	71.42	13	72.22
Cold intolerance	2	50	10	71.42	12	66.66
Puffiness of face	2	50	10	71.42	12	66.66
Body aches	2	50	8	57.14	10	55.55
Weight gain	2	50	7	50	9	50
Constipation	2	50	9	64.28	11	61.11
Depression	2	50	8	57.14	10	55.55
Paresthesia	2	50	6	42.85	8	44.44
Menorrhagia	-	-	5	35.71	5	27.77
Thyroid gland size enlarged	1	25	5	35.71	6	33.33
Hair loss	1	25	4	28.57	5	27.77

Table 2. Prevalence of Symptomatology of Hyperthyroidism in the Study Group

Symptoms and signs	Male (n = 2)		Female (n = 3)		Total (n = 5)	
	No.	%	No.	%	No.	%
Nervousness	2	100	3	100	5	100
Sweating	2	100	2	66.66	4	80
Hypersensitivity to heat	1	50	3	100	4	80
Palpitation/ Increased heart rate	2	100	2	66.66	4	80
Fatigue	1	50	2	66.66	3	60
Goiter	1	50	2	66.66	3	60
Hyperdefecation	1	50	1	33.33	2	40
Weight loss	1	50	2	66.66	3	60

present in 3 patients (60%). One male and 1 female hyperthyroid patient had hyperdefecation.

Twelve thyroid dysfunction patients with metabolic syndrome underwent FNAC of thyroid gland. Out of 12 patients, 8 patients (66.66%) had normal cytological findings. Two (1 subclinical hypothyroid and 1 overt hypothyroid) patients had simple colloid goiter and 1 overt hypothyroid had nodular colloid goiter. One hyperthyroid patient with metabolic syndrome had nodular hyperplasia of thyroid gland.

DISCUSSION

In our study, out of 60 patients of metabolic syndrome, 30 patients (50%) were euthyroid, 13 patients (21.66%) had subclinical hypothyroid and 12 patients (30%) had overt hypothyroid. Five patients (8.33%) of metabolic syndrome had hyperthyroidism. A cross-sectional study from South India by Shantha et al has shown prevalence of subclinical hypothyroidism as 21.9% and overt hypothyroidism in 7.4% cases of metabolic syndrome.

The female-to-male ratio in our study was 2.25:1 in subclinical hypothyroidism and 2:1 in overt hypothyroidism patients. The female-to-male ratio in hypothyroidism ranges from 2:1 to 8:1 in various epidemiological surveys. Some surveys indicate hypothyroidism to be more prevalent in elderly population, reaching as high as 20%. Shrestha et al observed the association of metabolic syndrome in 21, 5 and 6 cases in 48 euthyroid, 24 hyperthyroid and 28 hyporthyroid groups, respectively.

The commonest symptom in hypothyroid patients was lethargy (77.77%). This was consistent with case-control study by Khurram et al in which 67.9% cases had lethargy. In our study too, dry and coarse skin was mentioned by 72.22% of patients like 70-79% cases in another study. Similarly, cold intolerance, that was found in 89% of patients in one series and 93% of another series, was prevalent in 66.66% of our cases, which is quite comparable to the 58.25% in Watanakunakorn's. Five out of 14 (35.71%) females had menorrhagia as in the study by Khurram et al. In a cohort study by Scott and Mussey, 28 women (56%) complained of menstrual disturbance, with the most common complaint being menorrhagia (occurring in 18 [36%] of the women). Other symptoms like body aches, weight gain, constipation, paresthesia, hair loss were similar to what has been described in various studies.

In our study, 66.66% patients had puffiness of face as compared to 63.3% in the study by Khurram et al, 79% in Lerman's series and 67% in Watanakunakorn's series.

Thyroid was enlarged in 6 hypothyroid patients (33.33%) as compared to 6.6% in the study by Samanta.

The most common symptom in hyperthyroid patients was nervousness (100%), followed by sweating (80%), hypersensitivity to heat (80%), palpitation (80%), weight loss (60%), fatigue (60%), hyperdefecation (40%) and goiter (60%), which was statistically comparable with the study by Trivalle et al.

Out of 12 patients who underwent FNAC of thyroid, 8 patients (66.66%) had normal cytological findings. Two (1 subclinical and 1 overt) hypothyroid patients had simple colloid goiter and 1 overt hypothyroid patients had nodular colloid goiter. One hyperthyroid patient with metabolic syndrome had nodular hyperplasia of thyroid gland.

In this study, we found that out of 60 patients of metabolic syndrome, 24 (40%) were male and 36 (60%) were female. Male-to-female ratio was 2:3 proving that disease was more dominant in females. Most of the patients of metabolic syndrome were belonging to age group 40-60 years. Mean age of males was 49.6 ± 8.0 years and mean age of female patients was 46.2 ± 7.1 years. Mean age of patients with metabolic syndrome in a study by Bacon and colleagues was 47 years and similarly another study also noted mean age of 54 years. About 23.3% of the patients met all the five diagnostic components of metabolic syndrome. Waist circumference was elevated in almost all (80%) the cases. Other components of metabolic syndrome were distributed in 50-70% of the patients.

Majority of male patients (45%) had waist circumference in range of 90-100 cm. Mean waist circumference of males was 97.9 ± 7.2 cm. Most of the female patients (40%) also had waist circumference in 90-100 cm range. Mean waist circumference of female patients was 97.8 ± 2.1 cm. In previous studies, mean waist circumference of males and females was 102 cm and 92 cm, respectively. About 62% of the patients had triglyceride level between 150 and 174 mg%. Only 14.3% had elevated triglyceride level more than 200 mg%. Mean triglyceride level of males was 160.1 ± 22.6 mg%. Mean level of triglyceride in females was 162.7 ± 27.2 mg%. Liese et al noted hypertriglyceridemia in 50% of the cases. In previous studies, it was observed that mean triglyceride level in the patients of metabolic syndrome was 191.8 mg%.

About half of the patients (50.0%) had HDL level between 30 and 39 mg/dL. Mean HDL level of males was 40.8 ± 6.4 mg/dL. Female patients had mean HDL level 43.4 ± 7.5 mg/dL. There was a significant variation in mean HDL level between male and female patients. Similar studies in the past observed HDL abnormalities in 63.5% of the patients.

In our study, 40% patients of metabolic syndrome were diabetic. Only 8.3% patients had blood sugar in impaired glucose tolerance (IGT) range, 16.6% patients were newly diagnosed diabetics. Maximum number of patients (41.7%) were diabetic for duration more than 10 years. Matteoni et al also performed a similar study and found diabetes mellitus in 23% of cases.

In our study, 53% of patients with metabolic syndrome were hypertensive. In all, 25% were newly diagnosed hypertensives. About 37.5% had hypertension for duration more the 10 years. Kaplan and colleagues noted prevalence of hypertension in 58% patients of metabolic syndrome.

CONCLUSION

The present study concludes that 50% metabolic syndrome patients had thyroid dysfunction. Subclinical hypothyroidism was present in 21.66% and overt hypothyroidism 20% patients. Hyperthyroidism was observed in 8.33% of metabolic syndrome patients.

The most common symptom in metabolic syndrome patients with hypothyroidism was lethargy/sleepiness followed by dry and coarse skin.

The most common symptom in hyperthyroid metabolic syndrome patients was nervousness (100%) followed by sweating, heat intolerance and palpitation (80%). Thyroid dysfunction patients with metabolic syndrome presenting with goiter underwent FNAC of thyroid - 8 patients (66.66%) had normal cytological findings. Two (1 subclinical and 1 overt) hypothyroid patients had simple colloid goiter and 1 overt hypothyroid patient had nodular colloid goiter. One hyperthyroid patient with metabolic syndrome had nodular hyperplasia of thyroid gland.

Metabolic syndrome and thyroid dysfunction are independent risk factors for cardiovascular disease. Their co-existence may even compound the risk of cardiovascular events. Hence, it is worthwhile to screen metabolic syndrome patients for thyroid dysfunction at the earliest for further decrease in cardiovascular events.

SUGGESTED READING

1. Trivalle C, Doucet J, Chassagne P, Landrin I, Kadri N, Menard JF, et al. Differences in the signs and symptoms of hyperthyroidism in older and younger patients. J Am Geriatr Soc. 1996;44(1):50-3.
2. Dillmann WH. Mechanism of action of thyroid hormones. Med Clin North Am. 1985;69(5):849-61.

3. Shantha GP, Kumar AA, Jeyachandran V, Rajamanickam D, Rajkumar K, Salim S, et al. Association between primary hypothyroidism and metabolic syndrome and the role of C-reactive protein: a cross-sectional study from South India. Thyroid Res. 2009;2(1):2.
4. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486-97.
5. Helfand M, Crapo LM. Screening for thyroid disease. Ann Intern Med. 1990;112(11):840-9.
6. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, et al. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf). 1977;7(6):481-93.
7. Sawin CT, Chopra D, Azizi F, Mannix JE, Bacharach P. The aging thyroid. Increased prevalence of elevated serum thyrotropin levels in the elderly. JAMA. 1979;242(3):247-50.
8. Shrestha S, Das BKL, Baral N, Chandra L. Association of metabolic syndrome and its components with thyroid dysfunction in females. Int J Diab Dev Ctries. 2007; 27(1):24-6.
9. Khurram IM, Choudhry KS, Muhammad K, Islam N. Clinical presentation of hypothyroidism: a case control analysis. J Ayub Med Coll Abbottabad. 2003;15(1):45-9.
10. Lerman J, Means JH. The gastric secretion in exophthalmic goitre and myxoedema. J Clin Invest. 1932;11(1):167-82.
11. Watanakunakorn C, Hodges RE, Evans TC. Myxedema; A study of 400 cases. Arch Intern Med. 1965;116:183-90.
12. Scott JC Jr, Mussey E. Menstrual patterns in myxedema. Am J Obstet Gynecol. 1964;90:161-5.
13. Samanta BB. Clinical profile of hypothyroidism. Available at:www.endocrineindia.comClinical%20Profile%20Of%20 Hypothyroidism %20-PDF.pdf
14. Bacon BR, Farahvash MJ, Janney CG, Neuschwander-Tetri BA. Nonalcoholic steatohepatitis: an expanded clinical entity. Gastroenterology. 1994;107(4):1103-9.
15. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care. 1991;14(3):173-94.
16. Liese AD, Mayer-Davis EJ, Haffner SM. Development of the multiple metabolic syndrome: an epidemiologic perspective. Epidemiol Rev. 1998;20(2):157-72.
17. Alshkri M, Elmehdawi R. Metabolic syndrome among type-2 diabetic patients in Benghazi-Libya: a pilot study. Libyan J Med. 2008;3(4):177-80.
18. Saely CH, Koch L, Schmid F, Marte T, Aczel S, Langer P, et al. Adult Treatment Panel III 2001 but not International Diabetes Federation 2005 criteria of the metabolic syndrome predict clinical cardiovascular events in subjects who underwent coronary angiography. Diabetes Care. 2006;29(4):901-7.
19. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ. Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology. 1999;116(6):1413-9.
20. Kaplan NM. The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. Arch Intern Med. 1989;149(7):1514-20.

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Five States Account for More Than 84% of Total Active COVID-19 Cases in India

The total number of active COVID-19 cases in India currently stands at 1.68 lakh with five states accounting for 84.16% of the total active caseload.

Six states and UTs - Maharashtra, Kerala, Goa, Chandigarh, Punjab and Gujarat - have reported a weekly positivity rate higher than the national average of 2%. Maharashtra and Kerala account for 67.84% of the active case numbers, stated the Union Health Ministry. Maharashtra has a weekly positivity rate of 10.02%, leading all the states. The active caseload in the country constitutes 1.51% of the total number of cases. Five states account for 80.33% of new COVID-19 infections… (*ET Healthworld – PTI*)

65 Plus Individuals can Now Get AstraZeneca COVID-19 Vaccine in France

The French government has said that older individuals with pre-existing conditions can now receive AstraZeneca COVID-19 vaccine. The country's health minister stated that those affected by comorbidities can now be vaccinated with the AstraZeneca vaccine, including those aged 65-74 years. Last month, the country had approved use of the vaccine for those aged below 65 only, stating that there was a dearth of data for older people. Studies have revealed, since then, that the vaccine is highly effective among the older people. The Health Minister mentioned that those aged over 75 years will continue getting either Pfizer or Moderna vaccines in a vaccination center… (*BBC*)

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To Study Endothelial Dysfunction by Brachial Artery Flow-mediated Dilatation and Its Relationship with Microalbuminuria in Hypertensive Individuals

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ABSTRACT

Introduction: Hypertension remains a central pathophysiologic contributor to cardiovascular morbidity and mortality. In its earliest stage, the principal endothelial alteration is merely functional and addressed as "endothelial dysfunction". Flow-mediated dilatation (FMD) of the brachial artery has been widely used as a noninvasive marker to vascular reactivity. Both microalbuminuria and endothelial dysfunction are expressions of an endothelial pathology; however, it is still uncertain whether they are interrelated, or if the two phenomena are caused in parallel by the cardiovascular risk burden. **Aim:** To study the relationship of brachial artery flow-mediated dilatation (BAFMD) with microalbuminuria in hypertensive subjects. **Method:** Total 120 subjects were included in the study comprising 80 hypertension cases and 40 controls. All subjects were subjected to anthropometric measurements and routine biochemical tests – hemogram, urea, serum creatinine, liver function test, lipid profile, BAFMD and urinary albumin to urinary creatinine ratio (30-300 mg/g Cr). **Conclusion:** Mean % FMD was lower in patients with abnormal microalbuminuria compared to normal and this was statistically verified, with p = 0.016, thereby verifying the central hypothesis of this study.

Keywords: Hypertension, microalbuminuria, brachial artery flow-mediated dilatation

Hypertension remains a central pathophysiologic contributor to cardiovascular morbidity and mortality. Although the precise cascade of events from the development of hypertension to adverse cardiovascular events remains to be elucidated, cardiovascular risk factors, including hypertension, are clearly associated with the development of vascular endothelial dysfunction. Endothelial dysfunction is a phenotypical alteration of the endovascular lining of blood vessels that is characterized by a prothrombotic, proinflammatory and proconstrictive phenotype. Endothelial function is readily measurable through multiple modalities and is an established barometer of cardiovascular risk. Further, interventions aimed at reducing cardiovascular risk, including antihypertensive therapy, are more effective if they concomitantly improve endothelial function. These data support the provocative hypothesis that reductions in cardiovascular risk secondary to antihypertensive therapy may relate independently to a particular intervention's beneficial effects on endothelial function as well as to its absolute effect on blood pressure.[1]

Recent studies have established microalbuminuria as an important cardiovascular risk factor. Data reported thus far clearly underpin the importance of measuring urinary albumin in patients with hypertension.

More importantly, patients with hypertension may benefit from prevention of the onset or progression of albuminuria, and to this end, further characterization of albuminuria in hypertensive patients or of possible risk factors affecting urinary excretion of albumin, could provide useful information.

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In disease conditions, including cardiovascular risk factors, the vascular endothelium undergoes functional and structural alterations. In its earliest stage, the principal endothelial alteration is merely functional and addressed as "endothelial dysfunction". The fundamental feature of this condition is impaired nitric oxide (NO) bioavailability. This can be evaluated in humans by measuring the downstream effects, namely vasodilatation through vascular reactivity tests. In the last decade, flow-mediated dilatation (FMD) of the brachial artery has been widely used as a noninvasive marker for this purpose.[2]

Both microalbuminuria and endothelial dysfunction are expressions of an endothelial pathology; however, it is still uncertain whether they are interrelated, or if the two phenomena are caused in parallel by the cardiovascular risk burden. Although endothelial dysfunction is constantly present in advanced renal disease, its association in mild renal dysfunction is still uncertain.[3]

AIMS AND OBJECTIVES

- To assess endothelial dysfunction by brachial artery flow-mediated dilatation (BAFMD) in hypertensive individuals and normotensive controls.
- To study microalbuminuria in the study population.
- To study the relationship of BAFMD with microalbuminuria.

MATERIAL AND METHODS

The present study was conducted in the Dept. of General Medicine, Cardiology and Radiology, Gajra Raja Medical College, Gwalior (Madhya Pradesh) in between January 2016 and September 2017.

Target sample size of 120 was divided into the following groups according to their age:

- Cases: Eighty individuals (40 male and 40 female) between age 30 and 50 with hypertension.
- Controls: Forty individuals (20 male and 20 female) between age 30 and 50 without hypertension.

Hypertension among the subjects was defined as per the seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC VII) (systolic BP [SBP] >140 mmHg and diastolic BP [DBP] >90 mmHg).

All subjects were subjected to anthropometric measurements and routine biochemical tests – hemogram, urea, serum creatinine, liver function test and lipid profile.

Patients were subjected to BAFMD study in the Dept. of Radiology. The procedure involved placing a pneumatic sphygmomanometer cuff on the forearm distal to the brachial artery and inflating it to suprasystolic levels and subsequently releasing it 5 minutes later. FMD was assessed by Doppler ultrasound with high resolution. FMD_{max} value was used in the present study.

Patient's urine sample was collected for detection of microalbuminuria. A single-void, urine sample was used to measure urinary excretion of albumin. Urinary albumin concentrations were measured by turbidimetric immunoassay and were as ratio of concentrations of urinary albumin to urinary creatinine (UACR). Microalbuminuria was defined according to recommendations of the American Diabetes Association and National Kidney Foundation (300 > UACR >30 mg/g Cr).

Inclusion Criteria

- **Cases**: Individuals having age between 30 and 50 years suffering from hypertension.
- **Controls:** Individuals having age between 30 and 50 years with no history of hypertension.

Exclusion Criteria

- Age below 30 and above 50 years.
- Documented or detected cases of type 1 or type 2 diabetes mellitus, chronic kidney disease, chronic inflammatory conditions, coronary artery disease, heart failure, acute febrile illnesses and on angiotensin-converting enzyme (ACE) inhibitors.
- Subjects who did not provide consent for the study.

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented as mean ± SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. Student *t*-test has been used to find the significance of study parameters between the two groups of patients. Chi-square/Fisher exact test has been used to find the significance of study parameters on categorical scale between the two groups. Pearson's correlation test was used for exploring correlation.

OBSERVATIONS

In cases and controls, most of the subjects belonged to age groups of 46-50 years (34 [42.5%]) and 36-40 years (13 [32.5%]), respectively (Table 1). Age of the study

Table 1. Distribution of Subjects According to Age and Gender

Age group	Cases		Controls	
	Male	Female	Male	Female
30-35	4 (5)	2 (2.5)	5 (12.5)	4 (10)
36-40	11 (13.8)	9 (11.2)	9 (22.5)	4 (10)
41-45	8 (10)	12 (15)	4 (10)	7 (17.5)
46-50	17 (21.2)	17 (21.2)	2 (5)	5 (12.5)

population was restricted to 30-50 years to avoid the confounding influence of age-related atherogenic changes on the measurement of BAFMD. Equal number of males and females were selected within the cases and controls for comparability.

Amongst the cases, 57.5% of the subjects belonged to the Stage 1 hypertension (HTN) group as per the JNC VII criteria (Table 2). More number of females than males was present in Stage 2 HTN group while the inverse was true for Stage 1 HTN. Subjects were distributed equally among the normal and prehypertensive categories in the control group with no female preponderance. Figure 1 depicts the distribution of study participants according to stage of hypertension.

Mean baseline lumen diameter (mm) in male and female cases and controls was 3.65 ± 0.86 vs. 3.75 ± 0.71 and 3.67 ± 0.66 vs. 3.70 ± 0.66, respectively. After occlusion cuff release, among male and female cases and controls, the diameter was 3.97 ± 0.92 vs. 4.15 ± 0.74 and 4.05 ± 0.71 vs. 4.10 ± 0.79, respectively. Mean BAFMD (%) in male and female cases and controls was 6.85 ± 2.86 vs. 10.75 ± 2.38 and 7.2 ± 3.12 vs. 10.35 ± 2.76, respectively (Table 3 and Figs. 2-4). Although the baseline diameter showed no significant difference among the hypertensive and normotensive groups, the mean post occlusion diameter was much lower in the hypertensive subjects, which was thereby reflected in a much lower mean % FMD amongst them. The lowest baseline diameter, post occlusion diameter and % BAFMD were recorded in the male hypertensives while the highest of these parameters were recorded amongst the male control group.

All cases of microalbuminuria were present in the hypertensive group. Among them, more males were observed to have abnormal levels than females (Table 4 and Fig. 5).

Mean values of body mass index (BMI), total cholesterol (TC), triglycerides (TGs), low-density lipoprotein

Table 2. Distribution of Subjects According to Blood Pressure

Blood pressure (mmHg)	Cases		Controls	
	Male	Female	Male	Female
Normal				
SBP <120 mmHg	0 (0)	0 (0)	10 (25)	10 (25)
DBP <80 mmHg				
Prehypertension				
SBP 120-139 mmHg	0 (0)	0 (0)	10 (25)	10 (25)
DBP 80-89 mmHg				
Stage 1 HTN				
SBP 140-159 mmHg	24 (30)	22 (27.5)	0 (0)	0 (0)
DBP 90-90 mmHg				
Stage 2 HTN				
SBP ≥160 mmHg	16 (20)	18 (22.5)	0 (0)	0 (0)
DBP ≥100 mmHg				

SBP = Systolic blood pressure; DBP = Diastolic blood pressure; HTN = Hypertension.

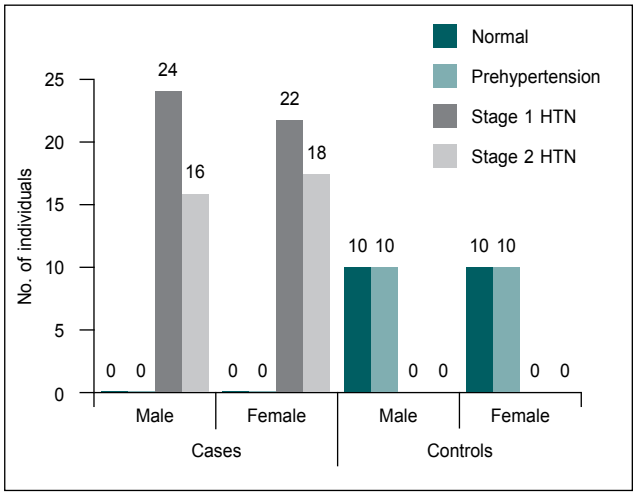

Figure 1. Distribution according to stage of hypertension.

cholesterol (LDL-C) and microalbuminuria (UACR) were higher in the case group when compared to the controls. Additionally, % BAFMD was lower in hypertensives when compared to the normotensive subjects (Table 5). On applying Students *t*-test, this difference in mean values between the cases and controls was statistically significant with each of them having a p value of <0.05.

Mean FMD (%) was significantly different across the age groups (p = 0.001), with FMD (%) showing a declining trend as age increases, whereas distribution of microalbuminuria was comparable across the age groups (p = 0.52) (Table 6; Figs. 6 and 7).

Table 3. Comparison of Assessment of FMD Between Cases and Controls

Variable	Cases		Controls	
	Male (mean ± SD)	Female (mean ± SD)	Male (mean ± SD)	Female (mean ± SD)
Baseline lumen diameter (mm)	3.65 ± 0.86	3.67 ± 0.66	3.75 ± 0.71	3.70 ± 0.66
Diameter after occlusion release (mm)	3.97 ± 0.92	4.05 ± 0.71	4.15 ± 0.74	4.10 ± 0.79
BAFMD (%)	6.85 ± 2.86	7.2 ± 3.12	10.75 ± 2.38	10.35 ± 2.76

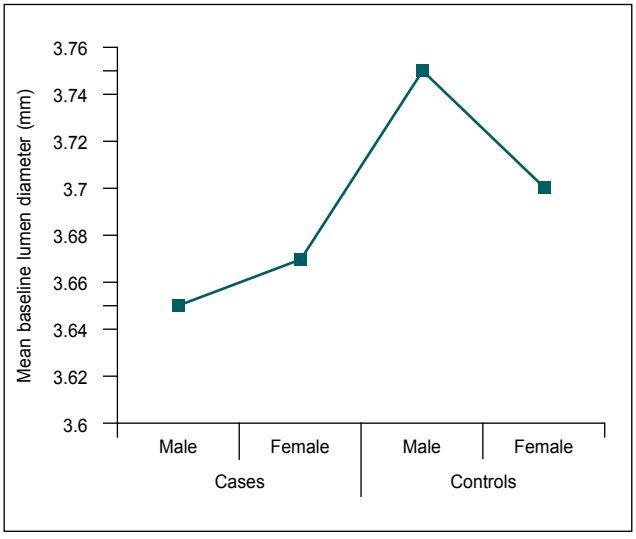

Figure 2. Mean baseline lumen diameter in study population.

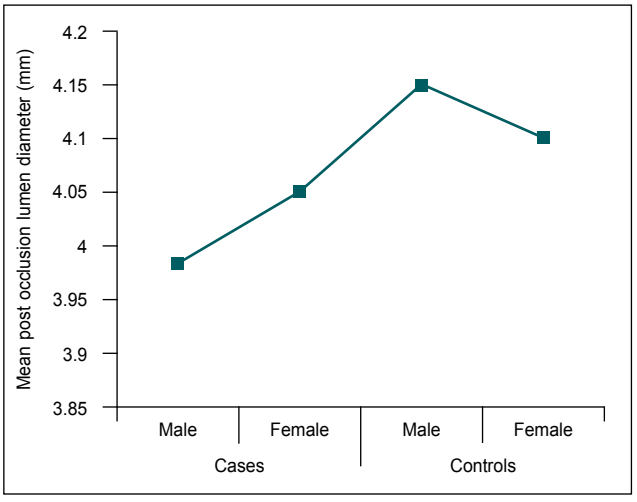

Figure 3. Mean post occlusion lumen diameter in study population.

Mean FMD was insignificantly higher among males (7.05 ± 2.55) compared to females (7 ± 3.38) (p = 0.87), whereas microalbuminuria was significantly higher among females (20 [25%]) compared to males (11 [13.8%]) (p = 0.039) in relation to smoking (Table 7).

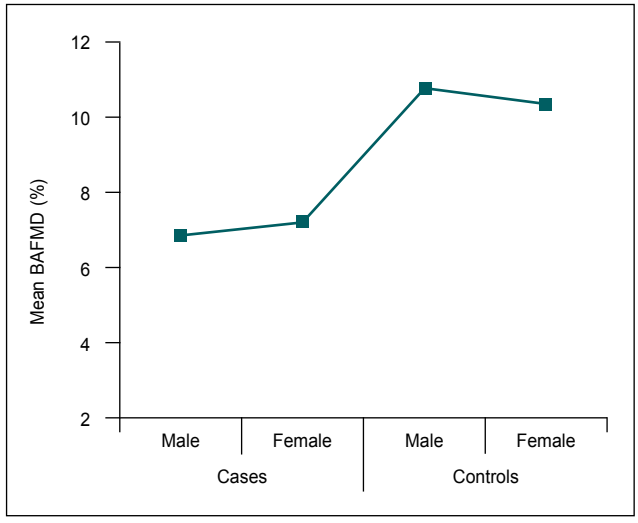

Figure 4. Mean BAFMD (%) in study population.

Table 4. Distribution of Subjects According to Microalbuminuria Levels

Microalbuminuria	Cases		Controls	
	Male	Female	Male	Female
Normal (<30)	20 (25)	29 (36.2)	20 (50)	20 (50)
Abnormal (>30)	20 (25)	11 (13.8)	0 (0)	0 (0)

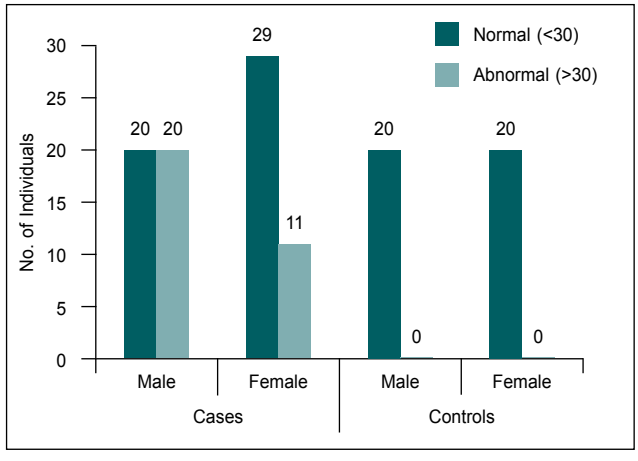

Figure 5. Distribution according to microalbuminuria.

Table 5. Comparison Between Cases and Controls

Variable	N	Mean	SD	P value
BMI				
Case	80	26.08	2.79	0.031*
Control	40	22.68	2.25	
TC				
Case	80	173.76	29.03	<0.001*
Control	40	162.77	6.19	
HDL-C				
Case	80	44.95	5.88	0.056
Control	40	44.08	28.83	
TG level				
Case	80	119.25	32.06	<0.001*
Control	40	97.58	23.50	
LDL-C				
Case	80	104.95	24.73	<0.001*
Control	40	97.57	16.25	
Microalbuminuria (ACR)				
Case	80	27.44	38.86	<0.001*
Control	40	3.73	0.68	
FMD %				
Case	80	7.04	2.173	<0.001*
Control	40	10.61	1.19	

*Significant

BMI = Body mass index; TC = Total cholesterol; HDL-C = High-density lipoprotein cholesterol; TG = Triglyceride; LDL-C = Low-density lipoprotein cholesterol; ACR = Albumin-to-creatinine ratio; FMD = Flow-mediated dilatation; N = Number; SD = Standard deviation.

Table 6. Relation of BAFMD and Microalbuminuria with Age in Cases

Age	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
30-35	9.2	3.09	6 (7.5)	0
36-40	9.27	3.54	12 (15)	8 (10)
41-45	8.03	2.7	10 (12.5)	10 (12.5)
46-50	7.1	3.27	21 (26.2)	13 (16.2)
P value	0.001*		0.52	

The FMD % showed a secular and significant decrease in mean value in the progressively higher JNC VII stages of hypertension with computed p value of 0.038 (Table 8 and Fig. 8). The prevalence of microalbuminuria

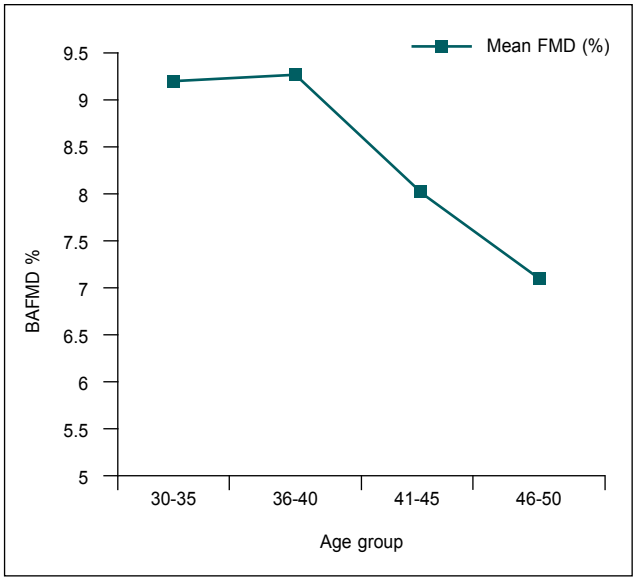

Figure 6. Age and BAFMD %.

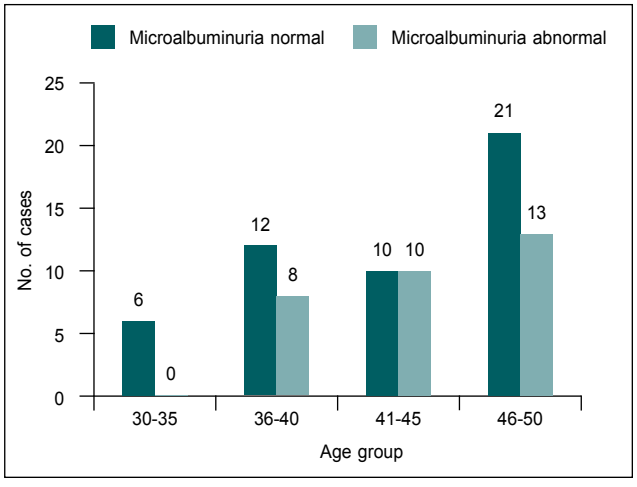

Figure 7. Age and microalbuminuria.

Table 7. Relation of BAFMD and Microalbuminuria with Smoking Habit in Cases

Smoking habit	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
Male	7.05	2.55	20 (25)	20 (25)
Female	7	3.38	29 (36.2)	11 (13.8)
P value	0.87		0.039*	

was higher in Stage 2 HTN than Stage 1 HTN, with a significant p value of 0.009 (Table 8).

Mean FMD was significantly lower in patients with abnormal SBP (>140 mmHg) compared to normal SBP (Table 9 and Fig. 9). Microalbuminuria was significantly

Table 8. Relation of BAFMD and Microalbuminuria with Stage of Hypertension in Cases

Blood pressure (mmHg)	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
Normal	10.61	3.72	0 (0)	0 (0)
Prehypertension	8.73	3.55	0 (0)	0 (0)
Stage 1 HTN	7.53	2.81	34 (42.5)	12 (15)
Stage 2 HTN	6.58	2.91	20 (25)	14 (17.5)
P value	0.038*		0.009*	

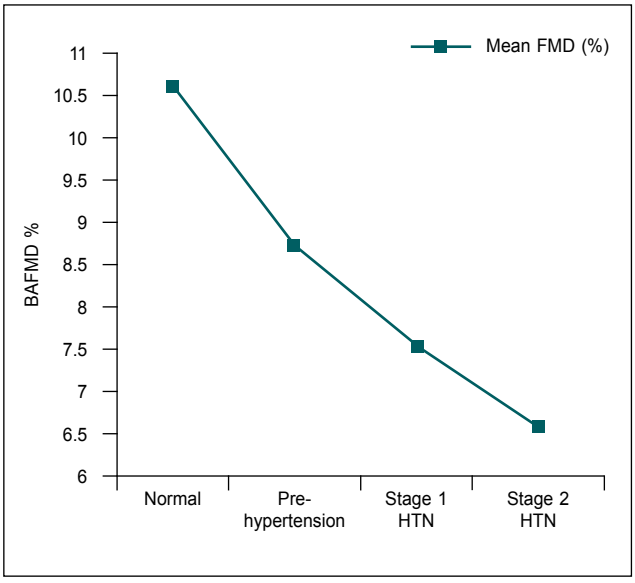

Figure 8. Stage of hypertension and BAFMD %.

Table 9. Relation of BAFMD and Microalbuminuria with SBP in Cases

SBP	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
Normal (<140)	8	2.91	12 (15)	1 (1.2)
Abnormal (>140)	6.84	2.97	37 (46.2)	30 (37.5)
P value	0.002*		0.001*	

higher in patients with abnormal SBP (p = 0.001) (Table 9).

Mean FMD was significantly lower in patients with abnormal DBP (>90 mmHg) compared to normal DBP (p = 0.027) (Table 10 and Fig. 10). Also, microalbuminuria was significantly higher in patients with abnormal DBP (p = 0.005) (Table 10).

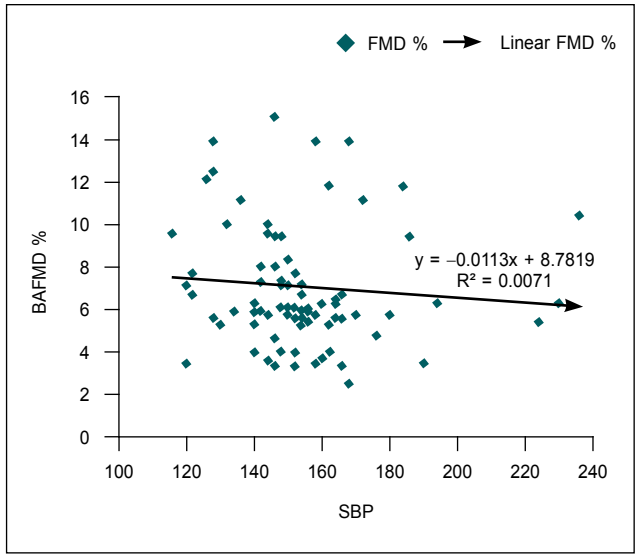

Figure 9. Systolic blood pressure and BAFMD %.

Table 10. Relation of BAFMD and Microalbuminuria with DBP in Cases

DBP	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
Normal (<90)	7.27	2.99	36 (45)	13 (16.2)
Abnormal (>90)	6.65	2.96	13 (16.2)	18 (22.5)
P value	0.027*		0.005*	

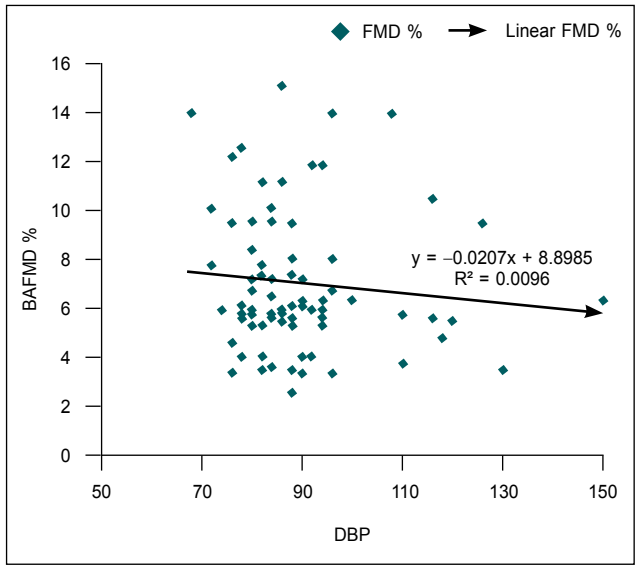

Figure 10. Diastolic blood pressure and FMD %.

Mean % FMD was significantly lower in patients with longer history of hypertension compared to patients with no history of hypertension (p = 0.022) (Table 11 and Fig. 11). The most precipitous dip in mean %

Table 11. Relation of BAFMD and Microalbuminuria with Duration of Hypertension

Duration of hypertension	FMD (%)		Microalbuminuria	
	Mean	SD	Normal	Abnormal
No history of hypertension (control group)	10.55	2.55	40 (100)	0
1 year	6.89	2.91	33 (41.25)	10 (12.5)
1-3 years	7.8	3.51	10 (12.5)	5 (6.25)
3-5 years	7.36	2.76	5 (6.25)	9 (11.25)
5-7 years	4.5	1.29	0 (0)	4 (5)
>7 years	3.91	1.01	1 (1.25)	3 (3.75)
P value	0.022*		0.036*	

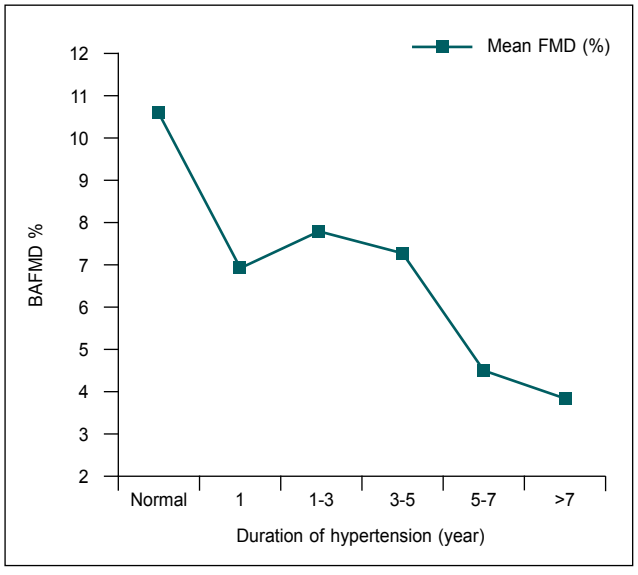

Figure 11. Duration of hypertension and FMD %.

BAFMD value in hypertensives occurred when the duration of hypertension exceeded 5 years. Similarly, the tendency for abnormal levels of microalbuminuria was significantly higher in patients with longer hypertensive history (p = 0.036) (Table 11).

When multiple cardiovascular risk factors (hypertension, dyslipidemia, smoking and obesity) were combined, it was noted that the cases tended to have a progressively lower mean % FMD and a higher mean level of microalbuminuria as the number of risk factors increased (Table 12; Figs. 12 and 13). In the case of % FMD, the decreasing trend was more or less secular in nature, with the most precipitous fall in % FMD value occurring when smoking was added as a risk factor. When the

Table 12. Impact of Various Risk Factors on BAFMD and Microalbuminuria

Risk factors	N	Mean FMD (%)	Mean level of microalbuminuria
Hypertension	80	7.03 ± 2.98	27.12 ± 38.58
Dyslipidemia	45	7.13 ± 2.96	67.49± 72.61
Smoking	23	7.06 ± 2.99	85.01 ± 71.23
Obesity	46	7.09 ± 2.89	56.23 ± 69.83
HTN + Obesity	46	7.09 ± 2.89	62.95 ± 69.83
HTN + Dyslipidemia	45	7.01 ± 2.97	73.82 ± 68.59
HTN + Smoking	23	7.06 ± 2.99	94.76 ± 71.23
HTN + Dyslipidemia + Obesity	25	7.05 ± 2.08	83.51 ± 70.12
HTN + Obesity + Smoking	13	5.78 ± 2.13	106.47 ± 75.88
HTN + Smoking + Dyslipidemia	10	5.69 ± 2.14	105.428 ± 69.87
HTN + Dyslipidemia + Obesity + Smoking	5	4.85 ± 1.89	103.74 ± 88.52

trend of mean levels of microalbuminuria was plotted, the trend showed general increase in the mean levels of microalbuminuria, and peaked at the points where smoking was added as risk factor.

Mean % FMD was lower in patients with microalbuminuria compared to those with normal values and this was statistically verified (Table 13 and Fig. 14), with p = 0.016, thereby verifying the central hypothesis of this study.

DISCUSSION

Our core question was whether hypertension related endothelial dysfunction detected in peripheral circulation by high frequency ultrasound measurement of BAFMD independently favors the progressive loss of albumin through urine, which shall be an indicator of early hypertensive renal disease. Moreover, we have also outlined the various cardiovascular determinants of BAFMD and microalbuminuria.

The present study limited the age of the participants within 30-50 years, with a deliberate intent of avoiding the confounding influence that age has been demonstrated to have on endothelial function. In spite of this, BAFMD showed a significant decline moving

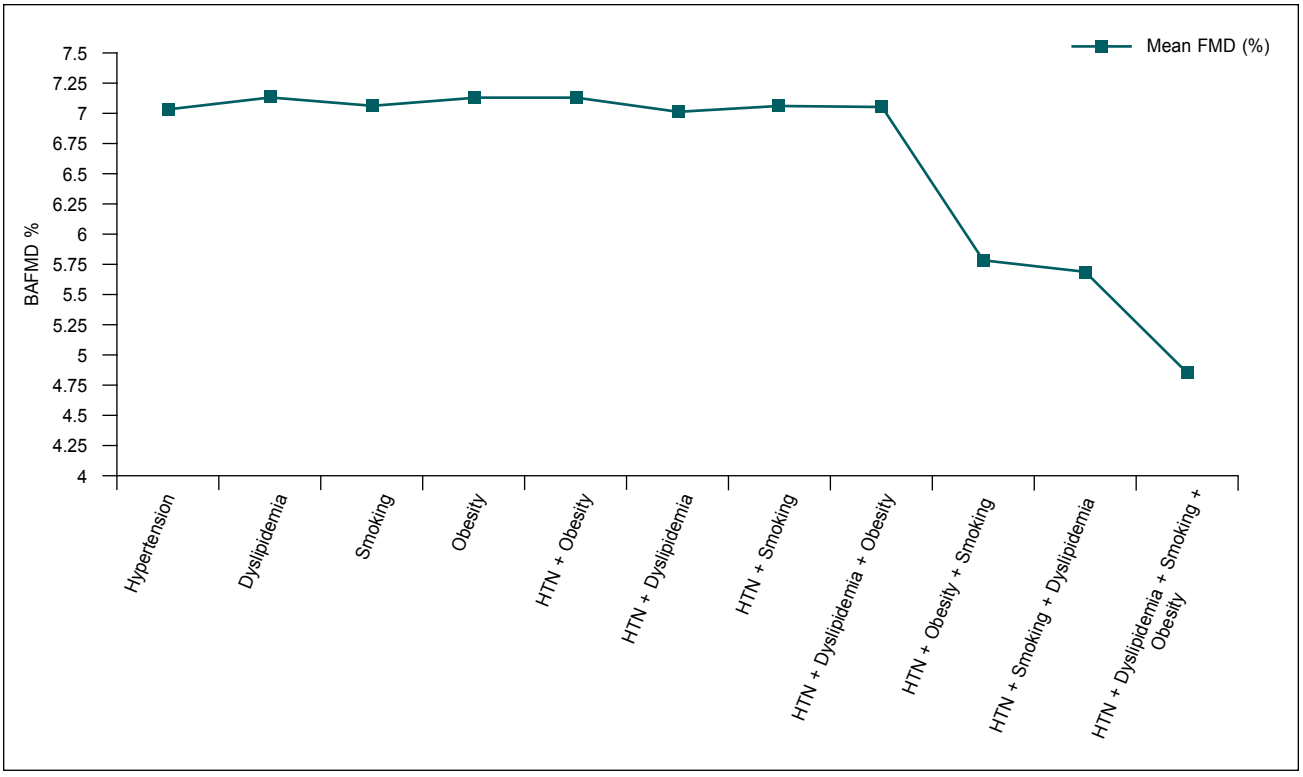

Figure 12. Combination of cardiovascular risk factors and BAFMD %.

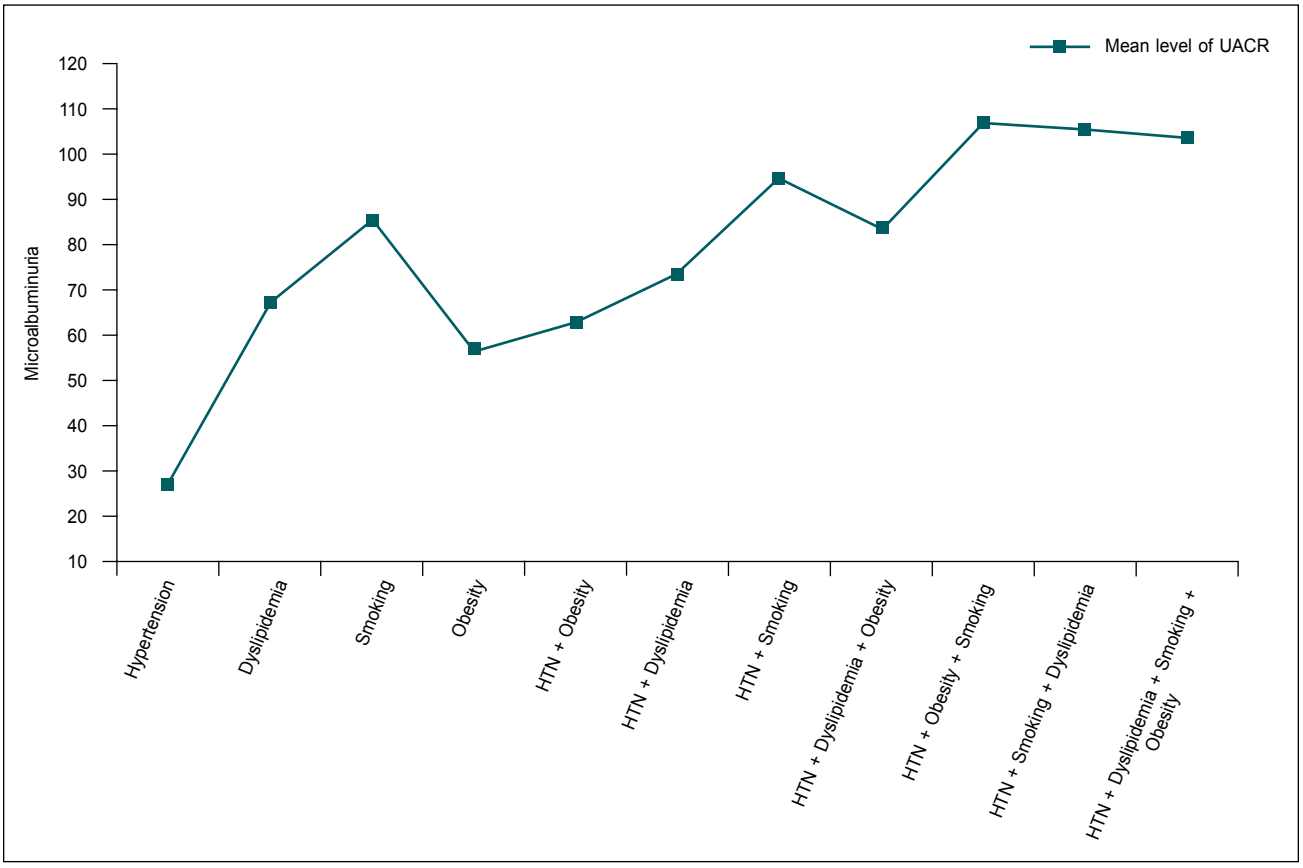

Figure 13. Combination of cardiovascular risk factors and microalbuminuria.

Table 13. Relationship of BAFMD and Microalbuminuria in Cases

Microalbuminuria	FMD %	
	Mean	SD
Normal	7.69	3.001
Abnormal	5.97	2.664
P value	0.016*	

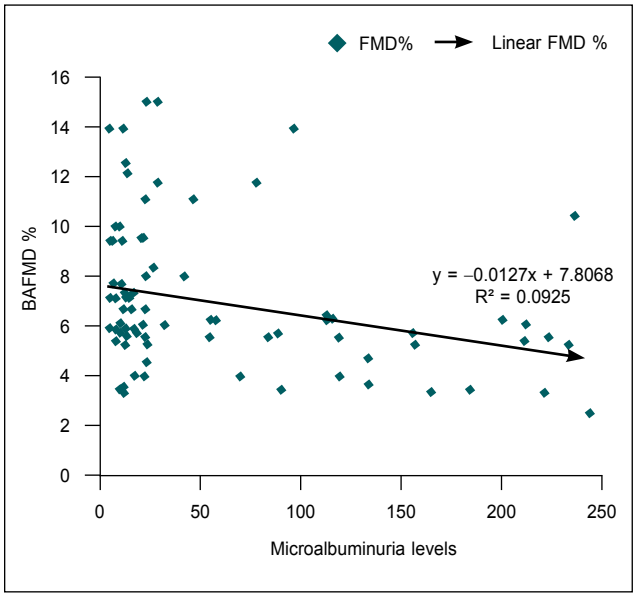

Figure 14. Microalbuminuria and BAFMD %.

towards the higher age groups, with a precipitous decline occurring at the 45 age cut-off. This trend across the age groups was statistically verified with a 'p' value = 0.001.

The number of males and females were equally distributed within the case and control group for comparability purposes. The prevalence of microalbuminuria reported by Sabharwal et al in males and females was found to be 34% and 30.7%, respectively.[4] In the present study, microalbuminuria was significantly higher among females (25%) compared to males (13.8%) (p = 0.039). Although various pathophysiological mechanisms have been propounded for this observation, it has to be pointed out that this may also reflect a certain fallacy arising in the nature of measurement of microalbuminuria, i.e., UACR. Urinary creatinine is a reflection of the overall body muscle mass and its metabolism, i.e., individuals with more muscle bulk tend to excrete higher levels of creatinine. In the measurement of UACR, as creatinine is placed in the denomination, and with middle-aged Indian females tending to have a decreased muscle bulk than their male counterparts, a higher UACR may be observed in females due to this inherent flaw.

Yang et al[5] studied the relationship of several cardiovascular risk factors (CVRF) to BAFMD in Chinese subjects and reported that according to multivariate analysis, negative FMD correlated with age ($\beta = -0.29$, $p < 0.001$), gender ($\beta = -0.12$, $p < 0.001$), BMI ($\beta = -0.12$, $p = 0.001$), waist circumference (WC) ($\beta = -0.10$, $p = 0.011$), SBP ($\beta = -0.12$, $p < 0.001$), fasting glucose ($\beta = -0.04$, $p = 0.009$), TC ($\beta = -0.04$, $p = 0.014$), smoking ($\beta = -0.05$, $p = 0.003$) and baseline brachial artery diameter ($\beta = -0.35$, $p < 0.001$). FMD decreased with increasing age in both genders. In women, FMD was higher than men and age-related decline in FMD was steepest after age 40; FMD was similar in men above 55 years old. In the present study, FMD was significantly different across the age groups (p = 0.001), lower among smokers (5.73 ± 2.69), higher among male (7.05 ± 2.55) compared to female (7 ± 3.38) (p = 0.87), lower in obese Grade I patients (7.16 ± 2.73) compared to obese Grade II (7.38 ± 2.72) and overweight (8.35 ± 3.37) (p = 0.007), lower in patients with Stage 2 HTN (6.58 ± 2.91) compared to Stage 1 HTN (7.53 ± 2.81) and prehypertension (8.73 ± 3.35) (p = 0.038), lower in patients with abnormal TC (>200 mg/dL), significantly lower in patients with abnormal TG (>150 mg/dL) compared to normal TC (p = 0.047) and significantly lower in patients with abnormal baseline diameter (>5) compared to normal baseline diameter (p < 0.001).

Multivariate analyses resulted in different conclusions. Schnabel et al noted that FMD was associated with age, sex, BMI, SBP, DBP, TC, HDL-C, TG, C-reactive protein, hypertension, hypertension treatment and dyslipidemia, whereas Philpott et al. argued FMD was only associated with SBP.[6,7] Although Mizia-Stec et al agreed FMD was associated with CVRF, he insisted that such correlations were limited among populations at high risk of cardiovascular disease.[8]

As observed in the current study, FMD was correlated with the traditional CVRFs including BP, blood lipid, obesity and smoking, in particular the baseline brachial artery diameter; however, it was not correlated with serum creatinine and uric acid. In our study, we further listed dyslipidemia, hypertension and smoking as the major risk factors. Grouping based on the number of risk factors showed that the FMD value declined along with the increase of the number of risk factors which means lower FMD was recorded in patients with multiple risk factors.

In the study by Yang et al, women had higher FMD values than men, which was consistent with a previous study,[9] suggesting the endothelial function is better in women than in men.[5,10] Contrary to these, in the present study, FMD was comparable between males (7.05 ± 2.55) and females (7 ± 3.38) (p = 0.87).

Gupta et al assessed the various factors affecting endothelial function in essential hypertensives and reported that endothelial dysfunction was significantly more quantified in Stage 2 HTN as compared with Stage 1 HTN (p < 0.01).[11] Similar to that, in our study, mean FMD was lower in patients with Stage 2 HTN (6.58 ± 2.91) compared to Stage 1 HTN (7.53 ± 2.81) and prehypertension (8.73 ± 3.35) (p = 0.038). Shimbo et al examined the cross-sectional and longitudinal relationships between endothelial dependent BAFMD and hypertension prevalence and incidence in 3,500 participants from the Multi-Ethnic Study of Atherosclerosis (MESA) and reported that reduced FMD was not an independent predictor of hypertension incidence, suggesting that impaired endothelial function does not play a major role in the development of hypertension.[12] Contrary to Shimbo et al, in the present study, FMD significantly decreased as we progressed to the higher stages of hypertension.

Mean FMD was significantly lower in patients with Stage 2 HTN (6.85 ± 2.91) compared to Stage 1 HTN (7.53 ± 2.81), prehypertension (8.73 ± 3.35) (p = 0.038) and the normotensive controls (10.61 ± 3.72). Whereas microalbuminuria was significantly distributed across the hypertensive ranges (p = 0.009). Mean FMD was significantly lower in patients with abnormal SBP (>140 mmHg) compared to normal BP, whereas microalbuminuria was significantly higher in patients with abnormal SBP (p = 0.001). Mean FMD was significantly lower in patients with abnormal DBP (>90 mmHg) compared to normal BP (p = 0.027), whereas abnormal microalbuminuria was significantly higher in patients with abnormal DBP (p = 0.005). Stehouwer et al concluded that both in nondiabetic and diabetic subjects, microalbuminuria is associated with an increased cardiovascular risk, independent of known risk determinants. As such, microalbuminuria is potentially useful for improved cardiovascular risk stratification.[13] Dinneen and Gerstein,[14] in a systematic review, showed microalbuminuria among individuals with type 2 diabetes to be associated with a 2.4-fold (95% confidence interval [CI] 1.8-3.1) increased risk for cardiovascular death as compared with normoalbuminuria. In addition, similar associations exist in hypertensive individuals (without diabetes) and in the general population.[15]

In the present study, mean FMD was lower in patients with abnormal microalbuminuria compared to normal (p = 0.016). Yokoyama et[16] measured FMD, carotid intima-media thickness (IMT) and pulse-wave velocity (PWV) in 158 subjects with type 2 diabetes (normo- 49, micro- 64, macroalbuminuria 45), explored the determinants of FMD and analyzed the relationship of FMD with traditional cardiovascular risk factors according to IMT and PWV levels.

They reported that microalbuminuria was significantly associated with lower FMD, higher IMT and higher PWV compared to normoalbuminuria (p < 0.001 for all). FMD was significantly correlated with IMT and PWV, and also with traditional risk factors, urinary albumin excretion (UAE), glomerular filtration rate, diabetic retinopathy and neuropathy. Multivariate regression analysis revealed that UAE remained a significant determinant of FMD independent of traditional risk factors, metabolic control and renal function. The relationship of FMD with IMT and PWV was less pronounced in subjects with increased IMT and PWV.[16] A report of Foster et al showed that microalbuminuria was associated with decreased hyperemic mean flow (47.2 ± 1.4 vs. 51.4 ± 0.5 mg/g, p = 0.005), but the association was not significant after multivariable adjustment (p = 0.09).[2] In agreement to this, in the present study, mean FMD was lower in patients with microalbuminuria compared to those with normal values (p = 0.016).

CONCLUSION

Traditional cardiovascular risk factors were significantly associated with both BAFMD and microalbuminuria. BAFMD had a significant inverse relationship with age (0.001), smoking (0.009), BMI (0.007), higher JNC VII stage of hypertension (0.038), duration of hypertension (0.002), SBP (0.027), DBP (0.022), abnormal TG levels (0.047) and a positive relationship with baseline diameter (<0.001).

Microalbuminuria was positively associated with female gender (0.039), smoking (0.001), stage of hypertension (0.009), duration of dypertension (0.001), SBP (0.005), DBP (0.036), abnormal TG levels (0.037), abnormal LDL-C levels (0.001).

Combination of more than one cardiovascular risk factor produced lower mean levels of BAFMD and higher levels of UAE.

BAFMD and microalbuminuria were significantly associated and the relationship was inverse in nature.

Based on the observations of the study, we can infer that:

- Both BAFMD as well as microalbuminuria can be used as surrogate markers in assessing increasing cardiovascular risk.
- BAFMD can be used as an effective tool to detect early hypertensive target organ damage, especially to the kidney.
- Hypertensive patients should be advised to maintain a within normal limit BMI.
- Effective therapeutic control of hypertension to prevent progress to higher stages of hypertension can prevent target organ damage.
- Hypertensive patients should be advised to cease smoking.
- Aggressive pursuit of target organ damage should be done in hypertensives, especially if the duration of hypertension exceeds 5 years.

REFERENCES

1. Modena MG, Bonetti L, Coppi F, Bursi F, Rossi R. Prognostic role of reversible endothelial dysfunction in hypertensive postmenopausal women. J Am Coll Cardiol. 2002;40(3):505-10.
2. Foster MC, Keyes MJ, Larson MG, Vita JA, Mitchell GF, Meigs JB, et al. Relations of measures of endothelial function and kidney disease: the Framingham Heart Study. Am J Kidney Dis. 2008;52(5):859-67.
3. Versari D, Daghini E, Virdis A, Ghiadoni L, Taddei S. Endothelial dysfunction as a target for prevention of cardiovascular disease. Diabetes Care. 2009; 32(Suppl 2):S314-S321.
4. Sabharwal KR, Singh P, Arora MM, Somani BL, Ambade V. Incidence of microalbuminuria in hypertensive patients. Indian J Clin Biochem. 2008;23(1):71-5.
5. Yang PT, Yuan H, Wang YQ, Cao X, Wu LX, Chen ZH. Correlations between brachial endothelial function and cardiovascular risk factors: a survey of 2,511 Chinese subjects. J Thorac Dis. 2014;6(10):1441-51.
6. Schnabel RB, Schulz A, Wild PS, Sinning CR, Wilde S, Eleftheriadis M, et al. Noninvasive vascular function measurement in the community: cross-sectional relations and comparison of methods. Circ Cardiovasc Imaging. 2011;4(4):371-80.
7. Philpott AC, Lonn E, Title LM, Verma S, Buithieu J, Charbonneau F, et al. Comparison of new measures of vascular function to flow mediated dilatation as a measure of cardiovascular risk factors. Am J Cardiol. 2009;103(11):1610-5.
8. Mizia-Stec K, Wieczorek J, Orszulak M, Mizia M, Gieszczyk-Strózik K, Sikora-Puz A, et al. Flow-mediated dilatation (FMD) and prevalence of cardiovascular risk factors: the value of FMD assessment in high risk patients is limited. Kardiol Pol. 2014;72(3):254-61.
9. Skaug EA, Aspenes ST, Oldervoll L, Mørkedal B, Vatten L, Wisløff U, et al. Age and gender differences of endothelial function in 4739 healthy adults: the HUNT3 Fitness Study. Eur J Prev Cardiol. 2013;20(4):531-40.
10. Virdis A, Taddei S. Endothelial aging and gender. Maturitas. 2012(4);71:326-30.
11. Gupta V, Sachdeva S, Khan AS, Haque SF. Endothelial dysfunction and inflammation in different stages of essential hypertension. Saudi J Kidney Dis Transpl. 2011;22(1):97-103.
12. Shimbo D, Muntner P, Mann D, Viera AJ, Homma S, Polak JF, et al. Endothelial dysfunction and the risk of hypertension: the multi-ethnic study of atherosclerosis. Hypertension. 2010;55(5):1210-6.
13. Stehouwer CDA, Smulders YM. Microalbuminuria and risk for cardiovascular disease: analysis of potential mechanisms. J Am Soc Nephrol. 2006;17:2106-11.
14. Dinneen SF, Gerstein HC. The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus. A systematic overview of the literature. Arch Intern Med. 1997;157(13):1413-8.
15. Jager A, Kostense PJ, Ruhe HG, Heine RJ, Nijpels G, Dekker JM, et al. Microalbuminuria and peripheral arterial disease are independent predictors of cardiovascular and all-cause mortality, especially among hypertensive subjects. Five-year follow-up of the Hoorn Study. Arterioscler Thromb Vasc Biol. 1999;19(3):617-24.
16. Yokoyama H, Sone H, Saito K, Yamada D, Honjo J, Haneda M. Flow-mediated dilation is associated with microalbuminuria independent of cardiovascular risk factors in type 2 diabetes - interrelations with arterial thickness and stiffness. J Atheroscler Thromb. 2011;18(9):744-52.

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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

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"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

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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

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Chromosome 3p Duplication: A Rare Chromosomal Anomaly

BRAJA KISHORE BEHERA*, RISHAV RAJ*, SAILABALA SHAW†, MITALI MAHAPATRA‡

ABSTRACT

Partial trisomy 3p results from either unbalanced translocation or *de novo* duplication. Common clinical features consist of dysmorphic facial features, congenital heart defects, psychomotor and mental retardation, abnormal muscle tone and hypoplastic genitalia. In this paper, we report a case of partial trisomy 3p with rare clinical manifestations. A full-term, female newborn was admitted to our hospital with complaints of repeated seizures and developmental retardation. On evaluation, chromosome 3p duplication was detected.

Keywords: Partial trisomy 3p, unbalanced translocation, seizures, developmental retardation, chromosome 3p duplication

Chromosome 3p duplication is an anomaly that occurs with an extra copy of genetic material on the short arm (p) of third chromosome. Another name for chromosome 3 duplication is trisomy 3p. It is a rare chromosomal disorder, where a portion of the short arm (p) of chromosome 3 is duplicated, so there are three copies of it rather than the normal two.

The severity along with the signs and symptoms depends on location and the size of duplication. Features that often occur in people with chromosome 3p duplication include developmental delay, behavioral problems, intellectual disability and distinctive facial features. Chromosome 3p duplication can be inherited from a parent with balanced translocation or *de novo* origin.[1,2] Treatment is based on the signs and symptoms on individual basis.

Signs and symptoms are brachycephaly, square face, frontal bossing, flat back of skull, small jaw, full cheeks, malformed auricles, widely spaced eyes, bushy eyebrows, downward slanting of eyes, short nose, large mouth, short upper lip, cleft lip and palate, short neck, short hand, stubby feet, excessive whorls, hemivertebrae, reduced muscle tone, seizure, congenital heart defect, esophageal atresia, hypoplastic kidney, ureteric duplication, growth retardation, speech retardation, mental retardation, feeding difficulty.

"*De novo*" duplications occur randomly during the formation of the egg or sperm. In these cases, a person would have no family history of the condition but could pass the duplication on to children. Other cases of chromosome 3p duplication are the result of a balanced translocation in one of the parents. Carriers of a balanced translocation generally do not have any unusual symptoms or health problems; however, they have an increased risk of having children with chromosomal abnormalities.

CASE REPORT

A 2½-year-old female child, a product of non consanguineous marriage with proper antenatal check-up and normal antenatal ultrasonography (USG) delivered through normal vaginal delivery (NVD) at hospital. Baby had not cried immediately after birth and was admitted to neonatal intensive care unit (NICU) and discharged after 3 days. At 2½ years, the baby came to the hospital with c/o delayed developmental milestones, repeated episodes of seizures at 20-25 days interval from the age of 7 months and poor weight gain. Baby recognized mother at 6 months, started neck holding at

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7 months, bi-syllable sound at 2 years, walked with support at 2 years. Baby was having head circumference of 40 cm, weight was 9 kg, mid-arm circumference was 12 cm, antimongoloid slant of eyes, brachycephaly, small jaw, broad and short nose, short neck, epicanthic fold, large mouth (Fig. 1), malformed auricle (Fig. 2),

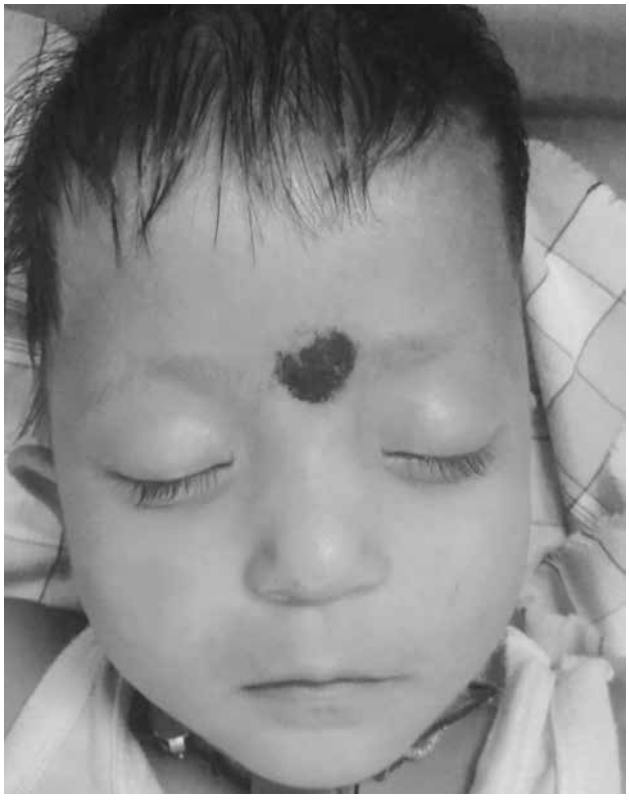

Figure 1. Facial anomaly.

Figure 2. Ear anomaly.

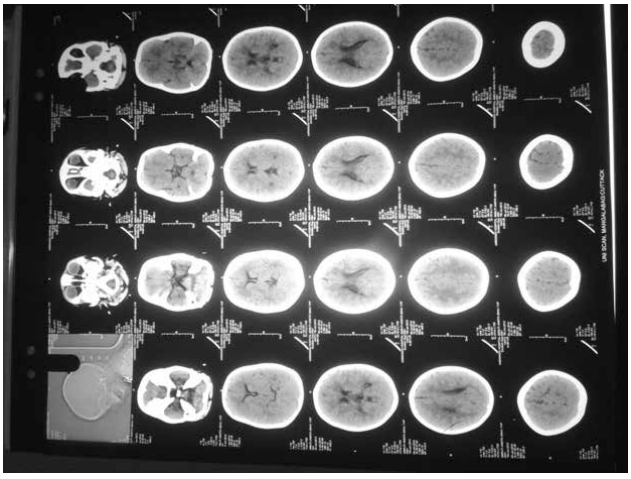

Figure 3. CT scan of brain.

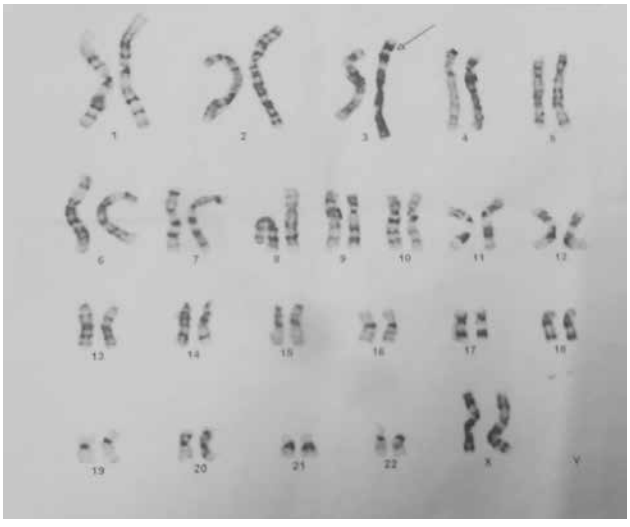

Figure 4. Chromosomal anomaly showing 3p duplication.

reduced muscle tone, seizures, growth retardation, mental retardation and speech retardation. On evaluating the child, complete blood count was normal. Electroencephalograms (EEG) showed normal sleep-wake cycle and normal EEG, CT brain showed no apparent anomaly (Fig. 3). On chromosomal analysis there was presence of duplication of segment between 3p22 and 3p25 (Fig. 4). For recurrent seizures, child was treated with levetiracetam and valproate, dietary modification advice and developmental counseling was properly given.

DISCUSSION

Our bodies are made of billions of cells. In each cell is a set of structures called chromosomes that carry all of the instructions (genes) for the cell to function. We generally have 23 pairs of chromosomes and inherit one in each pair from each parent. Sometimes,

a section from one chromosome of a particular pair changes places with a section from a chromosome of another pair. When the two breaks do not pass through a gene and there is no gain or loss of material when the chromosomes are looked at under a microscope, it is called a balanced translocation.

Some people discover from a blood test when they have had a child with special needs or health problems caused by a chromosome disorder. Some people have repeated miscarriages or other fertility problems. Some people have a blood test as part of family investigations. Others find out by chance when they have a chromosome test for other reasons. Occasionally, a balanced translocation is found in a baby during pregnancy. Translocations can be new or they can be passed down in families from parent to child through the generations. New translocations occur when sperm or egg cells are forming or just after fertilization during the copying of the early cells that will become an embryo, then a fetus and then a baby. One study suggests that most new balanced translocations arise during sperm production and particularly in older fathers. They are not caused by men's lifestyle, environment or work. Duplication of the short arm of chromosome 3 is associated with severe delay in mental development. More than 50% of children die within the first 2 years of life. Duplications may be due to paternal or maternal balanced translocation.

The list of signs and symptoms mentioned in various sources for trisomy 3p inlude:[3-5]

- **Skull**: Brachycephaly, holoprosencephaly, flat back of skull, temporal indentations.
- **Face:** Square face, frontal bossing, small jaw, facial clefts, full cheeks.
- **Eyes**: Widely spaced eyes, iris coloboma, small eyes, telecanthus, bushy eyebrows, downward slanting space between eyelids, cyclopia, epicanthal folds.
- **Nose:** Short nose, broad nose, flat nose, prominent philtrum, choanal atresia.
- **Ear:** Malformed auricles.
- **Mouth:** Large mouth, short upper lip, cleft lip, cleft palate.
- **Neck**: Short neck.
- **Extremities:** Short hands, stubby hands, short feet, stubby feet, camptodactyly, syndactyly, brachymesophalangy, clubfoot, excessive fingertip whorls, joint contractures.
- **Cardiac defects**: Congenital heart defects including tetralogy of Fallot, ventricular septal defect, hypoplastic heart and transposition of the great vessels.
- **Central nervous system**: Seizures.
- **Muscles:** Severe hypotonia.
- **Gastrointestinal**: Esophageal atresia, atresia of the colon and rectum.
- **Miscellaneous:** Hemivertebrae, reduced muscle tone, accessory nipples, esophageal atresia, atresia of colon, rectal atresia, hypogonadism, hypospadias, small penis, undescended testes, duplication of ureters, kidney hypoplasia, kidney cysts, hypercholesterolemia, growth retardation, motor retardation, speech retardation, mental retardation and feeding difficulty.

There are several different specialized tests that can be used to diagnose a chromosome 3p duplication. These include:

- **Karyotyping:** A karyotype is a laboratory test that produces an image of a person's chromosome. This test can be used to diagnose large duplications.
- **FISH:** A laboratory technique that is used to detect and locate a specific DNA sequence on a chromosome. A chromosome is exposed to a small DNA sequence called probe that has a fluorescent molecule attached to it. The probe sequence binds to its corresponding sequence on the chromosome. This test can be used in combination with karyotyping for duplications that are too small to be seen on karyotype. However, FISH is only useful if the person ordering the test suspects there is a duplication of a specific region of 3p.
- **Array CGH:** A technology that detects duplications that are too small to be seen on karyotype.

REFERENCES

1. Han DH, Chang JY, Lee WI, Bae CW. A case of partial trisomy 3p syndrome with rare clinical manifestations. Korean J Pediatr. 2012;55(3):107-10.
2. Natera-de Benito D, García-Pérez MA, Martínez-Granero MÁ, Izquierdo-López L. A patient with a duplication of chromosome 3p (p24.1p26.2): a comparison with other partial 3p trisomies. Am J Med Genet A. 2014;164A(2): 548-50.
3. Allen DL, Foster RN. Anaesthesia and trisomy 3p syndrome. Anaesth Intensive Care. 1996;24(5):615.
4. Kotzot D, Krüger C, Braun-Quentin C. De novo direct duplication 3 (p25-->pter): a previously undescribed chromosomal aberration. Clin Genet. 1996;50(2):96-8.
5. Walzer S, Favara B, Ming PM, Gerald PS. A new translocation syndrome (3/B). N Engl J Med. 1966;275(6):290-8.

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Huge Denture Causing Acute Obstruction in Esophagus and Stridor

SHAMENDRA KUMAR MEENA

ABSTRACT

We report a rare case of an unusually long foreign body (denture) impacted in the mid esophagus of a 62-year-old man. He was illiterate and drank wine regularly. He came to me with some attendants with history of taking wine with lunch, followed by acute obstruction since lunch at 12:30 pm and reached Kota by 9:30 pm. Till then, he was nil by mouth (NBM). Following investigations, we made a diagnosis of foreign body esophagus and with the help of rigid esophagoscopy under general anesthesia, we removed the foreign body. Next morning, he could swallow food and water without any difficulty, and we discharged him.

Keywords: Foreign body, esophagus, denture

A large number of ingested foreign bodies, especially smooth or <12 mm in diameter, tend to pass safely through the gastrointestinal tract. However, severe problems, such as perforation, may occur following ingestion of sharp objects, bone fragments, pins or long foreign bodies (>6.5 cm).[1,2] The postcricoid region is a common site of impaction of foreign bodies (in nearly 84% of the subjects). Impaction of a bolus of food in the distal esophagus in adults is often associated with a pre-existing stricture, diverticulum or tumor.[2] Adults with non-food foreign bodies have a high incidence of psychiatric and social derangements. Most foreign bodies pass through the pylorus; however, some objects may remain in the stomach for a long period. Once they have crossed the pyloric canal, most objects, even sharp-edged foreign bodies such as pieces of glass or nails, pass without harm. But, terminal ileum is again a site with predisposition for impaction. Sometimes, the ingested foreign bodies may remain fixed in the cecum, ascending colon or sigmoid colon.[2] Noncontrast computed tomography (CT) scan is done for diagnosing suspected upper esophageal foreign bodies that may not be visible on plain radiography,[3] and in order to rule out perforation.[4]

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CASE REPORT

A 62-year-old gentleman presented to the emergency services at night with complaints of difficulty in swallowing, pain on swallowing, drooling of saliva and pain in the chest following the accidental ingestion of denture while drinking wine and eating lunch. He reported that suddenly he swallowed a piece of denture, measuring approximately 4-5 cm, that caused acute obstruction and distress. He was also having problem in respiration. He came to me at 9:30 pm at night from Bundi. He could not retrieve it and landed in emergency department.

He was illiterate, without any chronic disease, and at presentation, there were symptoms of respiratory distress or hoarseness. The general physical examination was unremarkable except that he was looking anxious (Fig. 1). Examination of the ear, nose and throat was all within normal limits and on indirect laryngoscopy, there was pooling of saliva in both pyriform sinuses. An X-ray of the neck and chest region, anteroposterior (AP) and lateral view, was unremarkable (Fig. 2).

Subsequently, a CT scan of the neck and chest region revealed a long radio-opaque foreign body in the whole length of the esophagus and also impinging into the stomach. So, a diagnosis of foreign body esophagus was made and the patient was subjected to rigid esophagoscopy under general anesthesia. Using an adult esophagoscope, upper end of the foreign body was encountered just beyond the cricopharynx and it

Figure 1. Patient with respiratory distress and looking anxious.

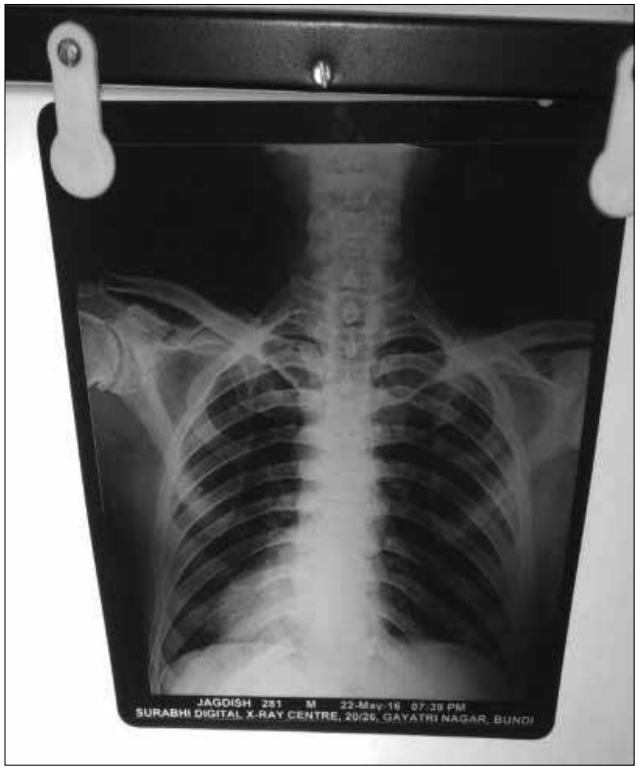

Figure 2. X-ray evaluation was unremarkable.

was grasped securely with a grasping forceps and the foreign body was removed with the Jackson's rigid esophagoscope (Fig. 3).

A check esophagoscopy was done and revealed no injury to the esophageal mucosa. The postoperative period was uneventful and the patient was allowed food orally after 12 hours.

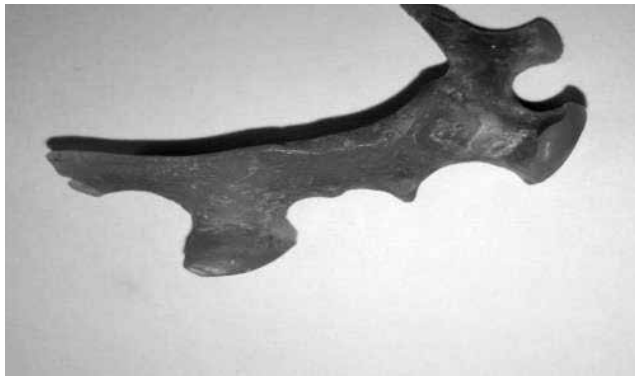

Figure 3. Foreign body removed.

DISCUSSION

A foreign body impacted in the esophagus calls for immediate attention and treatment. Dysphagia (92%) and tenderness in neck (60%) have been found to be the most common clinical features. A vast majority of patients come to the hospital within 24 hours of foreign body impaction. X-ray of the neck (lateral view) appears to be the most valuable investigation tool. Presence of air in the esophagus is a significant finding.[5] Most foreign bodies are radio-opaque and can be recognized on a plain radiograph. Their progress can be checked periodically in the bowel. Bone fragments look like linear or slightly curved densities with sharp margins. Small fish bones or pieces of plastic and wood; however, can appear only faintly radio-opaque calling for a CT scan for their detection.[2] Foreign bodies in hypopharynx and cervical esophagus such as chicken and fish bones often require radiologic evaluation. Noncontrast CT scan may show these small calcified esophageal foreign bodies when X-ray and barium swallow fail.[6]

Indirect signs that can be seen on plain radiography include soft tissue swelling and/or air due to edema or hematoma. In case of suspected perforations, esophagography should first be performed with hydrosoluble contrast medium to exclude perforation and can then be followed by a barium examination. The contrast medium may impregnate the surface of the foreign body and making it noticeable. Dilatation of the esophagus proximal to the obstruction with air fluid level and absence of air in the fundus of the stomach are signs of impaction in the distal esophagus, as evidenced on a radiograph.[2]

The postcricoid region was found to be the site of impaction of foreign bodies in 84% of the subjects in a study. Esophagoscopy was successful in 97% of the patients and failed in 3%. Coins appear to be the most common foreign bodies (60%), followed by meat-related

foreign bodies (22.5%) and dentures (5%). Complications were noted in 18% patients and were more common in adults (37.1%) in comparison with children (8.8%). Pneumomediastinum was the most serious of all complications. Maximum complications occur with dentures (80%) and bone chips (42%).[5] Foreign body in the esophagus is therefore a serious condition and warrants early removal by rigid esophagoscopy as it is a safe and effective procedure.

Other treatment interventions involve removal with a laryngoscope in case of foreign bodies impacted in the pharynx, or with a hypopharyngoscope for hypopharyngeal foreign bodies. Less easily, foreign bodies can be removed using a flexible esophagoscope. The common complications encountered with a rigid esophagoscope include injury to the lips, teeth, tongue, palate and esophageal perforation commonly at the level of cricopharyngeal sphincter.[2] Complications can; however, be limited if treatment is initiated within 24 hours of foreign body impaction.[7]

Sharp end of the foreign body has to be taken in the lumen of the endoscope to avoid complications. Partial dentures with sharp hooks, metallic springs and screws are the most difficult and dangerous objects to remove from the esophagus.[8] One can cause laceration and perforation during removal of such objects.

CONCLUSION

Early diagnosis and immediate removal of a foreign body are key to avoid any complications. Although 80-90% of the foreign bodies pass smoothly through the gastrointestinal tract, the nature of foreign body has to be determined. In case of a disc battery, it should be removed surgically if it remains in any one position for more than 24 hours. Sharp and large foreign bodies such as a screw have to be removed to prevent any further complications.

It is advisable to have a team approach while dealing with sharp and impacted foreign bodies.

REFERENCES

1. Taylor RB. Esophageal foreign bodies. Emerg Med Clin North Am. 1987;5(2):301-11.
2. Singhal SK, Arora V, Dass A. An unusual foreign body of esophagus. Online J Health Allied Sci. 2010;9(1):14.
3. Marco De Lucas E, Sádaba P, Lastra García-Barón P, Ruiz-Delgado ML, González Sánchez F, Ortiz A, et al. Value of helical computed tomography in the management of upper esophageal foreign bodies. Acta Radiol. 2004;45(4):369-74.
4. Mosca S, Manes G, Martino R, Amitrano L, Bottino V, Bove A, et al. Endoscopic management of foreign bodies in the upper gastrointestinal tract: report on a series of 414 adult patients. Endoscopy. 2001;33(8):692-6.
5. Khan MA, Hameed A, Choudhry AJ. Management of foreign bodies in the esophagus. J Coll Physicians Surg Pak. 2004;14(4):218-20.
6. Braverman I, Gomori JM, Polv O, Saah D. The role of CT imaging in the evaluation of cervical esophageal foreign bodies. J Otolaryngol. 1993;22(4):311-4.
7. Sittitrai P, Pattarasakulchai T, Tapatiwong H. Esophageal foreign bodies. J Med Assoc Thai. 2000;83(12):1514-8.
8. Holinger LD. Management of sharp and penetrating foreign bodies of the upper aerodigestive tract. Ann Otol Rhinol Laryngol. 1990;99(9 Pt 1):684-8.

■■■■

US President Urges States to Prioritize Vaccinations for Teachers

US President Joe Biden has urged all states to give priority to teachers for COVID-19 vaccinations in order to ensure that children could go back to school quickly and safely. He stated that every educator should be administered at least one dose by the end of this month.

With three vaccines now available, the President was confident that enough vaccines would be available for every adult in the country by the end of May. He also stated that Merck & Co Inc would assist in making Johnson & Johnson's single-dose COVID-19 vaccine. The President said that he was optimistic that they would attain the goal of delivering 100 million vaccine doses in his first 100 days in office. However, he recommended that people should remain vigilant in wearing masks and observing social distancing… (*Reuters*)

Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

Acute Intermittent Porphyria: A Frequently Misdiagnosed Chameleon!

ARVIND VYAS*, DIVYA GOEL†

ABSTRACT

Acute intermittent porphyria (AIP) is an inborn disorder of heme biosynthesis, autosomal dominant in inheritance. It is a frequent occurrence in young females of reproductive age group. While abdominal pain is the most frequent presentation of this disorder, it can present with a myriad of clinical and biochemical features, frequently leading to misdiagnosis of this condition. We present a case of a 17-year-old young female who presented with an acute onset weakness in all four limbs along with absent deep tendon reflexes but characteristically preserved ankle jerks, who was initially diagnosed as Guillain-Barré syndrome (GBS), treated with intravenous immunoglobulin (IVIg), succumbed to a chronic progressive course of weakness and put on oral steroids. Lack of improvement and subsequent development of abdominal pain led us to investigate her for urine for porphobilinogen which came out to be positive, thus leading to a final diagnosis of AIP.

Keywords: Acute intermittent porphyria, abdominal pain, Guillain-Barré syndrome

Porphyrias are a group of relatively uncommon metabolic disorders produced by defective biosynthesis of heme. There are broadly two categories, i.e., hepatic and erythroid and clinically they can be classified as neurovisceral, cutaneous or mixed. Acute intermittent porphyria (AIP) is the most common of all and results from partial deficiency of porphobilinogen deaminase enzyme. Being an easily missed entity, it should be looked for with high index of suspicion in any patient presenting with acute onset weakness and abdominal pain. There have been case reports on misdiagnosis of AIP mostly as Guillain-Barré syndrome (GBS) due to acute presentation of the disease. We report a case here with acute presentation of weakness of all four limbs, subsequently attaining a progressive form of weakness and wasting, mimicking chronic inflammatory demyelinating polyneuropathy (CIDP). Based on our literature search, this transition from acute to chronic phase in AIP has not been described before.

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CASE REPORT

A 17-year-old young female presented with history of subacute onset weakness of all four limbs in the form of difficulty in carrying out overhead activities and performing fine activities, along with difficulty in rising from sitting position, for the last 4 months. There was no associated sensory complaint, difficulty swallowing, bowel or bladder involvement. She was treated 4 months back as a case of acute motor axonal neuropathy (AMAN) variant of GBS with intravenous immunoglobulin (IVIg) on the basis of her neurophysiological study, which revealed pure motor axonal affection of the tested nerves. She developed acute abdominal pain during hospital stay along with vomiting and was treated as a case of acute cholecystitis. After 15 days, as no significant improvement was found, she was subjected to nerve biopsy and started on oral corticosteroid treatment thinking of CIDP. She had minimal improvement with steroids; her nerve biopsy report was inconclusive and after 4 months, she presented to our institute with residual and static weakness. On asking about her family, she revealed that her younger sister suffered with fever, abdominal pain and seizures last year, which lasted for a month, followed by her sad demise.

On examination, the patient was tachypneic and had resting tachycardia. On neurological examination, there was wasting of posterior fibers of deltoid; both anterior and posterior compartments of arms and

Figure 1. Bilateral wrist drop.

Figure 2. Urine sample turned cola-colored on exposure to sunlight.

forearms bilaterally; interossei, chiefly the first dorsal interosseous; anteromedial compartment of thighs and calf muscles. Generalized hypotonia was present along with bilateral wrist drop (Fig. 1). Power was 4/5 in upper limbs at shoulder and elbow joints, 0/5 at dorsiflexors of wrists, 4/5 in lower limbs at hip and knee joints, 5/5 at ankle bilaterally. Deep tendon reflexes were absent, except ankle jerk which was 2+ bilaterally. Sensory and cerebellar examination was unremarkable. Her urine sample was sent for porphobilinogen and a sample was also kept in sunlight to see for change in its color (Fig. 2) considering the past history of acute abdominal pain, vomiting, neuropathy along with suspected positive family history. The report came out to be positive and patient was advised high carbohydrate diet and avoidance of all the drugs that precipitate porphyria. Thus, after a great diagnostic odyssey, the patient was finally labeled as AIP and advised high carbohydrate diet. On follow-up after 2 months, the patient has shown marked improvement in her functional status.

DISCUSSION

Porphyrias are heme biosynthetic disorders leading to accumulation of toxic porphyrin precursors and porphyrin itself, the excess of which accumulates in various tissues giving rise to a myriad of clinical features. There are eight main varieties of hepatic and erythroid porphyrias, amongst which AIP is the most common. It is caused by the deficiency of porphobilinogen deaminase leading to excessive accumulation and urinary excretion of porphobilinogen. AIP is most prevalent in young females of reproductive age group and crises mostly occur after puberty. This disease is manifested by acute gastrointestinal manifestations like abdominal pain, nausea, vomiting, constipation; neurological manifestations like neuropathy involving both motor and sensory nerves, psychiatric symptoms, seizures; cardiovascular manifestations like arrhythmias and autonomic disturbances.

The symptoms can range from acute crisis to chronic progressive neurological weakness, thus making it difficult to be diagnosed timely. AIP can mimic many other illnesses like in our case, the patient was initially thought to have GBS with co-existent cholecystitis. Subsequently, when she attained a chronic progressive course of weakness, she was treated as CIDP but all in vain. Misdiagnosis of GBS in a case of porphyria has been reported previously, highlighting the fact that muscular weakness progressing to quadriparesis can mimic GBS in a case of porphyria.

CONCLUSION

This case establishes the fact that AIP can be a great masquerader and thus easily misdiagnosed in clinical settings. Thus, a high index of suspicion is required when confronted with a blend of gastrointestinal and neurological manifestations in a patient in order to prevent a delayed diagnosis and grave outcomes.

SUGGESTED READING

1. Foran SE, Abel G. Guide to porphyrias. A historical and clinical perspective. Am J Clin Pathol. 2003;119 Suppl:S86-93.
2. Thadani H, Deacon A, Peters T. Diagnosis and management of porphyria. BMJ. 2000;320(7250):1647-51.
3. Kauppinen R. Porphyrias. Lancet. 2005;365(9455):241-52.
4. Anderson KE, Bloomer JR, Bonkovsky HL, Kushner JP, Pierach CA, Pimstone NR, et al. Recommendations for the diagnosis and treatment of the acute porphyrias. Ann Intern Med. 2005;142(6):439-50.
5. Oomman A, Gurtoo A. Acute intermittent porphyria as a cause of acute respiratory failure. J Indian Med Assoc. 2002;100(1):44, 46.
6. Suarez JI, Cohen ML, Larkin J, Kernich CA, Hricik DE, Daroff RB. Acute intermittent porphyria: clinicopathologic correlation. Report of a case and review of the literature. Neurology. 1997;48(6):1678-83.
7. González-Arriaza HL, Bostwick JM. Acute porphyrias: a case report and review. Am J Psychiatry. 2003;160(3):450-9.

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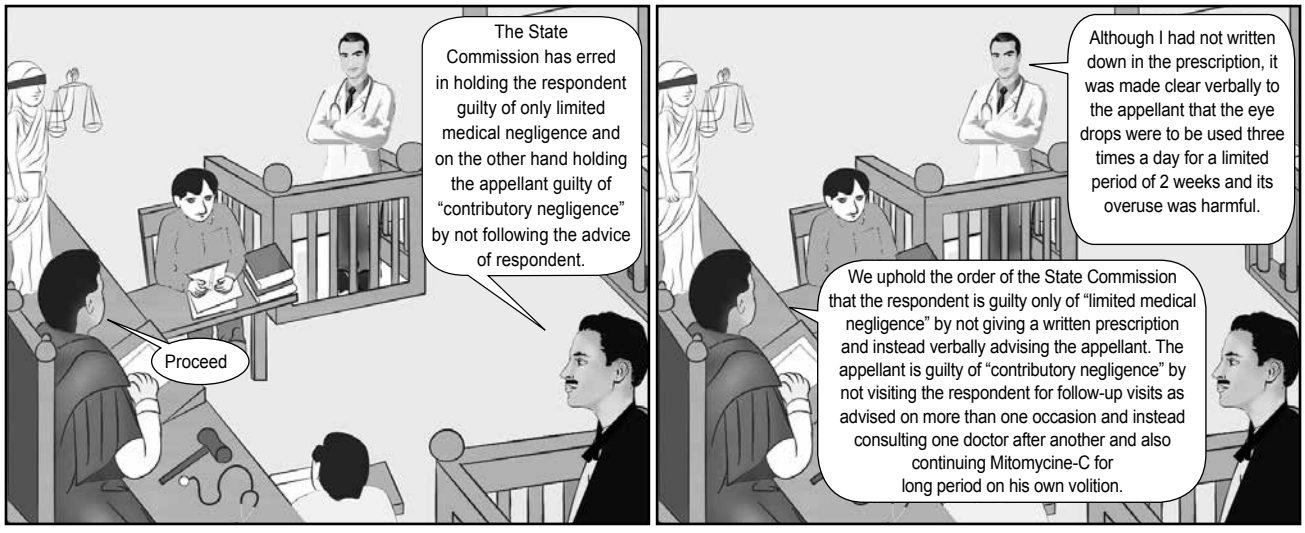
Case of Limited Negligence on Part of the Doctor and Contributory Negligence by the Patient



Lesson: The order dated 31.08.2006 in Complaint Case No. C-21/95 of the State Consumer Disputes Redressal Commission Delhi stated "By not prescribing in writing in the prescription that medicine Mitomycine-C should be used, at first instance, only for 2 weeks, OP has committed an offence of limited medical negligence as complainant also cannot be excused for contributory negligence by not approaching the treating doctor after few days and hopping from one doctor to another and continued using the medicine for long resulting in dry-eye syndrome causing loss of vision in the eye."

COURSE OF EVENTS

- June 1993: Following a minor complaint of a cosmetic nature in his left eye, the appellant consulted respondent, who is an eye surgeon, in his clinic in Daryaganj, who after examining him informed that he was suffering from an innocuous growth known as pterygium and since there was likelihood that the growth may increase, excision was advised through a minor surgery, which would ensure that the appellant's eye would become normal within 5 days. Appellant, therefore, agreed to undergo this surgery.
- October 1993: The respondent conducted the surgery on the appellant at his clinic and the appellant was thereafter prescribed medicines for both local application, which included Mitomycine-C, as also oral medication. However, soon after, the appellant's left eye became red and there was acute pain and irritation, which persisted, and therefore he consulted the respondent, who assured him that if he continues to regularly use Mitomycine-C, his eye would become normal. However, during the course of using this medicine, appellant's eye further deteriorated and became very dry and there was loss of vision in that eye. Appellant complained about this to the respondent, who changed the medicine, which only further aggravated the condition.
- The appellant consulted another ophthalmologist Dr G, who informed him that his left eye had become very dry due to wrong prescription of Mitomycine-C and he was advised to consult Dr P at Hospital A, New Delhi.
- Dr P confirmed that the eye had got damaged due to prolonged use of Mitomycine-C.
- The appellant thereafter went to hospital B where this diagnosis was confirmed by a cornea specialist, Dr A. He was advised to stop using all the medicines, including Mitomycine-C.
- Being aggrieved because of the medical negligence and deficiency in service on the part of respondent, because of which the appellant's eye became dry,

he issued a legal notice to respondent to pay him Rs. 10 Lakhs as compensation but received no response.

- Appellant, therefore, approached the State Commission with a complaint of medical negligence and deficiency in service against respondent and requested that he be directed to pay Rs. 10 lakhs as damages and compensation since there was total loss of vision in appellant's left eye, which had adversely affected both his professional and personal life, as also any other relief as deemed appropriate.
- Respondent on being served filed a written rejoinder denying the above allegations, which he termed as false, frivolous and vexatious. It was contended that appellant approached him with a condition known as pterygium, which is a growth of extra skin and if it reached the pupil area of the eye, it could permanently hamper the appellant's vision. Surgery was, therefore, necessary, which was satisfactorily conducted. The appellant thereafter advised both oral medication as also medicine through local application.
- After a week, when the healing of the appellant's eye was completed, respondent advised the respondent to use Mitomycine-C for 2 weeks since this was necessary to prevent recurrence of pterygium. This medicine, which comes in the form of injection, was converted into eye drops for use three times a day and appellant was verbally told that over use of this medicine for more than 2 weeks is harmful.
- Unfortunately, the appellant did not heed this advice and instead of coming back for a further check up appears to have continued using Mitomycine-C and taking treatment from various other doctors as per his own whim and fancy.
- It was only on 03.03.1994 i.e. after over 4 months that appellant visited the respondent and told him that he was still continuing the use of Mitomycine-C. Respondent immediately asked him to discontinue the same and to come back after 15 days.
- The appellant again did not heed this advice and consulted the respondent after 3 months i.e. on 22.06.1994 when he was prescribed natural tear drops and lacri-lube ointment.
- A perusal of these facts clearly indicate that it was the appellant who was responsible for the damage caused to his left eye by prolonged use of Mitomycine-C on his own volition and against medical advice given by respondent. There was, therefore, no deficiency in service or medical negligence of respondent.
- The State Commission after hearing the parties and on the basis of evidence produced before it held the respondent guilty of "limited negligence" by not advising the appellant in writing to use Mitomycine-C only for a particular limited period. The relevant part of the order of State Commission reads as follows:

"*By not prescribing in writing in the prescription that medicine Mitomycine-C should be used, at first instance, only for 2 weeks to OP has committed an offence of limited medical negligence as complainant also cannot be excused for contributory negligence by not approaching the treating doctor after few days and hopping from one doctor to another and continued using the medicine for long resulting in dry-eye syndrome causing loss of vision in the eye. OP is guilty of this limited medical negligence amounting to deficiency in service due to which the complainant has lost his vision of one eye though he can also be not absolved from contributory negligence which is a mitigating circumstance for awarding compensation.*"

The State Commission, therefore, held that a lump-sum compensation of Rs. 50,000/- to the appellant would meet the ends of justice.

- Being aggrieved by the lesser compensation, the present first appeal has been filed before National Consumer Disputes Redressal Commission (NCDRC).

ALLEGATION OF THE APPELLANT

- Learned counsel for the appellant contended that the State Commission erred in holding the respondent guilty of only limited medical negligence and on the other hand holding the appellant guilty of "contributory negligence" by not following the advice of respondent.
- Following the surgery, the appellant did visit the respondent doctor for further check-up prior to 03.03.1994. According to appellant, respondent had prescribed him Mitomycine-C on 18.10.1993 and the prescription did not indicate either the duration for taking the medicine or its possible harmful side effects.
- The appellant was also not advised when he should come back for a follow-up check. Further, when the appellant visited the respondent on 03.03.1994 with a serious complaint regarding his operated

eye, respondent again sought to hide the correct facts by recording that the condition of appellant's eye as also the vision was normal.

- Since the appellant had already started losing his eyesight and he was having acute pain in his eye, he was constrained to approach other doctors, who advised the appellant to immediately stop the use of Mitomycine-C. It was these doctors who informed him that the problem in his left eye had occurred due to over use of Mitomycine-C, which should not have been used for more than 2 weeks.
- Counsel for the appellant further stated that the conduct of the respondent was suspect before the State Commission as is evident from the fact that he did not produce the necessary documents on the ground that these had been destroyed in a fire. Because of the medical negligence and callousness on the part of respondent, appellant lost the vision in his left eye causing him a great deal of mental agony and adversely affecting his work as a senior clerk in the Supreme Court of India.

REJOINDER OF THE RESPONDENT

- Learned counsel for respondent denied the above allegations and stated that it is not factually correct that respondent had prescribed Mitomycine-C to the appellant on 18.10.1993 i.e. immediately following the surgery. In fact, he was prescribed other medicines and ointments after the surgery and it was only after a week when the eye had healed that Mitomycine-C was prescribed to the appellant.
- It is a proven fact in ophthalmology medical literature that Mitomycine-C is successful in checking the recurrence of pterygium, which has a very high incidence of recurrence and is routinely prescribed for limited periods following such surgeries. It was under these circumstances that respondent rightly prescribed this medicine to the appellant. Although not written down in the prescription, it was made clear verbally to the appellant that the eye drops were to be used three times a day for a limited period of 2 weeks and its over use was harmful.
- This is further confirmed by the fact that respondent converted only one vial of Mitomycine-C injection into eye drops, which would have lasted at the most for a little over 2 weeks. From this fact alone, it is clear that the Appellant had been procuring this medicine and getting it converted into eye drops from some other doctor(s) and in this way using it for several weeks i.e. till 03.03.1994 when he next visited the respondent, who immediately directed him to discontinue the use of this medicine.
- Learned counsel for respondent pointed out that a senior ophthalmologist of hospital A, Dr M, has confirmed to him in writing that appellant had consulted him and also informed him that he was continuing to use Mitomycine "on his own".
- Appellant continued to disregard medical advice of Respondent even after 03.03.1994 by not coming for follow-up visits, which he was advised to do by respondent, who had prescribed him some other medicines and wanted to assess their effect.
- From the above facts, it is clear that appellant, who was not an illiterate person and who had been clearly orally advised to use Mitomycine-C eye drops only for a limited duration by respondent, failed to follow this advice and continued to use the medicine on his own, for which respondent cannot be held responsible, particularly since appellant did not even come for the follow-up visit after 2 weeks. There was no medical negligence or deficiency in service on the part of respondent, who had prescribed the right medicine and given correct advice regarding its limited period of use. The present first appeal, therefore, having no merit deserves to be dismissed.

OBSERVATIONS OF NCDRC

- The appellant visited the respondent's clinic with a complaint in his left eye and was detected with pterygium, for which a minor surgery was conducted is not in dispute.
- It is also a fact that appellant was prescribed Mitomycine-C by respondent, which is a drug of choice, to ensure that pterygium does not recur since it has a high degree of recurrence.
- While it is a fact (as also observed by the State Commission) that no directions were given by respondent in writing to appellant regarding the duration for which the drug should be used or any written precaution against its prolonged use, we find force in the contention of respondent that since he had converted only one vial of Mitomycine injection into eye drops, this itself indicates that the intention was clearly for its limited use for about 2 weeks and not for several months.
- When specifically asked by us, learned counsel for the appellant also fairly conceded that respondent had converted only one vial of Mitomycine injection into eye drops, thus confirming the respondent's clear intention regarding its use for a limited period. It is, thus, apparent that appellant

had been using this medicine for several weeks by getting the Mitomycine injection converted into eye drops through some other source and not by the respondent, for which respondent cannot be held responsible.

- It was under these circumstances that the State Commission had held the respondent guilty of only "limited medical negligence" for not having put down in writing the dosage and duration of the medicine in the prescription slip.

ORDER OF THE NCDRC

We agree with this finding. We further agree that the appellant is guilty of "contributory negligence" by not visiting the respondent for follow-up visits as advised on more than one occasion and instead consulting one doctor after another and also continuing Mitomycine-C for long period on his own volition, which resulted in the dry eye syndrome and consequent loss of vision in the left eye. To sum up, we uphold the order of the State Commission that respondent is guilty only of "limited medical negligence" by not giving a written prescription and instead verbally advising the appellant, for which a compensation of Rs. 50,000/- is reasonable and we, therefore, confirm the same. The present first appeal is dismissed. Respondent is directed to pay a sum of Rs. 50,000/- to the appellant within 6 weeks, failing which it will carry interest @ 6% per annum for the period of default. No costs.

REFERENCE

1. Case no. 692 of 2006, NCDRC; Order date 16.01.2013.

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One in Four People Estimated to have Hearing Problems by 2050: WHO

One in four people, or close to 2.5 billion individuals globally, are projected to be living with some degree of hearing loss by the year 2050, cautions the WHO's first World Report on Hearing.

According to the report, around 700 million of these people will need access to ear and hearing care as well as other rehabilitation services. The report has been released ahead of World Hearing Day on March 3, and emphasizes the need to accelerate efforts for preventing and addressing hearing loss by means of investment in ear and hearing care services and also by expanding access to such key services. The report outlines the evidence-based interventions that all countries must include in their health systems… (*WHO*)

WHO Panel Advises Against Hydroxychloroquine use for COVID-19

A WHO expert panel has advised against the use of hydroxychloroquine for prevention of COVID-19 and has stated that the drug has no significant effect on patients who have already contracted the infection.

The agency's Guideline Development Group (GDG) expert panel wrote in the *BMJ* that hydroxychloroquine should not be used in the fight against COVID-19. It further stated that it will not be beneficial to explore the drug in further research studies of possible COVID-19 treatments. As per experts, this "strong recommendation" comes after high-certainty evidence from six randomized controlled trials that included over 6,000 individuals, both with and without exposure to COVID-19… (*Reuters*)

Unrealistic to Think this Virus will be Finished by Year-end: WHO

The WHO has cautioned that it is unrealistic to think that the COVID-19 pandemic will be over by the end of the year.

Michael Ryan, WHO emergencies director, stated that it might be possible, however, to decrease hospitalizations and deaths. Ryan said that it would be premature and unrealistic to think that we will be able to finish this virus by the end of this year, adding that we may be able to finish with the tragedy associated with the pandemic. He further stated that vaccinating frontline healthcare workers and the people who are most vulnerable to severe disease would take the fear out… (*NDTV - Agence France-Presse*)

Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

Medtalks with Dr KK Aggarwal

CMAAO Coronavirus Facts and Myth

Can Vaccination be Mandated?

Yes

- Even if one country has a persistent infection, the mutations will occur continuously.
- The available evidence suggests that vaccines are very safe. The public health data suggests that coronavirus disease 2019 (COVID-19) is a considerable health risk, and hence people should be vaccinated to protect themselves.
- It is a novel virus and hence will infect 100% population if the person gets exposed.
- It is the individual choice to choose between corona or vaccine!
- Vaccine mandates may become necessary once we have more vaccines than people willing to take them.
- An employer can mandate vaccine on the job as long as they are not applying it in a discriminatory fashion and making it mandatory for all.
- Vaccine is now available for all healthcare workers as hospitals can mandate it, and patients may ask for treatment only from vaccinated individuals.
- COVID-19 neutralizing antibodies tests are now available and can be a real vaccine passport.

No

- With supplies of the vaccines currently available falling well short of demand, mandating vaccination is not a realistic scenario possibly.
- Queries to be answered: Is it legal for states, private employers and even airlines to mandate a vaccine that has only been approved for emergency use? Who could be held responsible if something goes wrong after getting the shot?
- A vaccine mandate that requires that every man, woman and child in America get a particular vaccine would be relatively unprecedented. Usually, when vaccine mandate is considered, it may be restricted to if you wish to send your child to school; or if you want to work for a specific type of employer, like a hospital.
- The limited case law existing in the USA, which mainly goes back to this one case from 1905, Jacobson v. Massachusetts, does say that states and municipalities have vast powers to compel vaccination for the benefit of public health.
- When it comes to these vaccines, they have not yet received full authorization. Is it legal to require something that has not been fully authorized?
- But will it stand up to a challenge of somebody saying: "Hey, if you want to compel me to take something, you have to make sure that it is safe and effective through the proper channels." That is going to be an interesting question that will play out in the next year or so.

HCFI Round Table Expert Zoom Meeting on "Adverse Events Including Deaths Following Vaccinations"

6th February, 2021 (11 am-12 pm)

Participants: Dr KK Aggarwal, Dr Ashok Gupta, Dr Suneela Garg, Prof Mahesh Verma, Dr Anita Chakravarti, Dr DR Rai, Mr Bejon Misra, Ms Balbir Verma, Dr KK Kalra, Dr Anil Kumar, Dr Suresh Mittal, Dr S Sharma

Consensus Statement of HCFI Expert Round Table

- Vaccines are universally tested and monitored and are among the safest medical products in use. Although evidence supports the safety of vaccines, there are rare instances where the causal relationship between vaccines and complications, including deaths has been established or plausible theoretical risks exist.
- Vaccines have saved millions of lives. Like any other drug, some adverse events (common, severe, serious) are associated with vaccinations. One should be aware about them and it is also important to know how to tackle them.
- Convert any contraindication to an indication. This will remove vaccine hesitancy. Try to identify vaccine intolerant patients and see how to proceed to give them the vaccine.
- Two patients in Brazil have tested positive for more than one strain of coronavirus. This is a matter of concern.

- India has overall only 25% seropositivity.
- Mutations are causing more mortality. The UK Prime Minister has said that the new UK variant may be more deadly.
- In India, out of 28 lakh vaccinations, 13-16 deaths (between 25 and 56 years of age) have occurred (Uttar Pradesh, Karnataka, Andhra Pradesh, Rajasthan, Telangana, Haryana, Odisha, Kerala and Gujarat); the vaccine taken in each case was Covishield. All had cardiovascular problems or brain stroke.
- In Norway, 33 elderly (≥75 years) and frail individuals died in a short time after receiving the first dose of the vaccine.
- Evidence from South Korea shows that people can die after flu vaccine; 23 persons, out of 13 million people who received the flu vaccine, died after being vaccinated.
- Ten people died in Germany, 79-93 years of age.
- A person can develop anxiety, vasovagal attack after seeing the vaccine injection.
- When a vaccine is taken, the antigen-presenting cells (APCs) will present the vaccine antigen to CD8+ T cells (cytotoxic) and CD4+ T cells. Th1 cytokines stimulate CD8+ T cells and in turn acquire the ability to attack the infected cells. Th2 response helps in the differentiation of B cells. The activated B cells can produce neutralizing antibodies. However, imbalanced immune responses can cause pulmonary immunopathology, partially due to aberrant Th2 response or antibody-dependent enhancement (ADE).
- Different reactions are seen after a vaccine: Allergy to vaccine or any of its ingredients, reactogenicity, reacto-immunogenicity (exaggerated Th1 and Th2 response), antigenicity or immunogenicity, reaction to pre-existing antibodies, development of disease enhancing antibodies/non-neutralizing antibodies.
- Before giving the vaccine, ask:
  - Will you develop and tolerate vasovagal reaction? If there is a history of syncope, the vaccine should be given in the lying down position and stay hydrated.
  - Are you prone to develop and tolerate immediate (IgE) and/or delayed (non-IgE) allergy? Allergy occurring in the first hour is IgE-mediated; if it is occurring after 1 hour and specifically after 6 hours, it is non-IgE-mediated allergy. In India, delayed reaction is being seen.
  - If likely (non-IgE-mediated): pre-load with montelukast + H1 + H2 blocker. If known IgE allergy: Get absolute eosinophilic count and IgE levels, do a scratch test/intradermal challenge.
  - Will you get exacerbation of thrombo-inflammation? If baseline C-reactive protein (CRP) >1 mg/L, it will cause rise in CRP, interleukin (IL)-6, IL-1β. In such cases, preload the patient with ACS (aspirin, colchicine and statin). CRP may rise by 30% on Day 2. If rise is more or CRP is >10 mg/L, then add mefenamic acid or any other immunomodulator.
  - Will you get oversympathetic response? (abnormal HR variability, 6 MWD/T less than 700 feet or over sympathetic response to walking): Pre-load such patients with a β-blocker.
- For non-IgE-mediated reactions, the following protocol comprising of H1 and H2 antihistamines and sometimes montelukast, aspirin or glucocorticoids will help.
  - Cetirizine (10 mg orally) is given 30-120 minutes before the start of the procedure.
  - Famotidine (20 mg IV or orally) is given 30-60 minutes before the start of the procedure.
  - Aspirin (325 mg orally) is given to patients with flushing during their initial reaction. This is administered the night before the procedure and again 1 hour before the start of the procedure.
  - Montelukast (10 mg orally) is given the night before the procedure and again 1 hour before the start of the procedure.
  - When desensitizing to chemotherapy or biologic agents, any premedications (such as steroids) that would be given to a nonallergic patient should be incorporated into the planned premedications as well.
- Reduce the precipitating factors for coronary artery disease (CAD) - hypertension, fever, tachyarrhythmias, thyrotoxicosis, anemia, polycythemia, hypoxemia and valvular heart disease.
- Ask for a history of cocaine use in young people; even casual use of cocaine may be associated with acute or chronic cardiovascular toxicity. Cocaine can precipitate myocardial infarction.
- Smoking will increase the sympathetic response; it will increase BP by 20 mmHg. A person, who smokes before taking the vaccine and has an

underlying heart disease, both can precipitate acute cardiovascular event.

- The amount of alcohol taken the previous night can also precipitate oversympathetic response.
- Frail individuals with comorbid conditions will not be able to tolerate even mild sympathetic overactivity. They need to be premedicated.
- The response to vaccine is the same as with COVID natural infection.
- The AEFI (adverse event following immunization) definition does not mention the time.
- Every death within 3 months of vaccine should be investigated.
- The long-term effects of the vaccine are unknown.
- We need to prevent post-vaccine complications. They are manageable and preventable.

Round Table – Expert Group on Environment Zoom Meeting on "Issues and Challenges in Implementation of Biomedical Waste Management Rules"

7th February, 2020 (1-2 pm)

Participants: Dr KK Aggarwal, Dr Anil Kumar, Dr Dipankar Saha, Dr M Dwarkanath, Mr Pankaj Kapil, Mr Pradeep Khandelwal, Mr Neeraj Tyagi, Dr Shyam Gupta, Dr Suresh Mittal, Dr Meenakshi Soni, Ms Ira Gupta, Dr S Sharma

The meeting was chaired by Dr M Dwarkanath and co-chaired by Mr Pradeep Khandelwal.

Key points from the discussion

- COVID-19 has increased the volume of biomedical waste (BMW) generated. With patients in home care, this subject has become very important and needs attention because hazardous waste is being disposed of mixed with domestic waste.
- Expired medicines, broken mercury thermometers, used batteries, used needles and syringes, contaminated gauze, etc., generated in home care of patients are covered under Solid Waste Management Rules, 2016 as "domestic hazardous waste" and not under BMW management.
- The Central Pollution Control Board (CPCB) should come out with SOPs about domestic hazardous waste. Awareness should be there so that it is properly handled and disposed.
- There are three types of waste in household: Wet waste, dry waste and domestic hazardous waste.
- NDMC and SDMC have started collecting the domestic hazardous waste. EDMC has started work on this. Indore has done a lot of work on this.
- Domestic hazardous waste includes paints and varnishes, expired medicines, sanitary pads, batteries. These are collected separately and segregated at materials recovery facilities (MRF).
- Indore model can be adopted and a separate system for domestic hazardous waste collection can be established.
- Big chemist stores or stockists should keep a box where the expired and left over medicines can be put under the extended producers responsibility (EPR) by a pharmaceutical company. They can be then collected and transported for safe disposal.
- Special e-waste collection bins had been put to collect electronic waste. Along similar lines, Delhi Pollution Control Committee (DPCC) can tie-up with market trader/drug stockist associations and put collection bins at various places for domestic hazardous waste, at least for expired medicines.
- For synchronization of segregation and collection system, it is important to have education and awareness for all. Education should start at the school level itself; there should be regular programs and courses round the year.
- People should know where the waste should be disposed.
- The Residents Welfare Association (RWA) should be asked to keep collection bins for domestic hazardous waste, especially with many patients in home care/quarantine.
- Implementation is poor because chain is incomplete. All things should move parallel to each other to achieve sustainability.
- Even if segregation is done, people do not know where it should go. Domestic hazardous waste has to go to Hazardous Waste Treatment, Storage and Disposal Facilities (TSDFs). Delhi does not have a TSDF.
- A suggestion was given to write to CPCB/Central government/Delhi government to undertake a survey for lifecycle analysis of e-vehicle batteries.
- There is a lack of space for landfills; hence, lot of waste is dumped in the open. Awareness needs to be generated about domestic hazardous waste and not just limited to penalization.
- Monitoring of autoclaving and steam disinfection should be done.

- A BMW nodal officer should be appointed in each hospital. However, most hospitals (≥50 beds) already have a BMW management committee including a nodal officer (at doctor level); there are advisory committees at district level and multi-departmental teams are there for inspection.
- COVID waste needs to be segregated (in double bags) with proper labeling, treated and disposed of expeditiously, within 24 hours, as per latest revision of CPCB guidelines (31st July, 2020).
- The generation of BMW must be reduced. This should be our first emphasis. For example, to reduce discarded medicine waste, medicines should be dispensed in the quantity that has been prescribed by the doctor.
- EPR should be implemented; chemists must be regulated to take back discarded medicines.
- Write to Insurance Regulatory and Development Authority (IRDA) that when reimbursing for home care, there should be a written assurance that they have followed BMW and other waste management guidelines. Doctors should also prescribe these guidelines – how to handle the home generated BMW. Adherence to these guidelines should be mandated.
- DPCC/CPCB should write to the National Medical Commission in this regard.
- Can masks be washed, disinfected and reused? A procedure should be prescribed and can be standardized and should be included in CPCB guidelines. Fabric masks can be washed with detergent and re-used. N95 masks are single use masks. The masks can be discarded in domestic waste after 72 hours of keeping in a paper bag.
- For collection boxes (for discarded medicines, etc.), along with EPR, all hospitals, medical associations, nursing homes, schools and colleges should be included.
- Wherever first aid is provided, there should be a collection facility either in the form of a box or room.
- Time for collection should be fixed; there should be helpline numbers.
- MCD vehicles that collect waste should be compartmentalized to avoid mixing of different kinds of waste. The compartments should be of appropriate volume and size.

Second Dose Reactogenic – Are COVID Vaccines Too Risky for Some People?

- The second dose of the vaccine appears to be more reactogenic than the first dose. Most symptoms occur within the first 3 days of receiving the dose and often resolve within a couple of days. The most common side effects appear to be pain, fatigue, headache and myalgias.
- It appears to be associated with the antibody response. With the first dose, most people don't have much of a reaction. There might just be a little bit of soreness at the injection site. Most people develop more side effects after the second dose. Probably after the first dose, the body starts developing an antibody response or an immune response. When the second dose is given, the body is ready to act against the antigen provided by the vaccine. This leads to an inflammatory response from the body.
- The side effects like pain or fatigue are not allergies. They're normal side effects of the vaccine.
- Most allergic reactions will occur within 30 minutes of vaccine administration. They present with urticaria or hives, angioedema and wheezing. One or two of these symptoms along with a low blood pressure or fast heart rate is anaphylaxis.
- New data shows that anaphylaxis appears to be not as common as previously thought.
- The frequency of anaphylaxis is around 5 cases per million doses of the Pfizer vaccine and nearly 2.8 cases per million doses of the Moderna vaccine.
- People have allergies to several allergens. Food products, pet dander, venom to bees or even latex, none are contraindicated. Even if one has anaphylaxis to these products, he can safely get the mRNA vaccines.
- The only major contraindication to the mRNA vaccines is if one has had an immediate allergic reaction to the first dose of the vaccine or if one has had such a response to a component of the vaccine previously. This includes polyethylene glycol. This is a component of both the vaccines and some people may react to it.
- Another contraindication is if one has had anaphylaxis to polysorbate. Polysorbate can cross-react with polyethylene glycol.

(Source: *Medpage Today*)

Variant Strain in UK More Severe

- The UK variant of coronavirus is probably more fatal and leads to more hospitalizations compared to nonvariant coronavirus cases, suggest data published on a British government website. The report stated that there was increased severity of COVID-19 cases caused by the B.1.1.7 variant compared to nonvariants of concern. The B.1.1.7 cases have been reported to be 30-70% deadlier than the actual wild-type strain.
- The concerns were first raised in January, when the initial data suggested that cases with B.1.1.7 were deadlier than nonvariant cases.
- The London School of Hygiene & Tropical Medicine noted a relative hazard of death within 28 days of 1.58 for variant cases compared to nonvariant cases. The Imperial College London stated that the mean ratio of case fatality for variant cases was 1.36.
- Public Health England conducted a matched cohort analysis to note a death risk ratio of 1.65 for variant versus nonvariant infected people.
- Public Health Scotland employed the S-gene target failure as a proxy to ascertain variant cases. The risk of hospitalization was found to be higher among S-gene target failure cases versus S-gene positive cases.
- Intensive Care National Audit and Research Centre (ICNARC) and QRESEARCH also noted that there was a greater risk of ICU admission for variant cases.
- Evidence thus suggests that B.1.1.7 is tied to an increased risk of hospitalization and mortality compared to infection with nonvariant virus.
- CDC modeling in January estimated that the UK variant would dominate in the US by the end of March. A new modeling study indicates that the incidence of variant cases is increasing two-fold every 10 days in this country.

(Source: *Medpage Today*)

With input from Dr Monica Vasudev

UK Strain: Longer Duration of Infection

- It was believed that B.1.1.7 variant's increased infectiousness is due to higher viral load. New data suggest that it is related to delayed clearance, and longer duration of infection.
- Infection duration appears to be longer for B.1.1.7, with a mean of 13.3 days (90% confidence interval [CI] 10.1, 16.5), compared to 8.2 days for non-B.1.1.7.
- A study evaluated if acute infection with B.1.1.7 is associated with higher or more sustained nasopharyngeal viral concentrations. Longitudinal polymerase chain reaction (PCR) tests conducted in a cohort of 65 individuals with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) undergoing daily surveillance testing were evaluated. These included seven infected with B.1.1.7.
- For patients with B.1.1.7 variant, the mean duration of proliferation phase, clearance phase and overall duration of infection was 5.3 days, 8.0 days and 13.3 days, respectively. The corresponding figures for non-B.1.1.7 virus were mean proliferation phase of 2.0 days, a mean clearance phase of 6.2 days, and a mean duration of infection of 8.2 days.
- The peak viral concentration for B.1.1.7 was 19.0 Ct vs. 20.2 Ct [19.0, 21.4] for non-B.1.1.7. This represents 8.5 $\log_{10}$ RNA copies/mL [7.6, 9.4] for B.1.1.7 and 8.2 $\log_{10}$ RNA copies/mL [7.8, 8.5] for non-B.1.1.7.
- The variant B.1.1.7 thus appears to result in longer infections with similar peak viral concentration compared to non-B.1.1.7.
- The longer duration may result in increased transmissibility of the variant.

Comments

- These variants probably carry non-spike mutations that affect their sensitivities to type I (or III) interferon.
- Not related to higher viral load as higher load is consistent with worse outcomes. Mitigation efforts should be just as effective.

(Source: https://dash.harvard.edu/bitstream/handle/1/37366884/B117Trajectories_10Feb2021.pdf?sequence=1&isAllowed=y)

With input from Dr Monica Vasudev

One in Five Diabetics Hospitalized with COVID Die in 28 Days

- While about half of the patients with diabetes hospitalized with COVID-19 will be discharged from hospital within a month, one-fifth of the patients will have died, reports the French CORONADO study.
- Early findings published in May last year revealed that 10.6% of patients with type 2 diabetes and COVID-19 and 5.6% of those with type 1 diabetes and COVID-19 succumbed within 7 days of hospitalization.

- Two thousand seven hundred ninety-six patients with diabetes were hospitalized with COVID-19 at 68 institutions in France from March 10 to April 10, 2020, and were followed for 28 days.
- Approximately 44.2% of patients had microvascular complications and 38.6% had macrovascular complications.
- After 28 days, 20.6% patients were reported to have died and 50.2% were discharged. The median duration of stay in the hospital was 9 days.
- Increasing age was the most important risk factor that augured poorly, followed by a history of microvascular complications, dyspnea on admission and inflammatory markers (white blood cell count, elevated CRP and increased aspartate transaminase).
- Routine treatment with metformin and a history of COVID-19 symptoms before hospitalization were among the positive risk factors.
- Blood glucose level was a neutral prognostic factor. Another one in this category was treatment with dipeptidyl peptidase-4 (DPP-4) inhibitors. Statin therapy was a negative prognostic factor.
- The data are published in *Diabetologia*.

(*Source: Medscape*)

Single High Dose of Vitamin D3 not Tied to Reduced Hospital Stay in Moderate-to-severe COVID-19

A study published in the *Journal of the American Medical Association* has revealed that among patients hospitalized with moderate-to-severe COVID-19, a single high dose of vitamin D3 did not significantly reduce hospital stay in comparison with placebo. The trial was conducted in 2 sites in Sao Paulo with 240 hospitalized patients with COVID-19 who had moderate-to-severe infection at the time of recruitment from June 2 to August 27, 2020. Patients were randomized to receive a single oral dose of 2,00,000 IU of vitamin D3 or placebo (n = 120 in each group).

(*Source: DG Alerts*)

Life Expectancy in the United States Declined by a Year in the First 6 Months of 2020

Life expectancy in the US reportedly came down by a year in the first-half of 2020. This represents the largest drop since World War II. This provides the complete picture of the pandemic's impact on expected life spans of Americans. They declined to 77.8 years from 78.8 years in the year 2019.

Life expectancy of Blacks came down by 2.7 years in the first-half of last year, after rise noted for 20 years. The gap between Black and White Americans, which was seen to be constricting, now stands at 6 years, which is the widest since 1998.

Contrary to the decline caused by the complex issue of drug overdoses, this one, guided mainly by COVID-19, will perhaps not last as long since deaths due to the virus are declining and people are getting inoculated. In 1918, when thousands of Americans died in the flu pandemic, life expectancy fell 11.8 years compared to the previous year, down to 39. The numbers completely bounced back the next year.

(*Source: NY Times*)

Minutes of Virtual Meeting of CMAAO NMAs on Corona Update: Country Experiences

20th February (Saturday, 9.30 am-10.30 am)

Participants: Member NMAs: Dr KK Aggarwal, President-CMAAO; Dr Yeh Woei Chong, Singapore Chair-CMAAO; Dr Alvin Yee-Shing Chan, Hong Kong, Treasurer-CMAAO; Dr Ravi Naidu, Malaysia; Dr Marthanda Pillai, India, Member-World Medical Council; Dr Angelique Coetzee, President-South African Medical Association; Dr Marie Uzawa Urabe, Japan Medical Association; Dr Md Jamaluddin Chowdhury, Bangladesh Medical Association; Dr Qaiser Sajjad, Secretary General-Pakistan Medical Association; Dr Debora Cavalcanti, Brazil; Dr Prakash Budhathoky, Treasurer-Nepal Medical Association

Invitees: Dr Akhtar Husain; Dr S Sharma, Editor-IJCP Group

Key points from the discussion

Malaysia Update: Malaysia has gone through the third wave of coronavirus infection. The total lockdown called the "movement control order" has been reduced in some states as the total number of cases is now declining. The vaccine (Pfizer) roll-out will begin from 26th February. One million doses will be received today. The frontline workers will receive the vaccine first. Malaysia expects to vaccinate 80% of population by April 2022. The total lockdown has made a difference to the number of cases.

Brazil Update: The cases are increasing, hospitals are full and there are no beds for new cases. People do not use masks. Vaccination has started with Oxford/AstraZeneca vaccine and the CoronaVac vaccine.

South Africa Update: Vaccination has started in all provinces 2 days back. Total daily cases are around

2,000 cases/day. Cases are now reducing because of lockdown measures. Some restrictions have been relaxed; schools have been reopened this week.

Hong Kong Update: The lockdown in Hong Kong has limited public gatherings to less than 4; lunch time just two people and only yesterday dining at restaurants has resumed. Gyms, cinemas, gaming arcades, beauty parlors, sports centers have now reopened. Vaccination has been launched with Sinovac vaccine. The Pfizer-BioNTech vaccine will arrive at the end of February and is expected to be administered in March. Many people are apprehensive about the Pfizer vaccine because of reports of deaths in Norway and Bell's palsy in Israel.

Japan Update: Japan has started to vaccinate the medical staff. The numbers are under control. Although a mild lockdown is still in place to control infection during the vaccination process.

Nepal Update: Numbers are reducing, serious disease is also reducing. There is; however, a risk of rise in cases because of political gatherings, processions, etc. Vaccination has started 3 weeks before for frontline workers. After 2 weeks, mass vaccination will start for persons above 60 years.

Singapore Update: There are around 0-1 case/day. People are not allowed to visit each other except 8 family members a day are allowed to visit two households. About 2,50,000 people have been vaccinated till date and around 1,10,000 having received their second dose; one person aged 72 years developed myocardial infarction (MI) after the first dose of vaccine (Pfizer). However, according to the initial assessment, this was not caused by the vaccine. The Moderna vaccine has also arrived in the country. Singapore aims to vaccinate the whole population by August this year.

Bangladesh Update: The infection rate is coming down to around 400 new cases/day, detection rate is <3%. There are political gatherings although there has been no increase in infection rates. More than 1% has been vaccinated; initially there was fear about the vaccine, but the situation has improved. Now there is a very good response.

Pakistan Update: The number of cases and deaths are decreasing. No serious cases; hospitalized cases have also reduced. However, people do not follow SOPs. The vaccination process (Sinopharm vaccine) has started for healthcare workers; although there is hesitancy among them. The Oxford-AstraZeneca vaccine is awaited.

India Update: The situation is optimistic with numbers reducing. Three states are contributing around 60% of cases. Sero-surveillance has shown that 21% people have developed antibodies. The healthcare workers have been accepting of the vaccine. There is a debate whether to delay the second dose by 8-12 weeks. Side effects have been very minor. Deaths that have occurred after vaccination are not directly related to the vaccine.

- Every country is worried about resurgence in cases.
- Factors such as mutations, COVID inappropriate behavior and super-spreader event, acting in combination, will lead to surge in cases.
- Two types of mutation: Substitution and deletion.
- Deletion mutation is permanent, while substitution mutation can be autocorrected by proof reading unless associated with deletion.
- Mutation in the state of Maharashtra in India is a substitution type of mutation and therefore is localized to that region. The UK strain has three deletions. Hence, it is of concern. South Africa and Brazil strains do not have deletions and therefore are not spreading globally.
- Newer mutations mean longer period of isolation.
- It has been suggested that humidity from masks may lessen severity of COVID-19. Face masks substantially increase the humidity in the air that the mask-wearer breathes in. This higher level of humidity in inhaled air may be why wearing masks has been linked to lower disease severity as hydration of the respiratory tract is known to benefit the immune system.
- It is important to shift from single gene testing to minimum three gene testing to be able to detect mutations.
- Reactivation of the disease has been reported in an immunocompromised patient 4 months after initial infection, documented by genomic sequencing.
- Allergic manifestations are same in all types of vaccines; reactogenicity is least in killed virus vaccine and maximum in RNA vaccines, while immunogenicity is lowest in killed vaccine and same in other vaccines. Killed vaccines are safer but less effective, so require more doses.
- In India, 744 doctors have died due to COVID, Pakistan 191, Bangladesh 130, South Africa 300, Nepal 6 and Brazil 440.
- Multiple doses of vaccine may precipitate multisystemic inflammatory disease.
- Swift and prompt policy is needed to determine the timing of the second dose.

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72nd Annual Cardiology Conference

CORONARY CALCIUM IN THE CATH LAB – HOW TO IMAGE WISELY?

Dr Pradeep Kumar Hasija, Chennai

- Coronary calcium requires accurate quantification for selecting appropriate therapy to ensure adequate stent implantation and optimal long- and short-term outcomes.
- Calcium imaging in cath lab by coronary angio alone is not adequate, and accurate assessment depends on intravascular ultrasound (IVUS) or optical coherence tomography (OCT).
- IVUS has higher tissue penetration useful to assess deep calcium, and OCT has a higher resolution for better quantification.
- OCT has higher sensitivity compared with IVUS in detecting both stent malapposition and under expansion. Future efforts should target consensus imaging guidelines.

AMBULATORY BP MEASUREMENT: HOW TO INTERPRET THE DATA?

Prof (Dr) Anjan Lal Dutta, Kolkata

Ambulatory BP monitoring (ABPM) displays 24-hour BP flow and HR dynamics that is particularly helpful to explain the disparity between BP level and end-organ damage in WCH, MH, Noct. Dippers/Nondippers early morning BP surge. It also helps assess BP variability, treatment response and treatment resistance. However, the proper utility of ABPM depends on proper data collection with a competent operator, patient's cooperation and quality of the device system.

CASE IN THE BOX: LEFT BUNDLE PACING – TIPS AND TRICKS

Dr Shunmuga Sundaram Ponnusamy, Madurai

Left bundle branch pacing is a recent innovation in the field of physiological pacing to overcome the limitations of his bundle pacing. Provides electrical and mechanical synchrony avoiding RV pacing related complications. It can be performed with or without EP setup by the deep placement of a 4.1 F sized lead in the proximal interventricular septum. Provides excellent lead stability and pacing parameters; Can be used as an alternative to conventional RV pacing. Left bundle branch pacing is an effective alternative to cardiac resynchronization therapy.

MINOCA – WHAT NEXT?

Dr Smit Shrivastava, Raipur

Myocardial **I**nfarction with **N**ormal **C**oronary **A**rtery. Every sixth to ninth myocardial infarction is MINOCA. Young and female are at more risk. A coronary angiogram misses 95% of the coronary circulation. MINOCA can have multiple potential mechanisms for causation – Vasospasm, dissection, myocardial dysfunction. Cardiac MRI can pick up the underlying cause in 87% of MINOCA. Treatment with statin and RAAS blocker benefits MINOCA. Only a LAZY CARDIOLOGIST would not investigate further or a CRAZY CARDIOLOGIST!

STRESS CARDIOMYOPATHY – NEWER INSIGHTS

Dr VK Katyal, Rohtak

Stress cardiomyopathy (TAKOTSUBO cardiomyopathy) develops in postmenopausal females with acute mental or physical events. Presents like acute coronary syndrome (ACS) often with complicated course with sudden death. Characteristic ECG changes with elevated troponin-I and natriuretic peptides are highly suggestive of Takotsubo syndrome. INTERTAK diagnostic score identify large no. of patients correctly. 2D echocardiography criteria has largely replaced invasive workup. Management depends upon type of involvement with LVOTO and MR posing difficulties in management with attendant cardiogenic shock.

BEST INDICATIONS FOR INTRACORONARY IMAGING

Dr Lorenz Raber, Switzerland

Stent failures, ambiguous ACS patients, intermediate left main stenosis, percutaneous coronary intervention (PCI) guidance for complex lesions (long lesions, LM, CTO, 2-stent bifurcation) represent key indications for IC imaging that are also supported by guidelines, consistent clinical benefits can be expected for PCI guidance, improved precision in the diagnostic workup.

DYSLIPIDEMIA

Prof Lale Tokgozoglu, Ankara

- Low-density lipoprotein (LDL) cholesterol is causal for cardiovascular disease (CVD) and the primary target. New ESC/EAS dyslipidemia guidelines recommend lower LDL goals. The guidelines suggest at least 50% reduction in LDL from baseline.
- Statins are the first-line of treatment while second-line of treatment includes ezetimibe, proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors, bempedoic acid, EPA, fibrates. There is a paradigm shift from high intensity statin to high intensity lipid-lowering.
- We have several existing and new lipid-lowering medications. The real challenge is using them effectively to get to guideline recommended goals and ensuring patient adherence.

CASE IN THE BOX: ISCHEMIC HEART FAILURE-VIABILITY ASSESSMENT

Dr Neha Sekhri, London, UK

- Myocardial stunning and hibernation are points on the same spectrum.
- Viability is still a retrospective assessment of left ventricular function post revascularization.

LDL-BASED MANAGEMENT: TARGET-BASED OR DOSE-BASED

Dr TR Muralidharan, Chennai

- Low-density lipoprotein (LDL) is causal of atherosclerosis – Evidence from meta-analyses of Mendelian randomization studies, prospective cohort studies and randomized controlled trials unequivocally establishes that LDL causes atherosclerotic cardiovascular disease (ASCVD).
- High-dose statin-indefinite use without monitoring: Predictable pharmacodynamics and kinetics; Proven superiority; Preferably without side effects; May be the only drug available.
- Statin therapy is remarkably safe: Typically, treating 10,000 patients for 5 years with a standard statin regimen is expected.
- Achievable reductions of LDL cholesterol as a function of the therapeutic approach: LDL cholesterol-lowering treatment impacts disease progression before clinical manifestation.
- To conclude - Monitor the lipids; Step down is a distant dream; Escalation is a startling reality.

SHOULD BP-LOWERING MEDICATIONS BE TAKEN AT NIGHT?

Prof Neil R Poulter, UK

- Raised BP continues to be the biggest contributor to the global burden of disease and to global mortality. BP control remains inadequate among hypertensives across the globe.
- According to ISH 2020 recommendations, ideal drug characteristics include "use a once daily regimen, which provides 24-hour BP control."
- Nocturnal BP is a better predictor of cardiovascular (CV) events.
- Evidence for nocturnal dosing – There is limited data on nocturnal dosing of BP-lowering drugs.
- Previous observational data suggest nocturnal dosing may give superior CV protection.
- HARMONY trial – In treated hypertensive patients with stable BP levels, the timing of antihypertensive drug administration did not affect mean 24-hour ABPM levels or quality of life.
- Hence, there are no good data to recommend nocturnal dosing.

PRIMARY ANGIOPLASTY (PAMI) IN ECTATIC CORONARIES

Dr Nakul Sinha, Lucknow

Ectatic coronaries (even bordering on aneurysms pose a unique challenge for PCI, more so when they have heavy thrombus burden in settings of acute myocardial infarction (MI). There is no uniform recommendation or guideline that can get a safe and effective outcome in most cases. The basic agreed approach is to use strong antiplatelets, antithrombotics (even consider GpIIb/IIIa inhibitors), and anti-spam measures. The key is to get the residual thrombus burden as low as possible (easier said than done). Early stenting or where there is an enormous thrombus burden can lead to stent thrombosis. The aim is to be able to get a good antegrade flow and maintain it! Do not aim for perfection but a reasonably good flowing vessel.

SHOULD WE RESTRICT TOTAL FAT FOR CVD PREVENTION?

Dr Ajay K Sinha, Patna

Reduce total fat intake to optimize types of dietary fat. Elevated consumption of saturated fats in the

diet would not be detrimental to CV risk and would not increase all-cause mortality. Mediterranean diet has shown a decrease in morbidity and mortality. New recommendations should emphasize food-based strategies that translate for the public into understandable, consistent and robust recommendations for healthy dietary patterns. Evaluating drugs is easy; assessing the healthfulness of food is not. Food-based dietary guidelines: No benefit of lowering total dietary fat in food or overall diets. Reducing total fat (replacing total fat with overall carbohydrates) does not lower CVD risk.

STATIN INTOLERANT POST-MI PATIENT – WHAT NEXT?

Dr SS Iyengar, Bengaluru

- Statin intolerance is rare. Statin intolerance is the inability to take statins to achieve the goal of LDL cholesterol either because of adverse effects or elevation of enzymes.
- Treatment of statin intolerance is to restart lower dose of the same statin, use an alternative statin, intermittent statin, low-dose statin *plus* ezetimibe or other nonstatins.

INNOVATIONS FROM INDIA DEFINING A FRESH PATH IN TAVR

Dr Ashok Seth, New Delhi

The Myval transcatheter aortic valve implantation (TAVI) system is designed and manufactured by Meril Lifesciences in India. The Myval valve is a next-generation balloon-expandable heart valve made up of a nickel-cobalt alloy frame and bovine pericardium leaflets. The valve has a unique hybrid honeycomb cell design, with open cells on the upper half to ensure the unjailing of the coronary ostia and closed cells on the lower half for high radial strength. Upon crimping, the design gives a unique "dark and light" band pattern, visible under fluoroscopy, ensuring accurate valve positioning and orthotopic deployment.

LEFT MAIN DISEASE – SURGERY IS THE BEST OPTION IN ALL

Dr OP Yadava, New Delhi

- Left main plaque is complex (Eccentric and heavily calcified) and usually extends into proximal left anterior descending coronary artery (LAD) and circumflex, besides over 90% having associated multivessel coronary artery disease (CAD).
- Associated comorbidities like diabetes mellitus, left ventricular (LV) dysfunction and chronic kidney disease (CKD) should factor in decision-making. Results of surgery are far superior to PCI in these comorbidities, as also when the Syntax score is ≥33.
- Coronary artery bypass grafting (CABG) has a survival advantage over PCI which unfolds on follow-up beyond 5 years and survival curves keep diverging beyond that period.
- EXCEL trial has been challenged as primary endpoint was changed during the trial and the definition of perioperative MI too was changed, thus raising an accusation that this was willfully done to prop-up PCI. Even 38% higher mortality with PCI over CABG was not given due cognizance.
- Off-pump, anaortic, total arterial revascularization is the gold standard treatment for left main stenosis.

PHARMACOLOGIC THERAPY TO REVERSE CARDIAC REMODELING IN HEART FAILURE WITH REDUCED EJECTION FRACTION

Dr Akshay S Desai, USA

- Cardiac remodeling is a key driver of heart failure progression.
- Reverse remodeling can be enhanced by appropriate application of guideline-directed heart failure therapy.
- Both the extent and pace of reverse remodeling are correlated with reductions in mortality and heart events.
- Replacement of angiotensin-converting enzyme (ACE) inhibition with ARNI reduces ventricular volumes and improves left ventricular ejection fraction (LVEF).
- Data regarding remodeling benefits of sodium-glucose cotransporter-2 (SGLT2) inhibitors is emerging.

VASCULAR DOSE OF RIVAROXABAN – EFFECTIVE STRATEGY TO REDUCE THROMBOTIC EVENTS IN POST-STEMI?

Dr Prabhat Kumar, Patna

Despite a great deal of interest in secondary prevention following an ACS, with particular attention on antiplatelet and antithrombotic therapies, the standard of care has remained essentially unchanged for the better part of a decade. Until recently, treatment of atherothrombosis focused on platelets with the use

of single or dual antiplatelet therapy. For secondary prevention, current guidelines recommend low-dose aspirin or clopidogrel if aspirin cannot be tolerated. Dual antiplatelet therapy (DAPT), consisting of aspirin plus a P2Y12 antagonist, is recommended for patients with ACS. Despite the use of single or dual antiplatelet therapy; however, there remains a significant residual risk of serious atherothrombotic events. The limitations of antiplatelet treatment raised the possibility that combining antiplatelet therapy with an anticoagulant might improve atherothrombotic outcomes.

An innovative low-dose of Rivaroxaban regimen (2.5 mg twice daily, known as vascular dose) or 5 mg twice daily was compared with matching placebo on a background of DAPT in phase III randomized trial (ATLAS-ACS-2 TIMI 51 trial) with 15,526 ACS patients for around 13 months, but up to 31 months. Compared with placebo, both doses of Rivaroxaban significantly reduced the primary efficacy endpoint, a composite of cardiovascular death, MI or stroke, by 16% relative risk reduction (RRR). In contrast to the twice daily 5 mg dose of Rivaroxaban, the twice daily 2.5-mg dose reduced the rate of cardiovascular death (2.7% vs. 4.1%, p = 0.002) and all-cause death. The trial does suggest that lower-dose strategies are advantageous in this setting, with the very low-dose group achieving overall better outcomes than the low-dose group. Based on these findings, the 2.5 mg twice daily dose of Rivaroxaban was licensed in Europe for use on top of DAPT in high-risk ACS patients.

Further, the importance of using low doses when direct oral anticogulants (DOACs) are combined with antiplatelet therapy is highlighted by the APPRAISE 2 trial findings. With the benefit of lower doses of Rivaroxaban established, the utility of DPI was evaluated in several phase III studies, the largest of which was the COMPASS trial, where Rivaroxaban was compared on top of aspirin (100 mg once daily) or aspirin alone for secondary prevention in 27,400 patients with stable CAD or peripheral artery disease (PAD).

Suggested Reading

1. Mega JL, Braunwald E, Wiviott SD, et al; ATLAS ACS 2–TIMI 51 Investigators. Rivaroxaban in patients with a recent acute coronary syndrome. N Engl J Med. 2012;366(1):9-19.
2. Alexander JH, Lopes RD, James S, et al; APPRAISE-2 Investigators. Apixaban with antiplatelet therapy after acute coronary syndrome. N Engl J Med. 2011;365(8):699-708.
3. Eikelboom JW, Connolly SJ, Bosch J, et al; COMPASS Investigators. Rivaroxaban with or without aspirin in stable cardiovascular disease. N Engl J Med. 2017;377(14):1319-30.

HOW TO CHOOSE THE IDEAL NOAC FOR VARIOUS CLINICAL SCENARIOS IN AF?

Prof (Dr) Saumitra Ray, Kolkata

- There is no "ideal" non-vitamin K oral anticoagulants (NOAC).
- NOACs vary in their efficacy, PK-PD properties and side effect profile. For stroke and systemic embolism prevention, superiority over warfarin has been proved for 150 mg b.i.d. dose of dabigatran and 5 mg b.i.d. dose of apixaban. Other molecules and other doses are noninferior to warfarin.
- All NOACs are better than warfarin for hemorrhagic complications, especially intracranial hemorrhage.
- Dabigatran is renally excreted and, as such, cannot be used in moderate-to-severe renal failure patients. Rivaroxaban may be used with lower dose and apixaban may even be used with advanced renal failure.
- When compliance is an issue, rivaroxaban scores over others due to its single daily dose.
- Food increases absorption of rivaroxaban, but has little effects with other molecules. On the other hand, drug-drug interaction is more with edoxaban.
- In all situations, regular monitoring for side effects and compliance is needed when a patient is on NOAC.

MY PATIENT ON NOAC FOR A PLANNED CORONARY INTERVENTION – HOW TO MANAGE?

Dr Nagamalesh UM, Bengaluru

Approximately 5-10% of patients undergoing PCI have atrial fibrillation (AF). Combining oral anticoagulation (OAC) with DAPT is a strategy known as triple antithrombotic therapy. Triple therapy is known to increase the risk of bleeding compared with OAC or DAPT alone. Multiple guidelines and consensus documents have been published over the past decade to inform clinicians on the optimal antithrombotic strategy for AF patients undergoing PCI. Long-term treatment of patients on OAC after revascularization: From PCI until Day 14 (max 30 days) NOAC (full AF dose) + aspirin + clopidogrel; Day 15 (day 31) until 12 months NOAC (full AF dose) + clopidogrel; After 12 months in ACS (after 6 months in CCS) NOAC.

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News and Views

Most People can Produce Neutralizing Antibodies Against SARS-CoV-2

A study published in *PLOS Pathogens* has stated that a large number of people have the potential to produce neutralizing antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in severe cases of coronavirus disease 2019 (COVID-19).

The study also supports the use of combination antibody therapy for the prevention and treatment of COVID-19. Michael Mor of Tel Aviv University, and colleagues made use of molecular and bioinformatics techniques and compared B-cell responses among 8 patients with severe COVID-19 and 10 patients with mild symptoms, 1.5 months following infection. Patients who were very ill had higher concentrations of receptor-binding domain (RBD)-specific antibodies as well as raised B-cell expansion. Twenty-two antibodies were cloned from two patients. Of these, 6 were found to have potent neutralization against SARS-CoV-2. It appears that most people can produce neutralizing antibodies against SARS-CoV-2 in severe cases of the disease… (*ET Healthworld*)

COVID Clot Prevention: Early Prophylactic Anticoagulation

A new study suggests that starting heparin prophylaxis within 24 hours of hospital admission for COVID-19 was tied to considerably better outcomes.

Investigators noted that starting anticoagulation early was linked with 27% lower relative risk of 30-day mortality compared to no anticoagulation (14.3% vs. 18.7%, hazard ratio [HR] 0.73, 95% confidence interval [CI] 0.66-0.81). Preventive heparin use was associated with similar positive outcomes for inpatient mortality (HR 0.69, 95% CI 0.61-0.77) and initiation of therapeutic anticoagulation (HR 0.81, 95% CI 0.73-0.90). Additionally, early prophylaxis was not linked with increased risk of bleeding that needed transfusion (HR 0.87, 95% CI 0.71-1.05). The study included 4,297 patients admitted to Veterans Affairs (VA) hospitals between March 1 and July 31, 2020, with confirmed severe COVID-19 and no history of anticoagulation. The findings are published in *The BMJ*… (*Medpage Today*)

Inhaled Hyaluronan may Help COPD Patients

Aerosolized high-molecular-weight hyaluronan (HMW-HA) appears to improve acute exacerbations of chronic obstructive pulmonary disease (COPD), suggests a new study.

In comparison with placebo, HMW-HA was found to be linked with a significantly shorter duration of noninvasive positive-pressure ventilation (NIPPV), lower systemic inflammatory markers and decreased measured peak airway pressure.

Researchers looked at 44 patients with a history of acute exacerbations of COPD requiring NIPPV. Three patients were excluded owing to heart failure. Twenty patients were given HMW-HA while 21 received placebo in association with NIPPV and standard medical therapy. Patients given HMW-HA were free from NIPPV sooner than those who were given placebo (mean, 5.2 vs. 6.4 days; $p < 0.037$). Patients given HMW-HA also had significantly shorter hospital stay compared to those in the placebo group (mean, 7.2 vs. 10.2 days; $p = 0.039$)… (*Medscape*)

Acute Malnutrition Estimated to Affect 2.3 Million Children Under 5 in Yemen in 2021

It is estimated that around 2.3 million children below 5 years of age in Yemen will likely suffer from acute malnutrition in 2021, warn four United Nations agencies.

Overall, 400,000 among these are estimated to have severe acute malnutrition and could even die if urgent treatment is not provided. These numbers represent an increase in acute malnutrition and severe acute malnutrition of 16% and 22%, respectively, among children under 5 years of age in comparison with 2020. The data come from the Integrated Food Security Phase Classification (IPC) Acute Malnutrition report that has been released by the Food and Agriculture Organization of the United Nations (FAO), UNICEF (the United Nations Children's Fund), the World Food Programme (WFP), the World Health Organization (WHO) and partners… (*WHO*)

Wide Variability in Blood Glucose Tied to More CVD in Diabetes Patients

Patients with type 2 diabetes with the highest variability in A1c levels over a period of 2 years were found to have significantly more first cardiovascular disease (CVD) events compared to similar patients with less A1c variability, reported a retrospective analysis of over 29,000 US patients.

Patients in the quartile with the greatest level of A1c variability were shown to have a 59% higher rate of CVD events, in comparison with patients in the quartile with the lowest level of A1c variability. Every 1 unit rise in A1c standard deviation was tied to a significant 18% increase in CVD events after adjusting for confounders. The results were published in *Diabetes Obesity and Metabolism*… (*Medscape*)

US CDC Issues Guidance for Reopening of Schools

The US Centers for Disease Control and Prevention (CDC) has issued new guidance for reopening of US schools. The agency recommends universal wearing of masks and physical distancing as important strategies to control COVID-19.

The guidelines also stress on facility cleaning, personal hygiene as well as contact tracing. CDC Director Rochelle Walensky stated that with the strategies suggested by the agency, there will be little to no transmission of COVID-19 in schools, if followed properly. The agency also recommended that priority should be given to teachers and school staff for COVID-19 vaccination.

US President Joe Biden had also assured that most K-8 schools would be reopened within 100 days of his taking office on January 20. The President lauded the agency's new guidance as he highlighted the problems faced by children due to school closure… (*Reuters*)

COVID Antibodies may Last for 8 Months After Vaccination, Says AIIMS Director

The Director of All India Institute of Medical Sciences (AIIMS) has stated that antibodies against the SARS-CoV-2 virus may last for up to 8 months or even longer following vaccination against COVID-19.

He further stated that scientists are exploring the long-term protection provided by the vaccines. He mentioned that antibodies will develop around 14 days following the second dose of the vaccine, adding that while it was not clearly known as to how long the protection will last, but it is believed to last for a duration of at least 8 months, or longer… (*ET Healthworld – IANS*)

Alien Cells may Account for COVID 'Brain Fog'

New research suggests that the long-term neurologic symptoms, such as brain fog, that some patients with COVID-19 experience, may occur as a result of the occlusion of brain capillaries by large megakaryocytes.

The findings, shared in a research letter, report on 5 post-mortem cases from patients who succumbed to COVID-19. Researchers noted large cells that resembled megakaryocytes in cortical capillaries. Immunohistochemistry validated that they were megakaryocytes. According to the researchers, megakaryocytes have not been seen in the brain previously. The report was published online in *JAMA Neurology*.

Lead author David Nauen noted these cells in the first evaluation of brain tissue from a COVID-19 patient. He found no viral encephalitis, but there were unusually large cells in the brain capillaries. He stated that he had never seen these cells in the brain before… (*Medscape*)

High Rates of Anxiety among Physician Mothers

A new report suggests that physician mothers are reporting increased rates of moderate-to-severe anxiety during the COVID-19 crisis. Among them, frontline workers and informal caregivers have the highest rates of anxiety.

A survey was conducted among the Physician Moms Group on Facebook. Among over 1,800 respondents, around 41% of them had scores above the Generalized Anxiety Disorder 7-item scale (GAD-7) cut-off for moderate-to-severe anxiety. Additionally, 18% were found to have severe anxiety. Frontline workers and informal caregivers had higher anxiety levels. About 46% of them scored on the higher end of the GAD-7. The data is published in the *American Journal of Psychiatry*… (*Medpage Today*)

Drug to Reduce Bone Marrow Suppression due to Chemotherapy Approved

Trilaciclib became the first drug in its class to be approved by the US FDA for reducing the incidence of chemotherapy-induced bone marrow suppression in patients being given chemotherapy for extensive-stage small cell lung cancer.

The drug may provide protection to the bone marrow cells against damage from chemotherapy by inhibition of cyclin-dependent kinase 4/6.

Three randomized, double-blind, placebo-controlled trials conducted in patients with extensive-stage small cell lung cancer randomized a total of 245 patients to either trilaciclib or a placebo prior to chemotherapy. Patients given trilaciclib were found to have reduced odds of having severe neutropenia in comparison with patients receiving a placebo. Among the patients who had severe neutropenia, those on trilaciclib treatment had it for a shorter duration on average, compared to patients who received a placebo… (*FDA*)

Humidity from Masks may Decrease Severity of COVID-19

A study, published in the *Biophysical Journal*, led by researchers at the NIH's National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), has noted that face masks considerably increase the humidity in the air that a person wearing the mask breathes in.

According to the investigators, this higher level of humidity in the inhaled air could possibly explain why wearing mask is tied to lower disease severity in those infected with COVID-19. Of note, hydration of the respiratory tract is beneficial for the immune system. High levels of humidity can potentially decrease the spread of a virus to the lungs by means of promoting mucociliary clearance (MCC)… (*HT – ANI*)

New SOPs Issued for Offices to Curb the Spread of Coronavirus

The Union Health Ministry has released a set of new "SOPs to contain the spread of COVID-19 in offices".

The SOPs suggest that if one or two cases of COVID-19 are reported at a workplace, the disinfection can be limited to the areas occupied and visited by the patient over the previous 48 hours. Work can resume following disinfection procedure according to the stated protocols. The ministry added that in case of a large number of cases at a workplace, the entire block or building need to be disinfected prior to resuming work. Staff residing in containment zones must inform their supervisors about the same and not report to the workplace until the containment zone is denotified. These staff should be allowed to work from home… (*ET Healthworld – PTI*)

Pfizer-BioNTech COVID-19 Vaccine Decreases Symptomatic Infection in Real World: Israeli Researchers

Researchers from Israel suggest that the Pfizer-BioNTech COVID-19 vaccine seems to decrease symptomatic COVID-19 infections by over 90% in the real world.

Preliminary findings indicate that the vaccine is highly effective in a mass vaccination campaign. The Clalit Research Institute looked at data on 1.2 million people; nearly half of these received the Pfizer-BioNTech vaccine. Patients receiving the vaccine were compared with those who didn't. The rate of symptomatic COVID-19 was found to reduce by 94% among those who were given two doses of the vaccine. Additionally, the rate of serious illness was found to be reduced by 92%.

The findings are in line with data obtained from Pfizer's vaccine trial, which stated that the vaccine yielded 95% protection against symptomatic COVID-19… (*CNN*)

Younger People Half as Likely as Adults to Contract COVID-19: Study

A new modeling study has shown that individuals below the age of 20 years have about half the odds of contracting COVID-19 infection, compared to adults. These individuals also have lesser odds of transmitting the disease to others.

The study looked at 637 households whose members had undergone polymerase chain reaction (PCR) testing in spring last year. Some of them also underwent serology testing for antibodies to SARS-CoV-2. It was noted that those below 20 had 43% lesser susceptibility to COVID-19 as compared to those above 20. Children appeared to have greater odds of getting a negative PCR result in spite of being infected. This could probably account for the reports from across the globe that lesser number of children are diagnosed in comparison with adults.

The findings are published in the journal *PLOS Computational Biology*… (*NDTV – PTI*)

About One-third of People with Mild COVID-19 have Symptoms Months Later: Study

A study published in *JAMA Network Open* assessed 177 people with confirmed COVID-19 infection for a period of up to 9 months. The study group included 150 outpatients with mild COVID-19 who were not hospitalized.

Researchers from the University of Washington noted that 30% of the respondents had persistent symptoms, the most common being fatigue and loss of smell or taste. Over 30% of the study respondents reported worse quality of life in comparison with that prior to falling ill. Additionally, 14 subjects (8%), including 9 who had not been hospitalized, had trouble performing at least one usual activity, like daily chores… (*CNN*)

Short Sleep Tied to Incident Dementia and All-cause Mortality

Novel evidence links sleep deficiency, dementia and mortality.

A new study included 2,812 adults, 65 years of age and older, from the National Health and Aging Trends Study (NHATS). The study subjects completed surveys about sleep disturbance and duration in 2013 and 2014. Investigators assessed the link between sleep

disturbance and deficiency and incident dementia and all-cause mortality over a period of 5 years. Fully adjusted Cox multivariate analysis revealed that subjects who slept 5 hours or less per night had about double the risk for incident dementia compared to those who slept longer (HR, 2.04). The risk of dementia was found to be higher among those who took 30 minutes or longer to fall asleep (HR, 1.45). The findings are published in *Aging*… (*Medscape*)

WHO Update on New Molecular Assays for Diagnosis of TB and Drug Resistance

The WHO has announced vital updates on new molecular assays in a Rapid Communication, which is expected to result in significant improvements in the diagnosis of tuberculosis (TB) and drug resistance among adults, adolescents as well as children.

A meeting of a Guideline Development Group was convened in December 2020 to update WHO policies on molecular assays employed for the diagnosis of TB and drug resistance. The evidence reviewed and presented in the Rapid Communication point to high diagnostic accuracy for 3 new technologies, including moderate complexity automated Nucleic Acid Amplification Tests (NAATs), to detect TB and resistance to rifampicin and isoniazid; low complexity automated NAATs to identify resistance to isoniazid and second-line anti-TB agents; and high complexity hybridization-based NAATs to detect resistance to pyrazinamide… (*WHO*)

Pulse Oximeters not to be used to Diagnose COVID-19: US FDA

The US FDA has cautioned that pulse oximeters should not be used to diagnose COVID-19. The devices could give inaccurate readings under some situations, stated the agency.

The WHO had included the use of pulse oximeter to detect patients who may require hospitalization in its clinical advice for treating COVID-19 in the month of January. The FDA has stated that the devices cannot be used to diagnose or exclude COVID-19. The agency further recommended not to depend on them to evaluate health. The agency recommended that attention should be focused on other indicators of low oxygen, including blueness of the face or a rapid pulse… (*Reuters*)

It is Unlikely That Food and Food Packaging Spread COVID-19

It is highly unlikely that food and food packaging can spread COVID-19, stated the US FDA, US Department of Agriculture and the CDC.

An FDA statement mentioned that available information and international scientific consensus support that foods that people consume and food packaging they touch are highly unlikely to spread COVID-19 infection. The agencies emphasized that there was a dearth of reliable evidence that could suggest that food or food packaging can transmit SARS-CoV-2. The FDA added that the amount of virus particles that could be picked up through touching a surface would be very small while the amount that is required to cause infection by means of oral inhalation would be very high. Therefore, the odds of catching infection by touching the surface of food packaging or eating food appear to be very low… (*CNN*)

A Third of Patients Recovered from COVID may have PTSD

A single-center study in Italy has shown that nearly 30% of the patients who recovered from COVID-19 developed post-traumatic stress disorder (PTSD).

Overall, 381 patients were followed. Women were more likely to develop PTSD (55.7%). Those who went on to develop PTSD had higher rates of history of psychiatric disorder (34.8%), and had higher odds of having had delirium or agitation during acute illness (16.5%). These patients were also reported to have more persistent medical symptoms following their initial illness (62.6%). Besides PTSD, it was noted that 17.3% had depressive episodes and 7% had generalized anxiety disorder. The study is published in *JAMA Psychiatry*… (*Medpage Today*)

Exposure to Air Pollution *in utero* Linked to Poorer Cognition Later

A study published online in the *Journal of Alzheimer's Disease* noted that *in utero* exposure to air pollution appears to be linked with poorer cognition later in life.

The longitudinal study noted that exposure to air pollution in early life seems to have a small yet detectable association with worse cognition from 11 to 70 years of age. The effect size, though, was small.

Investigators assessed data from 572 individuals in the Lothian Birth Cohort 1936 with information on lifetime residential history. Participants were subjected to the Moray House Test of cognitive ability at 11 years of age and again at 70, 76 and 79 years of age. A small association was evident between exposure to greater levels of air pollution in 1935, when participants were *in utero* and worse cognition between age 11 years and 70 years… (*Medscape*)

Heart Damage in COVID-19 Patients Discharged from Hospital: Study

A clinical study suggests that nearly half of the patients evaluated have had damage to their hearts after being hospitalized with severe COVID-19 and had raised troponin levels. The study, published in the *European Heart Journal*, assessed 148 patients from six acute hospitals in London. Injury was identified by magnetic resonance imaging (MRI) scans at least 1 month following discharge. Troponin levels were raised in all the patients in the study. The patients were followed up with MRI scans of the heart after discharge. Investigators noted high rates of heart muscle injury a month or two following discharge. Some of this may have been already present, but MRI scans revealed that some were new, and possibly caused by COVID-19… (*HT – ANI*)

No-fault Compensation Plan for COVID-19 Vaccines

The WHO and Chubb Limited (NYSE: CB) have agreed to a no-fault compensation program for 92 low- and middle-income countries that are getting support through the Gavi COVAX Advance Market Commitment (AMC) of the COVAX Facility.

The program represents the first and only vaccine injury compensation plan on a global level and intends to provide eligible people in these countries with a fast, fair and transparent process to obtain compensation for serious adverse events associated with the vaccines distributed by COVAX till June 30, 2022. The no-fault compensation program will be put into operation through the web portal www.covaxclaims.com by March 31, 2021… (*WHO*)

Teachers may have a Role in In-school Transmission of COVID-19, Says CDC

Quoting a study done in elementary schools in a Georgia school district, the US CDC has stated that teachers may have a vital role in the transmission of COVID-19 in schools. Mask use and social distancing measures were sometimes found to be lacking.

The study included around 2,600 students and 700 staff members from a school district's elementary schools. There were nine clusters of COVID-19 cases that included 13 educators and 32 students at 6 elementary schools. The CDC report states that the students sat at a distance of less than 3 feet, and inadequate use of masks had a role to play in spread in some cases. Additionally, students ate their lunch in classrooms, which could also have led to an increase in transmission. The report stated that based on the findings, it appears that teachers can play a key role in in-school spread of COVID-19… (*Reuters*)

Study Implies COVID-19 Vaccination should be Prioritized for People with Genetic Disorders

A team of researchers has found in a recent study that adults with Down syndrome had greater odds of death due to COVID-19, compared to the general population. The study suggested that vaccinating people with genetic disorders against COVID-19 should be the priority.

The study, published in The Lancet's *EClinical Medicine,* included over 1,000 COVID-19 patients with Down syndrome, and noted that these patients had more severe symptoms at hospitalization and had increased rates of lung complications associated with increased death rate. Adults suffering from Down syndrome had a 3-fold higher likelihood of death due to COVID-19 in comparison with the general population. It was also noted that the increased risk of death was particularly evident in the fifth decade of life… (*HT – ANI*)

People Above 60 to be Vaccinated on Priority in India, Says Official

As the second phase of COVID-19 vaccination is set to begin in mid-March in the country, priority will be given to individuals 60 years of age and above as well as to those with comorbidities for longer duration, said Dr Suneela Garg, an advisor to Indian Council for Medical Research (ICMR).

Dr Garg stated that the beneficiaries will be split up depending on different criteria and every sub-group will have separate vaccination timelines. She added that there will be a key role of the private sector in the vaccination drive. She further mentioned that individuals with comorbidities like diabetes, hypertension, CVD, stroke, cancer, chronic respiratory diseases will be given priority over people suffering from other diseases… (*NDTV*)

Ghana Receives First Shipment of COVID-19 Vaccine Doses *via* COVAX Facility

Ghana has become the first country to receive the COVID-19 vaccine doses through the COVAX Facility in a historic step towards ensuring that there is equitable distribution of COVID-19 vaccines across the globe.

In all, 600,000 doses of the AstraZeneca/Oxford vaccine were shipped by the COVAX Facility on February 23 from the Serum Institute of India (SII) in Pune, India to Accra, Ghana. The shipment arrived in Accra on

the morning of February 24. This is the first batch of COVID-19 vaccines delivered in Africa by the COVAX Facility. The program aims to deliver at least 2 billion doses of COVID-19 vaccines by the end of this year… (*UNICEF*)

Survey in England Finds High Antibody Levels with Pfizer Vaccine

People in England who have been administered two doses of the Pfizer-BioNTech COVID-19 vaccine have developed strong antibody responses, suggests a new survey.

The survey conducted by the Imperial College London revealed that 87.9% of the individuals above 80 years of age tested positive for antibodies following two doses of the Pfizer vaccine. The figure stands at 95.5% among those below 60 years of age and 100% for those below 30. Close to 95% of the individuals below 30 years of age tested positive for antibodies 21 days after one dose, though the figure declined in older age groups. This home surveillance study for COVID-19 antibodies included more than 1,54,000 participants… (*Reuters*)

New Coronavirus Variant Found in New York City

Two research teams have reported that a concerning new coronavirus variant has been found in New York City and in the Northeast.

The mutations in this variant help it evade the body's immune response, besides evading the effects of monoclonal antibody treatment. The variant has been named as B.1.526. It has been noted among individuals affected in varied neighborhoods of New York City and scattered in the Northeast. One of the mutations that this variant carries is the same as that seen in the variant first identified in South Africa (B.1.351). There has been a steady rise in the detection rate from late December till middle of February, while there has been an alarming increase to 12.7% over the last 2 weeks… (*CNN*)

Concomitant Glucocorticoids and PPI use Increases Fracture Risk in RA Patients

Rheumatoid arthritis (RA) patients treated with oral glucocorticoids and proton pump inhibitors (PPIs) had an elevated risk for osteoporotic fracture, reported a large cohort study published online in *Annals of the Rheumatic Diseases*.

Concomitant use of glucocorticoids and PPIs was found to be linked with a 1.6 times increased risk of osteoporotic fracture (adjusted HR 1.60, 95% CI 1.35-1.89), reported researchers. Use of either oral glucocorticoids or PPIs alone was associated with only a 1.2 times increased risk.

For glucocorticoid alone, the adjusted HR was 1.23 (95% CI 1.03-1.47), and that for PPI use alone was 1.22 (95% CI 1.05-1.42). This was statistically lower than that for concomitant use of the two drugs… (*Medpage Today*)

WHO Certifies El Salvador as Malaria-free

El Salvador has become the first country in Central America to be certified as malaria-free by the WHO.

The certification of malaria elimination comes after over 5 decades of commitment by the government of El Salvador and its people to eliminate the disease from the country that is densely populated and has a topography that is favorable for malaria.

The certification of malaria elimination is given when a country proves that it has broken the chain of indigenous transmission for at least 3 years in a row. From 1990 to 2010, the number of malaria cases had dropped from over 9,000 to 26 in the country, and there have been no indigenous cases since 2017… (*WHO*)

UN-backed Policy Brief Urges for Action Addressing Long COVID

A policy brief, published by the WHO's Regional Office for Europe and the European Observatory on Health Systems and Policies, states that 1 in 10 individuals still feel ill 12 weeks after having COVID-19, and that authorities need to do more to support these people.

The UN-backed policy brief talks about what we know about long COVID and also summarizes countries' efforts in addressing the condition. Long COVID is associated with symptoms like severe fatigue and increased damage to the heart, lungs and brain. The document emphasizes the development of new care pathways, devising appropriate services, and addressing the more extensive impacts like employment rights, sick pay policies and access to disability benefits… (*UN*)

FDA Allows More Flexible Storage, Transportation for Pfizer-BioNTech Vaccine

The US Food and Drug Administration (FDA) has stated that undiluted frozen vials of the Pfizer-BioNTech COVID-19 vaccine can be transported and stored at temperatures that are commonly found in pharmaceutical freezers, for up to 2 weeks.

This comes as an alternative to the storage of the vaccine vials at temperatures of -80ºC to -60ºC (-112ºF to -76ºF).

Pfizer Inc. had submitted data to the US regulator which stated that its COVID-19 vaccine remained stable after undiluted vials were stored for up to 2 weeks at standard freezer temperature. However, this alternative storage temperature for frozen vials does not apply to the thawed vials prior to dilution, or the storage of thawed vials following dilution… (*FDA*)

People Above 45 with Comorbidities Need Doctor's Certificate for Vaccination in India

Individuals 45-60 years of age having comorbidities will need a certificate from a registered medical practitioner, either from public or private sector, stating that they are suffering from a disease that could heighten the risk of infection, and therefore, are eligible to receive the COVID-19 vaccination on priority, stated officials.

A protocol for doctors is yet to be issued. Those in the stated age group who have one or more comorbidities such as uncontrolled diabetes, heart disorders, chronic pulmonary, kidney diseases, cancer, have undergone transplant, those taking immune medication and have morbid obesity conditions can be given the vaccine… (*ET Healthworld – TNN*)

Most Severe COVID Linked with Four Cardiometabolic Conditions

A new study has shown that the majority of hospitalizations due to COVID-19 in the United States can be attributed to four pre-existing cardiometabolic conditions.

Out of 9,06,849 COVID-19 hospitalizations seen among US adults as of November 2020, obesity accounted for 30% of them, hypertension accounted for 26%, diabetes for 21%, and heart failure accounted for 12% of the hospitalizations. It is estimated that around 63.5% of the hospitalizations were associated with these cardiometabolic conditions. Investigators stated that these hospitalizations would have been preventable if these conditions were not present in the first place. Investigators further estimated that a reduction of 10% in these cardiometabolic conditions would have prevented 11.1% of the hospitalizations due to COVID… (*Medscape*)

Canada Approves AstraZeneca COVID-19 Vaccine

Canada has granted approval for the AstraZeneca COVID-19 vaccine, including the one produced by the Serum Institute of India (SII). Overall, 5,00,000 doses of the vaccine are expected to arrive in the country next week.

This is the third vaccine to be approved by Health Canada after the approval of vaccines developed by Pfizer-BioNTech and Moderna in December. Prime Minister Justin Trudeau stated that with the three vaccines, the country will now get over 6.5 million doses before March end. Additionally, tens of millions of more doses will reach between April and June. Twenty million doses have been ordered by Canada from AstraZeneca, of which 1.9 million will be received through COVAX in the first half of this year… (*Reuters*)

Open a Window to Reduce COVID-19 Transmission, CDC to Schools

The US CDC has issued new recommendations highlighting the significance of good ventilation in preventing the spread of COVID-19 in schools and daycares. The key recommendation is "Open a window".

For the first time, the CDC has separately stressed on the role of ventilation in preventing the spread of coronavirus. While the agency had previously talked about ventilation in its guidelines to schools, this time, an entire page has been dedicated to the matter. The CDC states that if it is safe to open doors and windows, it should be done. However, if it poses a safety or health risk, like falling, they should not be opened. The agency also advises to open the windows in transportation vehicles… (*CNN*)

More Than 1.37 Crore Vaccine Doses Administered in India

The 42nd day of the country-wide COVID-19 vaccination program saw 2,84,297 vaccine doses administered to HCWs and frontline workers (FLWs), taking the overall number of vaccinations to more than 1.37 crores, stated the Union Ministry of Health and Family Welfare (MoHFW).

Overall 1,37,56,940 doses have been administered across 2,89,320 sessions, according to the provisional report till 6 pm on February 26. Overall, 66,37,049 (76.6%) HCWs have received the first dose while 22,04,083 (62.9%) HCWs have been administered their second dose. Additionally, 49,15,808 (47.7%) FLWs have received the first dose. The five states that have recorded the highest number of vaccinations include Uttar Pradesh, West Bengal, Gujarat, Karnataka and Maharashtra… (*NDTV – ANI*)

COVID Vaccination Tied to Decline in Intubation Rates: Real World Data

Since the nationwide COVID-19 vaccination program with the Pfizer-BioNTech vaccine started in Israel, the

rates of mechanical ventilation have been reported to decline about two-thirds among older adults with the disease.

Investigators compared adults 70 years of age and older, who had the highest two-dose vaccination coverage in February, to adults 50 years of age and below, who had the lowest coverage. They compared the rates of mechanical ventilation in the two groups during October to December last year to the rates in February this year. They reported in the *Morbidity and Mortality Weekly Report* that the rates of mechanical ventilation among COVID-19 patients aged 70 years and above dropped by 67% between fall 2020 and February 2021, in comparison with patients below 50 years of age.

The ratio of ventilated older patients to younger patients was reported as 1.9:1… (*Medpage Today*)

SEC Asks Bharat Biotech to Submit Covaxin Phase 3 Efficacy Data Before Seeking Approval for Kids' Trial

The Subject Expert Committee (SEC) that advises the Drugs Controller General of India (DCGI) has asked Bharat Biotech to submit efficacy and safety data from the ongoing Phase III trials of Covaxin prior to seeking approval for conducting the trials on children.

The SEC has also asked the company to revise and submit the protocol of the trial for children to a Phase II/III study.

Bharat Biotech had sought approval to conduct Phase III trials of their vaccine on children aged 5-18 years. The SEC stated that sample size and other consequential changes must be made to the protocol, and the company should submit the revised clinical trial protocol for review… (*ET Healthworld – TNN*)

Single Pfizer Vaccine Dose Yields Strong Protection for Those who've been Infected: UK Studies

Just a single dose of Pfizer-BioNTech COVID-19 vaccine can produce an immune response in people who have already been infected with COVID-19 which is robust enough to protect them from future infection, suggest two new papers published in *The Lancet*.

One of the two new papers involved data on 51 HCWs in London. Twenty-four of them had previously had COVID-19. All of these healthcare workers received a first dose of the Pfizer-BioNTech vaccine and were tested for antibodies 19-29 days later. Among the participants who had a previous natural infection, vaccination heightened their antibody levels over 140-times. The second paper presented data on 72 HCWs vaccinated in late December. Twenty-one of them had previous infection. Those who had a previous COVID-19 infection developed stronger immune responses to one dose of vaccine compared to those who had not been infected… (*CNN*)

Gym Sessions without Masks can Spread COVID-19: CDC

New studies from CDC suggest that gyms can be the hot spots for COVID-19 outbreaks if people don't wear face masks, even if social distancing guidelines are followed. The CDC released results from outbreaks at gyms that had a high attack rate during summer of 2020. In Hawaii, 21 people were reported to have caught COVID-19 infection in July after a cycling instructor infected with COVID-19 taught classes for 3 days and later tested positive. While the cycling stations were placed at a distance of over 6 feet from one another, none of the individuals wore masks. One of the participants was another instructor, and later taught kickboxing classes and conducted personal training sessions without a mask, leading to many COVID-19 cases.

In Chicago, 55 out of 81 individuals attending high-intensity fitness classes during the last week of August contracted COVID-19. The classes had only 10-15 people, and they were stationed over 6 feet apart. People were required to wear masks while entering the gym, temperature checks were conducted, and people were screened for symptoms at the facility. But, the people were allowed to remove the masks while exercising.

The CDC stated in the Chicago report that there is increased respiratory exertion in the enclosed spaces of indoor exercise, which assists in the transmission of the virus… (*Medscape*)

Risk of Human Spread of H5N8 Bird Flu Appears Low, Says WHO

The risk of human-to-human transmission of the H5N8 strain of bird flu appears to be low, after it was first identified in farm workers in Russia, stated the WHO.

Russia reported the first case of a strain of bird flu virus H5N8 being passed to humans from birds. The matter was notified to the WHO. Seven people in Russia were found to be infected with H5N8 strain after an outbreak on a poultry farm in Astrakhan. All of the affected individuals were asymptomatic, stated the WHO. Close contacts of the cases were monitored, and none of them showed signs of clinical illness. Therefore, on the basis of the available information, the risk of human-to-human transmission appears to be low, said WHO… (*Reuters*)

Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

The Vast Power of the Spirit

KK AGGARWAL

Om Poornamadah, "Om Poornamadah Poornamidam,
Poornaat Poornamudachyate
Poornasya Poornamaadaaya, Poornameva Avasihyate"

The whole is whole; if you take away the whole away from the whole the whole will still remain. (That is infinite, this is infinite, from the infinite, the infinite has come out. Having taken the infinite out of the infinite, the infinite alone remains).

In Vedanta, **"That"** represents super consciousness, God or the Brahman and **"This"** signifies the visible universe.

Atman makes up our body. It is 99.99% space, and the rest - it is also nothing but space or void. This void or 'akasha' is Brahman, God or consciousness and represents a web of energized information. This web of information of inner space called inner consciousness is the Atman or the Soul. This is connected with the outer space in the universe having a similar web of energized information called the Spirit or *Brahmand*.

This spirit has been given many names - Allah (Islam), Buddha (Buddhism), Brahman (Hinduism), Christ (Christianity) or Wahe Guru (Sikhism). They all signify the same. This spirit, the energized field of information, is a powerful expression of live energy which can move faster than the speed of light. Soul is nothing but an individualized expression of the spirit.

This energy containing information in the spirit cannot be seen, felt, touched, tasted or smelt. It cannot be destroyed with a weapon, fire, water or air. This consciousness is enshrined in the space of all cells of the body. It is like sugar added to the milk. Once added, you cannot find it as it gets mixed with each and every drop of the milk.

Soul originates from the spirit. Each soul differs from the other through subtle layer of consciousness called the *"sukshma sharira"* which is controlled by actions, memories and desires. Spirit is like light - always positive and removes darkness. The basic nature of the consciousness is "truth and bliss". The soul and the spirit do not have hatred, anger or jealousy and are full of unconditional love. They are a treasury of information about everything. This infinite information can achieve anything, including miracles. It is like the flame of a candle, which can light an infinite number of candles, and still retain its illumination.

Dr Deepak Chopra once said that the soul is like the voice of Lata Mangeshkar coming out of a radio, and even if you break the radio, you will not find Lata Mangeshkar in it. Similarly, even if you cut the body into pieces, you cannot find the physical presence of the spirit.

Spirit is present all over, be it the universe or the living beings. Any amount of spirit taken out from it will not make any difference to the spirit. In religious terms, the infinite or the vastness is equated and described by the blue color; hence, most of the gods are represented by the blue color, or are shown in the background of blue sky. This signifies the vastness and infinite character of the consciousness.

One of the Gurus explained to his disciple the description of the spirit by the following equation. 1 × 1 = 1, 1/1 = 1 or, in other words everything is one. It can also be explained by the equation that infinity when added, subtracted, multiplied or divided by infinity will result in infinity only.

This infinite potential in our mind is present in between the thoughts and can be experienced by enabling oneself to go in between the thoughts by a process called mediation. One can experience the silent gap between the thoughts either with the use of primordial sound mantra or by way of yoga. People who have learnt meditation and have achieved the ability to go into the silent gaps can accomplish everything in their life using the principles of intention and attention. After any intention is introduced in the silent gap, a new reality can be created.

"That which is born of the flash is a flash; that which is born of the Spirit is spirit" – John

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

Group Editor-in-Chief, IJCP Group

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 10, March 2021

List of Things We Dislike

A man and his girlfriend were getting married in an elaborate ceremony. All of their friends and family came to the wedding. Everyone had a wonderful time.

The bride looked beautiful in her white wedding gown and the groom looked handsome in his black tuxedo. Everyone could tell that truly lover each other.

A few months later, the wife came with a proposal to the husband. She had read somewhere about how they can strengthen their marriage. She proposed that both of them will write a list of the things that they find a bit annoying about the other person. Then, they would discuss about how to fix them together and make their lives happier together.

The husband agreed. They went to a separate room in the house and started penning down the things that annoyed them about the other.

The next morning they decided to go over their lists. The wife took out her list. It was a 3 page list. As she started reading the list, she noticed tears appearing in her husband's eyes. She asked him what was wrong.

The husband said that it was nothing and asked her to keep reading her lists. The wife continued to read and placed the list on the table once she was done.

Now she asked her husband to read his list. The husband stated that he had nothing on his list. He thought that his wife was perfect. He didn't want her to change anything for him.

The wife was touched by his honesty and the depth of his love for her. She burst into tears.

Many a times, we feel disappointed, depressed and annoyed. But we don't really have to go looking for such times.

This is a wonderful world full of beauty, light and promise. Don't waste time looking for the disappointing or annoying times when there are wonderful things around us.

We are the happiest when we acknowledge the good and try our best to forget the bad. Nobody's perfect; we can find perfection in them to change the way we see them.

You may never find a perfect partner to love you the way you wanted, only a person who's willing to love you more than what you are.

■■■■

Masks Don't Impact Oxygen Saturation in Individuals with Asthma

A new study has suggested that wearing a mask to protect against the spread of COVID-19 does not decrease oxygen saturation.

The study revealed that there was no decrease in oxygen saturation in over 200 mask-wearing individuals who attended an asthma and allergy clinic, irrespective of the type of mask and the duration for which they had been wearing the mask. Investigators obtained 223 surveys from adult and pediatric patients presenting to the University of Michigan Medicine Allergy Clinic from September 10 through October 23, 2020. Patients were asked if they had asthma, the degree of perceived control if they had asthma, the type of mask they wore, and how long they had been wearing it. Resting pulse oximetry readings were noted for all subjects. The mean SpO_2 was noted to be 98% in both asthma and nonasthma groups. Additionally, the mean SpO_2 was 98% for both a fabric mask and a surgical mask 98%, while it was 99% for N95 mask. The findings were presented at the Virtual Annual Meeting of the American Academy of Allergy, Asthma and Immunology… (*Medscape*)

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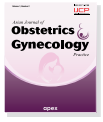
Asian Journal of Obs & Gynae Practice 	4	1,500/- ☐	550/- ☐
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Lighter Side of Medicine

HUMOR

WORK WISDOM

- Kauffman's Paradox of the Corporation: The less important you are to the corporation, the more your tardiness or absence is noticed.
- The Salary Axiom: The pay raise is just large enough to increase your taxes and just small enough to have no effect on your take-home pay.

PRISON VS WORK

Just in case you ever got these two mixed up, this should make things a bit more clear.

In PRISON you spend the majority of your time in an 8 × 10 cell.
At WORK you spend the majority of your time in a 6 × 8 cubicle.

In PRISON you get three meals a day.
At WORK you only get a break for one meal and you pay for it.

In PRISON you get time off for good behavior.
At WORK you get more work for good behavior.

In PRISON the guard locks and unlocks all the doors for you.
At WORK you must carry around a security card and open all the doors for yourself.

In PRISON you can watch TV and play games.
At WORK you get fired for watching TV and playing games.

GOOD TREATMENT

Bob went over to his friend Joe's house and was amazed at how well Joe treated his wife. He often told her how attractive she was, complimented her on her cooking and showered her with hugs and kisses. "Gee," Bob remarked later, "you really make a big fuss over your wife". "I started to appreciate her more about 6 months ago," Joe said. "It has revived our marriage and we couldn't be happier."

Inspired, Bob hurried home, hugged his wife and told her how much he loved her and said he wanted to hear all about her day. But she burst into tears. "Honey," Bob said, "what's' the matter?" "This has been the worst day," she replied. "This morning Billy fell off his bike and broke his ankle, then the washing machine broke. Now to top it off, you come home drunk!"

ROLLS ROYCE

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".

Dr. Good and Dr. Bad

SITUATION: A 70-year-old man with type 2 diabetes had increased glycemic variability. In addition, his kidney disease had worsened over a period of 2 years.

LESSON: In patients with type 2 diabetes mellitus, progression of kidney disease as well as increased glycemic variability are known to contribute to the pathogenesis of coronary plaque formation via inflammatory pathways.

Cardiovasc Diabetol. 2017;16(1):131.

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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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