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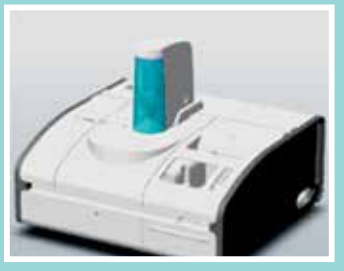

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HCFI DR KK AGGARWAL RESEARCH FUND

HCFI Round Table Environment Expert Zoom Meeting on "Biomining of Dumpsites, Bioremediation of Legacy Waste, Utilization and Pollution Control Aspects"

- Urban India accounts for one-third of India's population and generates 55 million tonnes of municipal solid waste annually. A major part is being dumped in the open since long time. There are three landfill sites in Delhi: Ghazipur, Okhla and Bhalswa. These dumpsites pose a threat to public health and the environment because they have grown in height and have become a huge source of pollution and greenhouse gas emissions, such as methane and other landfill gases.
- It is estimated that more than 10,000 hectares of land in India is locked in these dumpsites.
- The legacy waste in these dumpsites amounts to several lakhs of tonnes and needs to be remediated to make the city cleaner.
- It affects the health of people living around it, causes air pollution and the ground water also gets contaminated through leachate.
- The National Green Tribunal (NGT) in its order has also said that the legacy waste needs to be cleaned by biomining and bioremediation.
- This topic is critical in present times because unlocking the land which is lying under the dump is a very important activity. But at the same time, what are the steps to be done and how it can be helpful is also important.
- The government is willing to take this activity under the Swachh Bharat Mission.
- A lot of guidelines by Central Pollution Control Board (CPCB), CPHU have been published. But these guidelines need to integrate the practical problems.
- Government of India, under the phase 2 of the Swachh Bharat Mission, has declared 15,000 lakh crore for the Swachh Bharat Mission. A considerable amount will be spent to unlock the legacy waste or the dumpsites.
- A 35-year-old dumpsite spread across 332 acres of land in Hyderabad was handed over (contract) to us in 2010 with the objective to reclaim roughly 55 acres of land to construct a landfill and other processing plants in the reclaimed land. Fresh waste intake at that time was 3,500 tonnes, which today is 8,000 metric tonnes per day. About 125 acres of land could be reclaimed. Part of it was capped. A huge compost plant, 19.8-megawatt power plant, a compressed biogas plant were constructed, which are all operational. This has been a successful case

study of reclaiming the land and utilizing it for scientific landfill, pre-processing of waste and also recovery of certain materials with 80% of waste going under capping.

- The kind of waste that is generated and the nature of problem is humongous and beyond our imagination.
- Nearly 55 million tonnes of municipal solid waste from urban areas had been open-dumped historically.
- Today there are 10 cities with a billion population. The accelerated growth of population and increasing economic activities rule out the viability of open dumping.
- Environmental adjudication has also mandated the scientific remediation of dumpsites.
- Dumpsites generate leachate that kills vegetation and irreversibly pollutes groundwater. They also generate methane, which often auto ignites.
- The number of legacy dumpsites in India, as of 2020, is 3075 with Uttar Pradesh having the maximum number at 601, followed by Madhya Pradesh (328) and Maharashtra (327).
- Fifty dumpsites in Madhya Pradesh, 15 in Karnataka and 6 in Kerala have been reclaimed. One dumpsite each in Meghalaya, Rajasthan, Telangana and Chandigarh and 6 in Karnataka have been converted to secured landfill facility (SLF) and capped.
- NGT has directed bioremediation of all dumpsites by October 2020. NGT discourages capping or using the land for activities other than waste management.
- CPCB has been directed to prepare inventory of dumpsites as per NGT order and to compile information on legacy sites and identify gaps. The inventory has been prepared and gap studies have been done.
- The Ministry of Housing and Urban Affairs has said that more than 14 billion tonnes of waste is lying with 472 cities and number of dumpsites are 517.
- The solid waste management rules talk of bioremediation. As per the Rules, the local body is the authority. Capping is permissible in case of absence of potential of bioremediation and also reduction by biomining and placement of residues in new SLF. Any new dumpsite can have a new SLF capping with geomembrane, cut off walls or any other method.
- It is required to provide total number of dumpsites and number of dumpsites bioremediated/capped in annual report filed to CPCB. Inventory is the responsibility of the local authority and bioremediation and capping to be completed by March 2021.
- Timelines have been defined and what actions to be done by the urban local bodies (ULB) have been mentioned in the rules. In compliance with the Hon'ble NGT orders, guidelines on "Disposal of Legacy Waste" was to be prepared by CPCB, which have been prepared and the guidelines are uploaded on CPCB website.
- NGT has been quite vocal and directive in terms of where biomining and bioremediation is possible, which can be *ex-situ* or *in-situ*. It says capping of legacy wastes, which has huge environmental and health consequences is no option at all except inert waste, which is to be disposed in a scientific secured landfill.
- Inert waste has not been defined. The utilization of recoverable material has also not been defined. Bioremediation and biomining of dumpsites should be the preferred option and cities with more than 10 lakh population need special localized solutions.
- Duties and responsibilities of local authorities have been defined namely, desired objective of zero waste going to landfill, feasibility studies on open dumpsites and existing operational dumpsites for biomining and bioremediation potential, initiate necessary actions to biomine or bioremediate the sites.
- In the absence of the potential of biomining and bioremediation of dumpsite, it shall be scientifically capped as per landfill capping norms to prevent further damage to the environment.
- Impacts are high in terms of groundwater, water pollution, air pollution (SPM). These dumpsites do not have liner system; so lead to groundwater contamination. There is uncontrolled leachate generation and lack of systems to collect and treat.
- There is no provision of gas collection utilization. Fresh waste continues to be dumped at legacy dumpsites.
- There are some issues related to biomining. Utilization of appropriate machinery and process is not defined. Use of bioculture for stabilization of waste is kept open and the chemical used add to the pollution. Screening of different fractions

requires varied machinery, which need to be carefully checked. Other important issues include management of existing leachate under the dump while doing bioremediation and proper record or documentation of utilization or disposal of screened fractions from biomining.

- There are gaps in planning, data, technical guidance and execution or use of outputs. There is little or no planning prior to dumpsite rehabilitation. There is lack of data on characteristics of waste, bore hole testing, leachate and gas generation from dumpsite.
- There is a need for training of ULBs, State Pollution Control Boards (SPCBs), state Urban Dynamometer Driving Schedule (UDDS) for thorough checks and audits of disposal of the proceeds from biomining. This is a very critical requirement.
- The CPCB has issued directions to SPCBs/ Pollution Control Committees (PCCs) in January 2021 for complete listing of dumpsites, along with bioremediation in compliance with solid waste management Rules and CPCB guidelines, analysis of screened fractions before their utilization or disposal, leachate management, preparation of time targeted actin plan and very importantly, the maintenance of record for utilization/disposal of screened fractions, but it has not been defined. The CPCB has also directed to develop at least one model for bioremediation of dumpsite.
- Biomining is not relocation of a dumpsite. There are complex technical, economic and environmental considerations. Real estate redevelopment potential needs to be carefully evaluated.
- Dumpsite processing has an impact on people living near the dumpsite due to dust and noise pollution. Malodors from the biomining process can affect the surroundings as well as the worker. Masking chemicals may also generate alternate pollution. The movement of heavy machinery is also an issue.
- Each dumpsite cannot be same. Hence, waste characterization is a precursor to the selection of right technology for processing. Capex for technology cannot be arrived at without the characterization of waste.
- Theoretical and actual quantity of waste must be determined rather than relying on visual inspection/total station survey. The densities of all the waste components need to be determined to arrive at the right processing cost of the waste.
- Economics of project completion is more dependent on developing new and instant markets for any new products of the legacy waste other than the regular products (Refuse Derived Fuel [RDF]/ Enriched Soil/Compost, etc.)
- Carbon footprint of transportation is dependent on the design and scale of operations.
- Transportation is very important.
- The proceeds from the biomining are dependent on the age of the dumpsite. The waste in the legacy dumpsite stabilizes with age. The components of biomining are in the form of compost/RDF/inerts/ recyclables. Inerts are very high sometimes and can be more than 70%. Recyclables are negligible.
- Sustainable proceeds from the legacy dumpsite can only be determined by a proper scientific characterization of waste.
- Challenges encountered in dumpsite remediation projects include operational, infrastructural, contractual and financial challenges. Risks need to be properly defined. Land unlocking should have proper support from the ULB or the government.
- 100% land reclamation is difficult for large dumps.
- Clearing land is required for setting up of the biomining equipment within dumpsite for maneuverability of the equipment.
- Other operational challenges are existing litigation on project or land, opposition from local public, lack of clarity on volume vs. weight-based measurements, provision of power and water connections for the project, lack of familiarity with CPCB guidelines, delay in processing due to climatic conditions. Difficulty in quantifying the legacy waste below ground level is another challenge. Therefore, separate methodology has to be worked out to assess the quantity which needs another project. Guidelines need further detailing with the help of experts.
- Transportation costs can be more than the cost of remediation itself.
- For smaller ULBs of less than 1 lakh population, farming areas are close by so that mined soil enricher is taken by the farmers. But they are reluctant; so confidence building measures are required to remove hesitancy. Inerts are also used up by ULBs and citizens in building activities such as construction of drains, footpaths.
- Transportation of RDF from these ULBs to the points of usage, such as cement kilns, road

projects and Waste-to-Energy (WtE) plants, can be a costly task as the amount of RDF is small.

- The linkages for off take of by-products, like soil enricher, RDF, C&D waste, recyclables and inert to farmers, are still a big challenge for ULBs or operators in providing sustainable solution of dumpsite remediation.
- Customized machineries are not available for removal of legacy waste.
- There is a lack of experienced workers for carrying out biomining work. There is no incentive or reward for carrying out this work since the contractors have to work in unhygienic and hazardous dump yards.
- Cement companies are reluctant to take the RDF. Cost-benefit analysis has to be done.
- Unreasonable timelines proposed by ULB, lack of clarity of PCBs clearances are other issues of concern.
- Mostly, biomining projects are under budgeted; there are no grants or financial assistance from government.
- The ULBs could not bear the entire biomining cost from their own resources.
- Payment terms and methodologies vary with different ULBs. There is lack of clarity on the applicability of GST.
- The cost burden for transporting the soil and inerts is much higher than the cost of the remediation itself.
- Biomining is a complex problem and needs to be aligned with an integrated Solid Waste Management (SWM) approach. There is no one size fits all as each dumpsite has its own characteristics. The biomining proceeds vary, which affect the disposal routes. The best strategy has to be selected to address the legacy dump.

Participants: Dr Anil Kumar, Mr Vivek Kumar, Mr Sanjeev Kumar, Mr Premchandrahas, Dr M Dwarakanath, Mr Arun Kumar, Mr Neeraj Tyagi, Mr Vikas Singhal, Mr Ankit Sethi, Mr Varun Singh, Ms Ira Gupta, Dr S Sharma

(*Excerpts from presentation by Mr Sanjiv Kumar, Vice President, Ramky Enviro Engineers Ltd.; February 20, 2022 - 12 noon-1 pm*)

■■■■

FDA Authorizes New Monoclonal Antibody to Treat Omicron

The US Food and Drug Administration (FDA) has issued an emergency use authorization (EUA) for bebtelovimab, a monoclonal antibody that has been reported to retain activity against the Omicron variant.

Bebtelovimab has been granted EUA for the treatment of mild-to-moderate COVID-19 in people aged 12 years and above, who have a risk of progression to severe disease. The agency stated that laboratory tests have shown that bebtelovimab retains its activity against both the Omicron variant and the BA.2 Omicron subvariant.

The antibody treatment has not been approved for use in hospitalized patients or those who need oxygen therapy, as it has not been evaluated in this population and could possibly worsen the outcomes. The EUA is supported by results from the phase II BLAZE-4 trial.

The agency stated that COVID-related hospitalizations and deaths were found to be lower among patients who received bebtelovimab alone or in combination with other antibodies compared to those who were given placebo… (*Medpage Today, February 11, 2022*)

Coronavirus can Destroy Placenta, Cause Stillbirths

According to new research, the coronavirus can potentially invade and destroy the placenta and result in stillbirths in infected women. Investigators in 12 countries, including the United States, examined placental and autopsy tissue obtained from 64 stillbirths and 4 newborns who died soon after birth. All the cases involved unvaccinated women who contracted COVID-19 infection during pregnancy. Jeffery Goldstein, a pathologist at Northwestern University's Feinberg School of Medicine, said that the study indicates that damage to the placenta, rather than an infection of the fetus, likely leads to COVID-19-related stillbirths.

Study lead author, Dr David Schwartz, said that in many of the cases, more than 90% of the placenta was destroyed. The study is published in *Archives of Pathology & Laboratory Medicine…* (*Deccan Chronicle – AP, February 11, 2022*)

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Preparing for the Ramadan Fast During the Month of Shabaan

As we approach the month of Ramadan, believers begin to prepare for the fasting that is one of the five pillars of Islam.[1] Ramadan fasting is decreed for spiritual growth and self-control, discipline and empathy with the less fortunate. There are sudden changes in dietary pattern and composition, physical and spiritual activity and sleep practices. This change creates some difficulties in the initial days, especially for persons living with diabetes or other chronic diseases. The Quran exempts people with illness from fasting, especially if fasting can worsen their health. In view of the enormous spiritual benefits of fasting, many people will insist on fasting. It is also allowed to fast later in case you miss out on fasts during Ramadan, but people prefer fasting during Ramadan as the entire community observes the fast.

In this editorial, we discuss how the month of Shabaan which precedes the month of Ramadan can be utilized to prepare for Ramadan fasting, and how it can serve as a springboard for enhanced healthcare-related behavior.

INTERMITTENT FASTING

Intermittent fasting (IF) is considered a "modern" development by many, but the Ramadan fast is actually a prototype of IF.[2] IF includes a wide-spectrum of meal-related practices. One may fast for 12 to 16 hours daily or a few days every week. Certain dietary restrictions are also mandatory which are accepted by patients who follow IF. Shabaan can be used to inculcate the habit of IF, in a graded manner. This habit has been advocated from the time of the Prophet, but not really inculcated seriously. It must be noted that such a change should be carried out in consultation with the treating physician, especially for persons on antihyperglycemic therapy.

Some individuals may choose to try a "practice" fast for 3 days, on the 15th, 16th and 17th day of Shabaan. This helps persons with diabetes understand and monitor their response to fasting and allows for more efficient titration of medication, especially in case of hypoglycemia.

PHYSICAL ACTIVITY

Ramadan is also marked by offering of the Tarawih prayers (prolonged prayers), which are equivalent of structured physical activity or exercise. This may be a daunting task for the exercise-naïve devotee. Shabaan can be used to begin exercising, achieve physical conditioning and prepare for the coming month. Gradual escalation of prayers, perhaps on a weekly basis, can be kept as an individual goal.

HEALTH CHECK-UP

It is important to have a comprehensive pre-Ramadan check-up, and impart structured pre-Ramadan education.[3] This helps in better risk stratification[4] of the patient regarding the risk of fasting. Shabaan, and

Table 1. Shabaan as an Opportunity for Better Health, Prior to Ramadan

Diet	Lifestyle	Healthcare assessment
• Moderation in diet	• Physical conditioning/exercise	• Regular healthcare check-up
• Practice of intermittent fasting	• Spiritual health/stress management	• Risk stratification for fasting
• Practice dawn to dusk fast for 3 days	• Avoidance of substance abuse	• Adjustment and titration of medicine
	• Regular sleep hygiene	• Pre-Ramadan structured education
		• Awareness of healthcare support available during Ramadan

the preceding month, offer an opportunity for better patient-physician interaction and communication. This allows institution of practices such as annual preventive check-ups before Ramadan, investigations for screening and monitoring of chronic complications, and reinforcement of healthy lifestyle measures.

One must include optimization of healthcare seeking and healthcare accepting behavior as a prelude to Ramadan during Shabaan. An example may be completing one's vaccinations prior to the start of Ramadan. Availability of healthcare, including emergency services, can also be reinforced.

LIFESTYLE OPTIMIZATION

Undesirable habits, such as substance abuse (including betel nut chewing), poor sleep hygiene and negative stress coping styles can be tackled during Shabaan to ensure a fulfilling and meaningful Ramadan fast. Ramadan fasting stands for self-control, sacrifice and empathy for the unfortunate. These are achieved through discipline, determination and devotion. This discipline and determination should be fortified throughout the year. This reflection helps motivate persons to integrate healthy behaviors as part of daily life.

HEALTHCARE AND DIALOGUE

All this is possible only through dialogue.[5] Healthcare professionals should take the lead in speaking about Ramadan and health conversations should start weeks before the onset of the holy month and should extend to every member of the society. Shabaan is an opportunity that we must not miss.

Religious leaders can be involved to explain and clarify the exemptions from fasting that have been listed in the scriptures.

SUMMARY

Shabaan, and the preceding month of Rajab, can be used as a springboard for initiation and strengthening of healthy practices. This will help in observance of Ramadan in a safe and fulfilling manner.

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ORIGINAL RESEARCH

Impact of Real-time Assessment on the Training of Trainers for the Introduction of Rotavirus Vaccine in India

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ABSTRACT

Background and aim: The introduction of rotavirus vaccine (RVV) in the universal immunization program of India is a big feat as it became the first nation in the World Health Organization (WHO) Southeast Asia region to do so. The involvement of huge numbers of frontline workers in introducing new vaccines in India and the underlined deficits in skills and knowledge require efficient capacity building programs. In view of this, limited research is available on the effectiveness of capacity-building interventions for healthcare workers. There is a dearth of studies from India measuring the "on-spot" impact of immunization trainings on healthcare workers. This study aims to assess the effectiveness of training in RVV introduction in enhancing the knowledge of the participants. **Methods:** The study was conducted among the participants attending two training workshops for the introduction of RVV: a state workshop in Pune and a regional workshop in Guwahati. The participants who attended the workshops and participated in both the pre- and post-test were included in the study. Real-time data was collected via Google forms pre- and post-training sessions. **Results:** In both workshops, a comparison of pre- and post-test scores of all questions taken together showed a significant increase in the knowledge level of the participants ($p < 0.05$). In Guwahati, the knowledge of the participants regarding doses of RVV, inadequate dosing, vaccine vial monitor (VVM), open vial policy, operationalization of RVV and monetary incentive increased significantly. In Pune, the knowledge of the participants regarding doses of RVV, bundling approach, schedule and dose, storage temperature for RVV, VVM, open vial policy, vaccine delivery and operationalization of RVV increased significantly after the training. **Conclusion:** A pre-planned and well-designed knowledge assessment tool can be used to understand the impact of training workshops in enhancing the knowledge and practical skills of the participants prior to the introduction of a new vaccine.

Keywords: Rotavirus vaccine, capacity building, staff development, training support, training assessment, training of trainers

Rotavirus is a leading cause of moderate-to-severe acute diarrhea in India. The Global Burden of Disease Study showed that in India 21,357.6 (13,150.8-33,967.0) deaths occur in children below 5 years due to rotavirus infection. Hospitalizations due to rotaviral gastroenteritis among under-five children are estimated to reach up to 8,72,000 admissions every year. Rotavirus vaccine introduction in the national immunization program is the most effective intervention in preventing severe rotavirus disease.[1] India became the first nation in the World Health Organization (WHO) Southeast Asia region to introduce the rotavirus vaccine (RVV) in its Universal Immunization Program (UIP). By 2019, India had introduced RVV across 29 states and 8 union territories, covering a birth cohort of 26.7 million.[2]

Almost 2,00,000 auxiliary nurse midwives (ANMs) work on the ground to successfully implement the UIP as they vaccinate the children and pregnant women, and are supported by around 1 million accredited social health activists (ASHA), who provide counseling to the beneficiaries and help mobilize them.[3] Despite the increasing demands placed on the public health workforce due to the introduction of several newer

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vaccines, skill deficits are evident and may reflect as inadequate preparation leading to on-job trial and errors. Hence, an important pre-requisite of any new vaccine introduction is capacity building of the health functionaries, from the program managers to the frontline health workers (FLWs). Studies have shown that the knowledge, attitudes and practices of the healthcare providers, including the frontline workers and supervisors, as well as parents, are the determining factors for improving immunization coverage.[4-8]

However, limited research is available on the effectiveness of capacity-building interventions related to capacity building of health workers. To our knowledge, an evaluation of the effectiveness of capacity-building interventions in new vaccine introduction has not been done so far. Evidence related to the effectiveness of these strategies can go a long way in considering choices about strategies and training focus, leading to better training outcomes.[9] The pre-test and the post-test pattern help in evaluating the enhancement in the knowledge of the participants. The pre-test assessment may further help in improving the focus of the audience in those technical sessions or topics that they could not answer correctly during the pre-test. It may also enable the facilitators to emphasize specific topics during the technical sessions based on the questions-wise scores' analysis of the pre-test.[10]

Currently, there is limited evidence available from India and other regions of the world measuring the impact of training via pre- and post-assessment in the context of immunization and other public health programs. Also, there is a dearth of literature evaluating the efficacy of short-term training programs in new vaccine introductions. To the best of our knowledge, this study is the first attempt to assess the effectiveness of training in RVV introduction in enhancing the knowledge of the participants. We believe that the results will enable public health professionals and program managers to develop tailor-made training modules in new vaccine introductions to ensure better application of knowledge during the rolling out of new vaccines.

METHODOLOGY

Ethics Statement

The study was designed in accordance with the Declaration of Helsinki. Ethics approval was obtained from the MGM-ECRHS, MGM Medical College, Aurangabad, Maharashtra (Ref. No. MGM-ECRHS/2019/16).

In the study, an assessment of the pre and post scores of the participants attending a government organized training workshop (supported by development partners) was conducted. The government authorities nominated the participants, and the standard agenda was shared with them before the workshop. Before administering the pre- and post-test, the participants were briefed by the facilitators during the workshop. The participants gave their informed consent before study initiation. The analysis of the proportion of question-wise correct responses was shared with the participants real-time.

Study Design

The pre- and post-test were conducted as per the standardized agenda approved by the Ministry of Health and Family Welfare (MoHFW). The pre-test was conducted using a self-administered questionnaire before the start of the workshop to assess the participants' knowledge of selected program domains essential for introducing the RVV. The facilitators briefed the participants on the objective and the process of conducting the pre-test. The questionnaire, which had 10 questions, was then administered online using a Google form. At the end of all technical sessions on Day 2, the post-test using the same questionnaire was again self-administered to the participants using the Google form.

Questions were close ended with one correct answer for each question. The number of options for each question ranged from 2 to 5. The participants were allotted 20 minutes to complete the tests. To prevent data contamination, facilitators ensured that there was no discussion amongst the participants and that doubts, if any, were clarified individually. The participants were not allowed to refer to any training materials, like operational guidelines, for answering the questions. The participants had to answer every question before submission.

As the tool was linked to a live Google form, real-time analysis of the responses was done. In the final wrap-up session of the workshop, those questions where the proportion of correct responses were below 90% were again discussed, and the facilitators clarified all doubts of the participants.

To capture the difference in the formulation and the mode of administration of the two types of RVV, question numbers 2, 3 and 4 were different between the questionnaires used in the Guwahati and Pune training of trainers (ToTs).

Training of Trainers

In the year 2019, before the scale-up of RVV, a cascading approach was adapted to train health functionaries at all levels from regional through state and district to sub-district level. This model was conceptualized to complete the training of many healthcare workers in a short period of 2 months. To train the master trainers at the regional and state level, a national pool of facilitators, comprising senior officials from the MoHFW, immunization partner representatives, and senior faculties from academic or research institutions, was formed. A total of 7 ToTs were conducted at different geographical zones, and a pool of 778 master trainers was created. Out of these 7 ToTs, 4 were conducted to introduce lyophilized RVV at Pune, Hyderabad, Ahmedabad and Kolkata, while three ToTs were held at Guwahati, Chandigarh, and Raipur for the introduction of liquid frozen RVV. The training modules were appropriately customized for the introduction of the two different of RVVs.

The master trainers trained at the regional/state level facilitated the state, district and sub-district training. In these ToTs, the focus was on the capacity building of the participants. Each ToT was accompanied by assessing the participants' knowledge both before and after the technical sessions through a pre- and post-test questionnaire.

Study Participants and Sampling Technique

This study was conducted amongst participants attending a state-level ToT in Pune and another group of participants attending a regional ToT in Guwahati to introduce RVV in their respective regions. The sampling technique used in the study was the complete enumeration method. Table 1 depicts the demography of the participants in the two ToTs included in the study.

The Pune state ToT participants included state and district level government officials, including medical officers from government health facilities, pediatricians, supply chain managers and partner representatives from Maharashtra.

In the regional ToT at Guwahati, the participants were only state-level government officials, supply chain managers, and partner representatives from the seven states, namely Arunachal Pradesh, Meghalaya, Nagaland, Manipur, Mizoram, Sikkim and Bihar.

All participants in the two workshops who participated in both the pre- and post-test, respectively were included for the study. The participants who participated only in the pre-test or only in the post-test were excluded from the study.

Statistical Analysis Plan

As the Google form also captured each participant's name and mobile number to create the unique field, for each workshop, a database of participant-wise responses in pre- and post-test was available. To calculate the pre- and post-test scores, correct and incorrect responses to each question were assigned scores of 1 and 0, respectively. The pre- and post-test results were then plotted in a simple bar graph to compare the difference in the proportion of question-wise correct responses. Then, to understand whether these differences in correct responses in each question and the overall difference in correct responses were statistically significant, three tests of significance were done. These tests were administered separately on the data compiled for each of the two ToTs. Statistical package for the social sciences (SPSS) version 20.0 (Chicago, SPSS Inc.) was used for the final analysis.

The number of correct responses of the participants before and after the workshop, captured through the pre- and post-test, was compared for statistical significance using McNemar's test. As the scores could not be assumed to

Table 1. Demography of the Participants at the Two Study ToTs (Pune and Guwahati)

ToT City	RVV type	Participants
Pune	Lyophilized	• State- and district-level government officials - medical officers from government health facilities • Pediatricians • Supply chain representatives • Partner representatives from Maharashtra
Guwahati	Liquid frozen	• State-level government officials • Supply chain managers • Partner representatives from the seven states - Arunachal Pradesh, Meghalaya, Nagaland, Manipur, Mizoram, Sikkim and Bihar

ToTs = Training of trainers

be normally distributed, Wilcoxon signed-rank test was administered to test the significance of the change in the participants' level of knowledge, as measured by the median total score. We also found several ties in scores between the pre- and post-test, which may potentially dilute the comparison of the median score, as demanded by the Wilcoxon signed-rank test. Hence, paired *t*-test was applied to further validate the results.

RESULTS

The ToTs were 2-day workshops with a structured and standardized agenda and a customized adult learning-based training methodology. A total of 84 and 60 participants attended the ToTs at Pune and Guwahati, respectively. However, the total number of participants who completed both the tests was 59 and 53 participants in the Pune and Guwahati workshops.

Regional ToT at Guwahati

In the regional ToT held in Guwahati, it was found that the knowledge about doses of RVV in one vial (77%), inadequate dosing (28%), vaccine vial monitor (VVM) (68%), phasing in of RVV in the immunization schedule (74%) and full immunization incentive for ASHA (68%) were the least amongst the participants. Table 2 shows the difference in the participants' level

Table 2. Findings from McNemar's Test (Guwahati and Pune ToT)

Questions	Correct response	Guwahati ToT			Pune ToT		
		Pre-test N (%)	Post-test N (%)	P value (McNemar's test)	Pre-test N (%)	Post-test N (%)	P value (McNemar's test)
Rotavirus diarrhea prevention	Vaccination with RVV along with good hygiene, frequent hand washing, safe water and food consumption	48 (90.6)	49 (92.5)	>0.05	44 (74.6)	52 (88.1)	>0.05
Doses of RVV in one vial	5	41 (77.4)	53 (100)	<0.005	41 (69.5)	59 (100)	<0.005
Inadequate dosing due to less vaccine quantity in the vial	New vial to be opened and full dose repeated	15 (28.3)	35 (66)	<0.005		NA	
Bundle approach for each RVV vial	One diluent vial + one adapter + two 6 mL oral syringes		NA		47 (79.7)	56 (94.9%)	<0.05
Schedule and dose of RVV	6, 10 and 14 weeks - 5 drops each	50 (94.3)	50 (94.3)	>0.05	39 (66.1)	59 (100%)	<0.005
Storage temperature for RVV	+2°C to +8°C	50 (94.3)	53 (100)	>0.05	57 (96.6)	59 (100%)	>0.05
Vaccine vial monitor	Located on the cap of the vaccine vial	36 (67.9)	53 (100)	<0.005	44 (74.6)	59 (100%)	<0.005
Open vial policy	Cannot be used beyond 4 hours of vial opening	46 (86.8)	53 (100)	<0.05	52 (88.1)	59 (100%)	<0.05
Delivery of RVV	In all RI/VHND fixed and outreach session sites	53 (100)	52 (98.1)	>0.05	55 (93.2)	59 (100%)	>0.05
Phasing in of RVV in the immunization schedule	Co-administered with first dose of OPV, fIPV, and Penta	39 (73.6)	53 (100)	<0.005	46 (78)	58 (98.3%)	<0.005
Full immunization incentive for ASHA	Completion of the 3 RVV doses part of the criteria to avail the incentive	36 (67.9)	51 (96.2)	<0.005	50 (84.7)	46 (78%)	>0.05

RVV = Rotavirus vaccine; ASHA = Accredited social health activist; VHND = Village health and nutrition day; RI = Routine immunization; OPV = Oral poliovirus vaccine; fIPV = Fractional inactivated poliovirus vaccine.

of knowledge before and after completing the ToT. It also shows whether the difference in the knowledge level is significant or not. The analysis of post-test data revealed that the proportion of correct responses increased to more than 90% in all the questions except that on inadequate dosing (66%).

The knowledge regarding doses of RVV in one vial (77.4%), inadequate dosing (28.3%), VVM (67.9%), open vial policy (86.8%), phasing in of RVV in the immunization schedule (73.6%) and full immunization incentive for ASHA (67.9%), increased significantly to 100%, 66%, 100%, 100%, 100% and 96.2%, respectively.

Table 3 shows the change in the level of knowledge for each question before and after completing the training workshop. Paired *t*-test revealed a statistically significant increase in knowledge following the completion of the workshop in knowledge around doses of RVV in one vial ($p < 0.005$), inadequate dosing ($p < 0.005$), VVM ($p < 0.005$), open vial policy ($p < 0.05$), phasing in of RVV ($p < 0.005$) and full immunization incentive for ASHA ($p < 0.005$).

Table 4 shows the change in the overall level of knowledge before and after completing the training workshop. Wilcoxon signed-rank test revealed a statistically significant increase in knowledge following the completion of the workshop, $Z = -5.779$, $p < 0.05$, with a large effect size ($r = 0.94$). The median knowledge score increased from 8 to 10 after the training workshop.

State ToT at Pune

In the state ToT held in Pune, it was found that the knowledge about schedule and dose of RVV (66.1%), doses of RVV in one vial (69.5%), rotavirus diarrhea prevention (74.6%) and VVM (74.6%) were the least amongst the participants. Table 2 shows whether, for each of the questions, the difference in the level of knowledge of the participants before and after the completion of the ToT was significant or not. After the completion of all technical sessions in the workshop, the data captured in the post-test revealed that the proportion of correct responses increased to more than 90% in all the questions except the ones on rotavirus diarrhea prevention (88.1%) and full immunization incentive for AHSA (78%).

The knowledge regarding doses of RVV in one vial (69.5%), bundle approach for each RVV vial (79.7%), schedule and dose of RV (66.1%), storage temperature for RVV (96.6%), VVM (74.6%), open vial policy (88.1%), delivery of RVV (93.2%), and phasing-in of RVV in the immunization schedule (78.0%), increased significantly

Table 3. Findings from Paired *t*-test (Guwahati and Pune)

Question	Guwahati				Pune			
	Mean	SD	SE mean	Significance (P value)	Mean	SD	SE mean	Significance (P value)
Rotavirus diarrhea prevention	0.1887	0.36640	0.05033	>0.05	0.13559	0.50711	0.06602	=0.05
Doses of RVV in one vial	0.22642	0.42252	0.05804	<0.005	0.30508	0.46440	0.06046	<0.005
Inadequate dosing due to less vaccine quantity in the vial	0.37736	0.62716	0.08615	<0.005			NA	
Bundle approach for each RVV vial			NA		0.15254	0.44774	0.05829	<0.05
Schedule and dose of RVV	0.0000	0.27735	0.03810	>0.05	0.33898	0.47743	0.06216	<0.005
Storage temperature for RVV	0.05660	0.23330	0.03205	>0.05	0.03390	0.18252	0.02376	>0.05
Vaccine vial monitor	0.32075	0.47123	0.06473	<0.005	0.25424	0.43917	0.05717	<0.005
Open vial policy	0.13208	0.34181	0.04695	<0.05	0.11864	0.32614	0.04246	<0.05
Delivery of RVV	0.01887	0.13736	0.01887	>0.05	0.06780	0.25355	0.03301	=0.05
Phasing in of RVV in the immunization schedule	0.26415	0.44510	0.06114	<0.005	0.20339	0.44643	0.05812	<0.005
Full immunization incentive for ASHA	0.28302	0.49526	0.06803	<0.005	-0.06780	0.44969	0.05854	>0.05

RVV = Rotavirus vaccine; ASHA = Accredited social health activist.

Table 4. Wilcoxon Signed-Rank Test (Findings for Guwahati and Pune ToT)

Score	Guwahati		Pune	
	Pre-test	Post-test	Pre-test	Post-test
Median	8	10	9	10
Interquartile range	7-9	9-10	6-10	9-10
Wilcoxon test (Z)	-5.779		-4.996	
P value	<0.05		<0.05	
Correlation coefficient	0.94		0.73435118	

to 100%, 94.9%, 100%, 100%, 100%, 100%, 100% and 98.3%, respectively.

Table 3 shows the change in the level of knowledge for each question before and after completing the training workshop. Paired *t*-test revealed a statistically significant increase in knowledge following the completion of the workshop in knowledge around doses of RVV in one vial ($p < 0.005$), schedule and dose of RVV ($p < 0.005$), VVM ($p < 0.005$) and open vial policy ($p < 0.05$).

Table 4 shows the change in the overall level of knowledge before and after completing the training workshop. Wilcoxon signed-rank test revealed a statistically significant increase in knowledge following the completion of the workshop, $Z = -4.996$, $p < 0.05$, with a large effect size ($r = 0.73$). The median knowledge score increased from 9 to 10 after the training workshop.

DISCUSSION

This study was conducted to assess the effectiveness of ToTs in increasing the awareness and practical knowledge of the participants. A comparison of the pre- and post-test scores on all questions demonstrated an increase in correct responses from 78% to 95% in the Guwahati workshop and an average increase from 81% to 96% in the Pune workshop. The post-test average correct responses were similar in both the workshops, although the participant profile was different in state-level program managers in Guwahati and sub-state or district level program managers in the Pune workshop. The increase in the knowledge level in both workshops is statistically significant ($p < 0.05$). Uskun et al, in their study, concluded that training on immunization increased the knowledge of primary healthcare workers and the vaccination coverage in the study region. The results of this study showed that the technical sessions during the training led to a significant increase ($p < 0.01$) in the health workers' knowledge of immunization. It was also seen that the vaccination coverage increased significantly ($p < 0.001$) over 3 months post the training-based intervention.[11] Earlier studies have also established the positive effects of a training intervention, showing an increased score of the post-test compared to the pre-test.[12,13]

While conducting a capacity-building workshop helps in familiarizing the participants with the various aspects and domains of the new vaccine introduction, at the same time, monitoring the effectiveness of the technical sessions in enhancing the actual knowledge of the participants is an important activity during the workshop. There is a dearth of studies to assess the impact of training the cadre of supervisors or future master trainers. The WHO conducted a study to evaluate the training system and the processes followed in certain good and bad performing states in terms of immunization rates. In the study by WHO, Das et al suggested that the quality of the training in terms of large pools of facilitators, prior knowledge, training methodology and trainees' feedback were found to be salient enabling factors in such trainings.[14]

The overall study emphasizes the importance of a knowledge assessment format for the training in public health. On the one hand, the pre-test individually is important for both the participants and the facilitators of the training: (i) to intimate the participants towards the various topics to be covered during the training, (ii) to highlight in their minds those topics beforehand in which they scored less in the pre-test, (iii) for facilitators to adopt a more interactive and easier approach towards the same topic where the scores were less during the pre-test. The post-test, on the other hand, individually imparts confidence among the participants when they score well. Together, the pre-test and post-test, when viewed comparatively, gave the actual picture about the quality of the training.

An advantage of this study is that it methodologically deployed an ensemble approach by applying the three most appropriate tests of significance in a hierarchical way to assess the trainees' actual difference between pre- and post-training knowledge status. Though each method suffers from its limitations, this ensemble approach gives more confidence to the findings.

The results of this study show that after the intervention of a 2-day training, significant improvement is seen in the knowledge of the participants while answering the post-test as compared to the pre-test. However, the retention of this knowledge gain is not assessed after

a long gap, such as 6 months or 1 year. Similar studies have shown a progressive decline in the mean scores of the participants after 3 or 6 months of the intervention. Though a decline in knowledge is seen after the said time, the then scores were still higher than those before the training intervention.[15,16]

To create data-based evidence of the results of a training intervention, a periodic and systematic follow-up knowledge assessment after 3 months,[17] 6 months,[18] 9 months,[19] 12 months and 24 months[20] should be included in planning such interventions. Also, it has been seen that for short-term results, a single intervention of continuing education can be useful, but for long-term sustainability and effectiveness, additional interventions to address health system gaps and community issues should be planned.[21]

A limitation of this study is that it is a complete enumeration of the participants attending a particular workshop, and hence it may lack external generalizability. As the tests were done for "on the spot", immediate training needs assessment and post-session feedback and clarification. Our study also could not capture temporal change in participant's knowledge.

CONCLUSION

This study signifies and highlights the effectiveness of a pre-planned and well-designed knowledge assessment tool before and after a training workshop in bridging the knowledge gap and improving the practical approach needed for new vaccine introduction. The findings signify that the pre- and post-test tool can be effectively used to capture the participants' pre-training knowledge levels, suggest the key areas to focus during the training, and finally test the knowledge enhancement post-training. The post-test, being the last event of training, allows reinforcing the key take-home points. This study recommends that the same model of knowledge assessment through live pre- and post-test approach should be used in all the trainings of public health. It will help make an accurate real-time assessment of the participant's knowledge and make real-time corrections or modifications in the focus of the training to ensure the best outcomes in terms of knowledge and practical skills gained.

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FDA Approves 180-day Implantable Continuous Glucose Monitor

The US FDA has granted approval to the long-term implantable continuous glucose monitor (CGM) for use for up to 6 months, stated Senseonics Holdings. The Eversense E3 System can be used in adults aged 18 years and above with type 1 or type 2 diabetes. It is implanted subcutaneously into the upper arm under local anesthesia. It enables replacement of finger stick blood glucose measurements and finger sticks may be required along with this system only for calibration, when symptoms do not appear to match the CGM readings, or when the user is taking a tetracycline class drug. The system was initially approved for use for 90 days in June 2018. In the PROMISE study, presented at the 2021 virtual American Diabetes Association (ADA) Scientific Sessions, the Eversense E3 CGM System was reported to have a mean absolute relative difference (MARD) of 8.5% between clinic reference values and the device's primary sensor on the basis of nearly 50,000 paired CGM points. In the study, 90% of the sacrificial boronic acid (SBA) sensors lasted 180-day wear, 96% of SBA sensors lasted up to day 90 and day 120, and 94% lasted up to day 150… (*Medpage Today, February 11, 2022*)

Restless Legs Syndrome Increased Early During Pandemic

People with restless legs syndrome (RLS) experienced an increase in symptom severity in the early phase of the COVID-19 pandemic in the US in 2020, noted a study. However, this increase declined by 2021.

Investigators assessed data from 500 participants in the National Restless Legs Syndrome Opioid Registry. Participants reported RLS symptom severity prior to and during the pandemic at 6-month intervals. Responses were obtained from early phase of the pandemic in January-February 2020, then in April-May 2020, 6 months later from September 2020 to February 2021, and then 1 year later, from March 2021 through June 2021. A total of 153 participants completed surveys during January and February 2020, and 155 during April and May 2020. A between-subjects analysis for these time periods revealed significantly higher symptom scores on the International Restless Legs Syndrome Study Group severity scale (IRLS) in January to February 2020. Participants had around double the likelihood of having IRLS scores of 20 or higher compared to April-May 2020 (37.7% vs. 20.9%). Responses from the same participants were compared at baseline and 6 months later, from September 2020 through February 2021, and from March 2021 through June 2021. A within-subjects analysis revealed that 51.3% of the participants reported increased IRLS scores in spring 2020. Participants had a significantly higher likelihood of having IRLS scores of 20 or above in the early pandemic period in April and May 2020 compared to baseline (37.7% vs. 26.6%). Patient Health Questionnaire (PHQ-9) and General Anxiety Disorder-7 scale (GAD-7) scores were higher during early period of the pandemic in April and May 2020 compared to baseline.

Participants who completed surveys in January and February 2020 did not report an increase in RLS severity or other mental health questionnaire values on the 6-month surveys completed during the pandemic or 1 year later.

The results are published in *Sleep Medicine…* (*Medscape, February 11, 2022*)

REVIEW ARTICLE

Ragi Traditional But Nutritional Especially in the Era of COVID-19

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ABSTRACT

Finger millet is the name commonly used to denote the crop *Eleusine coracana*. It is known as Ragi in many parts of India, which is an important member of the family of cereals. In fact, it is superior to many cereals like wheat and rice in terms of its micronutrient content and bioavailability. Several indigenous processing techniques may be applied to finger millets allowing it to be processed into various value-added products, which may be better in appearance, taste, flavor and acceptability. Development of value-added products that contain Ragi as one of their major components can be beneficial for food and nutrition security of Indians. Ragi may contribute to solving the issue of micronutrient deficiency and nutrition security as it is an important source of micronutrients and can be easily incorporated in various recipes and value-added products. It can therefore be a part of various nutritional programs to enhance the nutritional density of foods.

Keywords: Finger millet, ragi, micronutrient, value-added products

The pandemic of SARS-CoV-2 (COVID-19) has had an enormous impact on India's healthcare infrastructure. It has been fierce battle fought with incredible courage and dedication by healthcare experts of the country and it is due to their conjoint efforts that the pandemic of COVID-19 was well-tackled even though the virus continued its menacing spread wave after wave.[1,2]

Thousands of doctors from every medical and surgical establishment were infected. Increasing COVID-19 infection amongst health workers revealed the need for effective control strategies, which was necessary for uninterrupted services of the health workers against the rapidly spreading outbreak.

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The pandemic's expansion did not lead to the exhaustion of healthcare institutions rather, it exposed existing flaws in healthcare systems around the world. "The Dead teaches the living", as the saying goes, and it was only after the brave sacrifices of several health workers who died treating the sick, the government and health systems realized that health workers are the most valuable resource in this pandemic and began taking appropriate measures to protect them.[3]

Drugs such as hydroxychloroquine, remdesivir, favipiravir, ivermectin and others have been used to prevent and treat SARS-CoV-2 (COVID-19),[4-7] with ivermectin being a particularly effective weapon in the anti-COVID-19 arsenal.[8] Several trials are being conducted in India and around the world for the approval of ivermectin in the COVID-19 treatment. A group of senior doctors from India with vast experience in the management of COVID-19 got together and published a white paper to propose ivermectin, a strong antiviral drug, as a therapeutic option in the prevention and treatment of mild, moderate and severe cases of COVID-19, which adds credibility to its use in the treatment as well as prophylaxis of COVID-19 virus following which it was added in the Government order of the state of Uttar Pradesh for management and prophylaxis of COVID-19.[9,10]

Almost 70% of the population in India resides in rural areas including those living in hilly and tribal areas. This population is prone to nutritional deficiencies and

hence more vulnerable to infectious diseases like COVD-19.[11] COVID-19 showed us the realm of nutrition and how it affects the daily life of an individual, role of immunity and Indian traditions (Namaste instead of Handshake, Yoga and Pranayama and being vegan). Being a developing country, there is a large majority of population, which cannot afford a meal with average nutritional value to improve and build their immune defense. Undernutrition can also lead to progression of latent infections like tuberculosis in post-COVID patients.[12] Undernourishment increases the severity of all infectious diseases and it is this vicious cycle of deteriorating sickness and worsening malnutrition that a good nutritional intervention must break.

Tough experiences teach us valuable lessons. An important take-away from this pandemic has been the need for a healthier lifestyle through adoption of healthy habits. Many of us have tended to embrace healthy behaviors and eat foods that are rich in nutrients like vitamin C and vitamin A, etc. that have allowed us to step outside and communicate. Considering this, ragi can play a vital role in taking care of all, whether from rural or urban India.

Ragi is an ancient grain that is popular in many households. But there is much more to the millet than just its flavor and texture. During the COVID pandemic, this millet has gained popularity as an immunity-boosting food.

Millets form an important dry land crop for a large population living in rural, tribal and hilly areas. Small millets include foxtail, kodo, proso and finger millet. These millets occupy 4.5% of the cultivated area in India.[13] The straw of millets becomes the main feed of cattle.

Finger millets (*Eleusine coracana*) or ragi or madwa (the name used for finger millet in the common dialect) is a routinely eaten food by people living in rain-fed hilly areas and also by the tribals of India. Amongst the various other names given to ragi, the oldest happens to be "nrtta-kondaka", which means the dancing grain in ancient Sanskrit literature.[14]

In India, finger millet is primarily farmed in the states of Uttarakhand, Odisha, Jharkhand, Maharashtra, Andhra Pradesh, Karnataka and Tamil Nadu.[15] Ragi is farmed across an area of 1.2 lakh hectares in Tamil Nadu. It is the finger millet or ragi, which has a high yield of 1909 kg/ha and provides food and nutritional security to farmers in dry regions, hilly and tribal areas.[16]

Amongst many people of India and Sri Lanka, the principal cereal food is ragi. Ragi can be ground into flour and sold to consumers who can use it in biscuits, cookies, bread, toast, rusks, cakes, muffins, chapatis, dosas or cheelas. It can be also used for making porridge, puddings and cakes. Similarly, finger millets can also be consumed in the form of ragi balls and ragi idlis.[14]

NUTRITIVE PROPERTIES OF FINGER MILLET

Finger millet, while being a gluten-free grain with a low glycemic index and nutritional and nutraceutical benefits, is overlooked and misused.[17] It contains 66.82 g of carbohydrate, 7.16 g of protein, 11.18 g of total fiber and 1.92 g of fat per 100 g of millet.[18] It has a significantly higher overall fiber and mineral content than wheat and rice. Finger millets are also a good source of calcium, which is an important macronutrient necessary for infants, children, pregnant women, as well as the elderly who are usually deprived of this macromineral. Essential amino acids including tryptophan, threonine and isoleucine are prominent in finger millet or ragi grains.[19]

The high fiber content helps to reduce risk of diabetes mellitus and gastrointestinal tract disorders.[20] The fermented grains of ragi are a rich source of vitamin B complex (riboflavin, pantothenic acid and niacin).[21] The ragi millet plant is often utilized in preparing folk medicine for treating liver disorders, measles infection, pleuritis and pneumonia.[22]

Ragi millet is vegan and gluten-free in nature. It can therefore be used as an alternative to wheat for patients with celiac disease and gluten sensitivity. The innumerous health benefits of finger millet are by virtue of the polyphenols, phytates, tannins and fiber that are present in it. The phenolic compounds in ragi that are responsible for its antioxidant and free radical scavenging activities are ferulic acid, epicatechin and catechin. Quercetin is the flavonoid which gives ragi its antimicrobial property as it has shown hindrance in the propagation of *Escherichia coli*, *Listeria monocytogenes*, *Bacillus cereus*, *Streptococcus pyogenes* and *Staphylococcus aureus*. Ragi is anti-inflammatory in nature and helps in healing of wounds, besides maintaining blood glucose homeostasis in people with diabetes. The water-soluble fibers present in ragi help reduce serum cholesterol levels and ebb the risk of atherosclerosis.[23]

Starch, which is extracted from ragi grains, is utilized in the pharma industries for making granules used for tablets and capsule dosage formulations.[24] These ragi or finger millet grains may be utilized in preparing baked products, composite flour, certain weaning foods for

infants, beverages and also some nonbeverage products.[25] Finger millets offer a variety of health benefits, some of which include delayed nutrient absorption, increased bulk of feces, lowering of triglycerides and lipids in blood, preventing colon cancer, action as a digestive barrier, mobility of intestinal contents, prolonged transit time of feces and the ability to ferment.[26]

The grains of finger millet have a seed coat, which is dark-brown in color and is high in polyphenols in comparison with other cereals like barley, maize, rice and wheat.[20] Consuming finger millets having polyphenols and dietary fiber on a regular basis is helpful in reducing the risk of diabetes and gastrointestinal disorders.

PROCESSING OF FINGER MILLET-BASED PRODUCTS

Methods of food processing have evolved over the last many years and can be adopted in order to create the ultimate product, which is more attractive in flavor, appearance, taste, consistency and several other factors. The food processing methods that are usually employed include milling, germination/sprouting, malting, fermentation, etc.

Each process alters the nutrient value of the final food product qualitatively and/or quantitatively. Besides the regular chapatis, ragi products may include expanded or puffed forms of ragi, ragi breakfast cereals and ragi flakes, extruded products, fermented products, sweets, ready-to-make instant mixes, pasta, bakery products like cakes, biscuits, rusks, etc., beverages, health foods and some special foods like weaning foods for infants.[14,27]

The grains of ragi millet offer many possibilities for diversified utilization and value addition in its products. Processing of finger millets will make it feasible to make a variety of food products by adopting appropriate milling, popping and other indigenous and modern technologies. Finger millet can also be utilized in various bakery products by partial supplementation of the regular wheat flour with ragi flour.

Sowbhagya and Ali[28] studied the process of making vermicelli noodles from ragi. The process involved hydration and dehydration under specific treatments, conversion to flour, addition of additives and preparation of dough under specified conditions, extrusion, further processing and drying.

The vermicelli noodles made from ragi can be given to children and also adults as a healthy option for breakfast. In Uganda, finger millet is consumed by making a porridge of a stiff consistency called 'Ugali' in their native language, which is eaten with vegetables, cowpea, groundnut, meat, chicken, etc. Ragi millet porridge can be served to lactating and expectant women and children.[29] This way finger millet will provide more micronutrients to these vulnerable groups in comparison to rice, wheat or other millets.

The possibility of using ragi malt in bread making has been studied.[30] The flour malt of this millet produced more reducing sugars in bread crumbs as compared to the regular malted wheat. This indicated that there was a decreased starch content and an increased amylase activity in ragi malt than normal wheat malt.[31]

PROSPECTIVE VALUE-ADDED PRODUCTS FROM FINGER MILLET

Chapatis

Wheat and finger millets can be mixed in a ratio of 7:3 to make chapatis. This will not only affect the taste and texture of the chapatis but also reduce the gluten content.[32] The chapati may be slightly darker in color. Being a low glycemic index food, finger millet chapatis can help to reduce the blood glucose in patients with diabetes. Also, adding ragi to normal wheat flour may give a feeling of fullness because of its fiber content and thus help to prevent and treat obesity and constipation.[33]

Chakli, Cheela and Khichri

These products may be prepared by blending the millet separately with green gram (moong) and soybeans in different ratios, which are acceptable in taste. Chaklis can also be prepared with puffed chickpea, finger millet, soybean flour and milk, which is skimmed and powdered; all in the ratio of 60:25:10:05.

This will prove to have a better nutrient composition than the conventional sattu with regard to protein, calcium and lysine. Hence, this may be recommended for growing children, pregnant and lactating mothers, who need additional calcium and proteins.[19]

Papads

Papads can be prepared with finger millets as a base material with other ingredients like black or green gram, rice and other spices. Around 15% to 20% (w/w) of finger millet can be added to make the papads. While making papads, the flour may be first cooked till it is gelatinized after which it may be kneaded into a dough and then rolled into thin sheets. The resultant papads will be darker in color as the starch is not separated from the pericarp.[20]

Puffed and Popped Millets

This is a well-liked method of making ready-to-eat millets of pleasing texture and appealing flavor. Ragi puffs can also be made by this process. The puffing and popping process of ragi millets will enhance the nutritive value of these ready-to-eat products by inactivating some of the antinutritional factors and thereby increasing their digestibility.[34]

Noodles and Vermicelli

The changing taste of children has brought about an increase in consumption of noodles in India and abroad.

Noodles can be prepared by using different proportions of whole or refined wheat flour, malted finger millet and/or soy flour.[35]

MALTING AND WEANING FOODS

The malt of ragi millet and milk-based beverage formulations can prove to be a well-liked beverage in India.

The favorable effects of malting in ragi are reflected by increased bioavailability of essential nutrients, lowering of antinutrient concentration and in improvising the texture, which was successfully exploited in developing malt-based human health foods.[36] Finger millets possess an appreciable malting quality. Although Tamil Nadu and Karnataka use this popular malting technique, it still has to reach the other states.

The health benefits of malting are because of the increase in the nutrients, fiber, fat, vitamin B, vitamin C and their availability.[36] Malted ragi millet, green gram and Bengal gram can be mixed together to formulate a malted weaning food for infants which is high in protein and calcium.[32]

Millet malts or ragi malts can be used as a base cereal for low dietary volume and caloric dense foods that can be utilized during the infant's weaning period, as a food supplement, in health boosting foods and as an amylase-rich food. Malting decreases the viscosity of flour paste more than several other heat treatments.[37] Malting finger millet greatly reduces tannin (brown millet) and phytic acid levels while significantly increasing ionizable iron and soluble zinc.[38] These malts can be simply eaten as a supplement by the elderly, who frequently have eating and digestive issues.

Innovative uses of finger millet may include its use in muffins, cake, cookies, laddoos, snack mix and various other snacks. It can be included in various feeding programs designed for vulnerable population, thus becoming a source of various micronutrients from a single item, which perhaps is its uniqueness in terms of its nutrient density as a millet.

CONCLUSION

Finger millet or ragi has a good potential to provide nutritional security to people as it is a rich source of micronutrients and certain minerals like calcium and iron. This millet is majorly consumed in and around areas where it is cultivated. Increasing the knowledge regarding the potential benefits of ragi will help overcome nutritional deficiencies and also many noncommunicable diseases.

The COVID-19 pandemic has increased the nutritional crisis in India. The undernourished have become more undernourished in the rural areas whereas in the urban areas, there has been an opposite effect on the health status of people as a consequence of lockdown cooking, lack of exercise and long hours of sitting. Supplementation of normal cereals with ragi amongst the low economic society may help in bridging the gap of undernutrition by providing the required essential nutrients. Addition of ragi-based products in the diets of urban populations can help them regulate diseases like obesity, diabetes, constipation, cardiovascular problems, etc.

The vulnerable groups as well as the elderly can also gain nutritional benefits by consuming the different varieties of products that finger millet offers.

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REVIEW ARTICLE

Role of Prostaglandins in Pathogenesis of Dysmenorrhea and Place of Mefenamic Acid and Dicyclomine in its Management

KAMINI A RAO*, SUNITA CHANDRA†, PRABHU N KASTURE‡

ABSTRACT

Despite being one of the most common gynecological issues faced by women of reproductive age, dysmenorrhea largely remains an ignored, underdiagnosed and untreated condition. It continues to be a public health issue and has a significant impact on the quality of life of the affected women in terms of inability to lead routine activities, absenteeism from academic activities or work and reduced social activities. Currently, existing evidence correlates and implicates the excessive synthesis of prostaglandins with the menstrual pain. Hence, treatment approaches that can inhibit prostaglandins' production or already formed prostaglandins can provide relief in dysmenorrhea. In this review, the impact of dysmenorrhea on the quality of life of women, the role of prostaglandins in the pathogenesis of dysmenorrhea, and how nonsteroidal anti-inflammatory drugs (NSAIDs) like mefenamic acid can be safe and effective in managing dysmenorrhea are discussed.

Keywords: Dysmenorrhea, primary dysmenorrhea, menstrual pain, NSAIDs, mefenamic acid, COX-2 inhibitors, quality of life

Dysmenorrhea is one of the most common gynecological issues faced by women of child-bearing age. It is classified as either primary dysmenorrhea, which does not involve a related organic disease, or secondary dysmenorrhea, which is related to attributable causes, such as endometriosis. The pain associated is described as lower abdominal pain of cramping nature, spreading to the thighs or lower spine, ranging from mild-moderate-severe intensity during the menstruation cycle. The pain in the lower abdomen may also be accompanied by vomiting, headache, back pain, diarrhea and fatigue.[1]

The global prevalence of primary dysmenorrhea ranges from 45% to 95% in women of reproductive age, while almost 2% to 29% experience severe pain.[2] In a study conducted among 550 female students in six universities, the prevalence of primary dysmenorrhea was 80.9%.[2] Studies from India have reported the prevalence range from 50% to 87.8%.[3]

THE IMPACT OF DYSMENORRHEA ON QUALITY OF LIFE

A study recently published in 2021 has reported that dysmenorrhea leaves a significant adverse effect on almost half of the dysmenorrheic females included in the study. The study participants reported that they experience a disruption of their daily activities and studying abilities. It has been reported that primary dysmenorrhea has a considerable impact on health-related quality of life, daily activities, work productivity and academic performance. Other significant adverse effects reported among the study participants were reduced engagement in social activities, limited activities, missing classes and poor concentration.[2] Primary dysmenorrhea without any obvious pathology occurs in almost 50% of menstruating females and causes significant disruption in quality of life and absenteeism from work or school.[4]

In earlier studies, it has already been suggested that approximately 52% of post-pubescent females suffer from dysmenorrhea; about 10% of these are incapacitated for 1 to 3 days every month. In fact, it

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was cited to be the largest single cause of lost working hours and school days among young women, with in excess of 140 million working hours estimated to be lost annually.[5] In another study conducted in 2004 in Canada, it was reported that among the study participants, 60% experienced dysmenorrhea with moderate-to-severe pain. Fifty-one percent reported restriction of activities, while 17% absenteeism.[6]

A survey-based study has also shown menstrual-related presenteeism to be widespread in the general female population. In fact, the annual productivity loss due to presenteeism is almost seven times more than the annual productivity loss due to absenteeism. This burden was most pronounced in women under 21 years of age. While absenteeism refers to time away from work or school, presenteeism is defined as loss of productivity while being present at work or school.[7]

Additionally, the psychological aspect of pain related to dysmenorrhea influences the reactive component of pain. The anticipation of severe dysmenorrhea each month in itself is a cause for lot of stress and unproductivity in women. It is reported that dysmenorrhea is more common in working women or those who have higher stress levels.[8]

Dysmenorrhea: An Untreated Condition?

Despite being one of the most common and recurring gynecological conditions, dysmenorrhea is usually underdiagnosed, and undertreated.[9,10] Besides, dysmenorrheic females do not get sufficient information about the condition, leaving it an inadequately addressed medical problem.[2] More often than not, women do not seek medical treatment for dysmenorrhea because they assume symptoms to be normal or tolerable, prefer to self-manage, have limited access to healthcare, they think healthcare providers would not offer help, they are unaware of treatment options, wary of available treatments, feel embarrassed or afraid to seek care, or they rarely take care of any medical ailment, irrespective of dysmenorrhea.[9] Sometimes, women undervalue the condition themselves, considering it part of the menstrual cycle, ignoring its implications on quality of life, and hence do not seek treatment for dysmenorrhea.[11] The high prevalence of primary dysmenorrhea indicates that it is a very common public health issue and should be addressed immediately. Primary dysmenorrhea is a common, neglected and undertreated gynecological disorder characterized by menstrual pain related to severe physical and psychological symptoms that impair regular daily activities.

Along with the lower abdominal or pelvic pain, it is also associated with other physical (menstrual migraine, lethargy, fatigue, sleepiness or sleeplessness, heaviness in the lower abdomen, nausea, vomiting, backache, pain in knee, muscle/joint/inner thighs) and psychological symptoms (anxiety, depression, irritability).[2] Hence, it has a wide range of symptoms typically lasting for 9 to 72 hours, severely disrupting a woman's quality of life. The plethora of recurring symptoms experienced by women makes dysmenorrhea a serious issue impacting the quality of life in women warranting immediate medical attention.

PATHOPHYSIOLOGY OF DYSMENORRHEA

In the case of primary dysmenorrhea, pain is caused due to excessive, pathological uterine contractions and is marked by the absence of palpable lesions within the lesser pelvis.[1] Dysmenorrhea is driven by a complex interplay of various pathogenetic mechanisms including behavioral and psychologic factors and thus is multifactorial.[8]

On the biochemical level, prostaglandins are a major factor causing the increased abnormal uterine activity. Because of the uterine muscle hypercontractility, the blood flow gets compromised leading to ischemia. Thus, the pain is thought to be due to these below 3 factors as: (i) increased abnormal uterine activity, (ii) uterine ischemia and (iii) sensitization of the nerve terminals by prostaglandins which lower the threshold of these nerves to the action of chemical and physical stimuli. Estrogen and progesterone stimulate the uterus to increase endometrial release of arachidonic acid, through lysosomal labialization and release of phospholipase A2, which in turn acts on the bilipid cell membranes to generate arachidonic acid (Fig. 1).

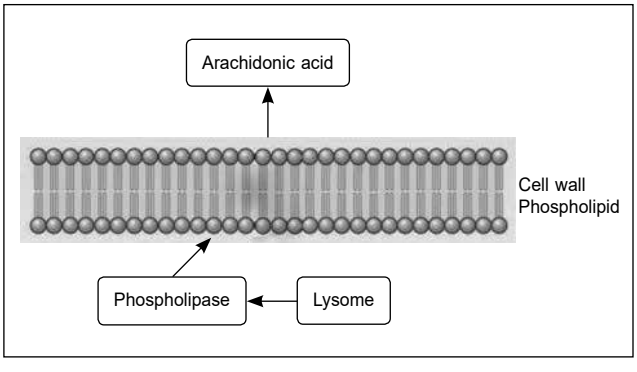

Figure 1. Release of arachidonic acid from lysosomes via phospholipids.

(Image adapted from Smith RP. The role of prostaglandins in dysmenorrhea and menorrhagia. In: Dysmenorrhea and Menorrhagia. 2018. Springer, Cham.)

During menstruation, prostaglandin F2α (PGF2α) and prostaglandin E2 (PGE2) induce prolonged uterine contractions that reduce blood flow resulting in uterine ischemia. Further contraction of bowel and vascular smooth muscle by PGF2α and PGE2 lead to nausea, vomiting and diarrhea.[12] On the other hand, secondary dysmenorrhea usually results from specific pelvic pathology.[13]

Role of Prostaglandin in Dysmenorrhea

The uterine activity induced by the excess prostaglandins in patients with primary dysmenorrhea can be very prominent. The normal resting pressure in the uterus is in the range of 5 to 15 mmHg. During normal menstruation, the uterine pressure increases up to 50 to 80 mmHg and helps in expulsion of blood and shed endometrial tissues. However, in women with dysmenorrhea, the uterine pressure peaks over 400 mmHg.[14]

The increased formation and secretion of uterine prostaglandins during menstruation increases abnormal uterine activity leading to uterine hypoxia and pain.[2]

Prostaglandins such as PGE2 and cyclic endoperoxides hypersensitize pain fibers in the pelvis and uterus to the action of pain-inducing substances or factors.[8] Advances during the last three decades and recent evidence suggests that increased secretion of PGF2α and PGE2 in the endometrium are the important mediators and are involved in increasing the myometrial contractions leading to ischemia and also sensitization of pain fibers to mechanical and physical stimuli.[2] PGF2α in dysmenorrhea causes uterine vasoconstriction and contraction of the myometrium, whilst PGE2 causes inflammation and contraction of the myometrium.[11]

The role of prostaglandin is supported by the fact that there is a similarity between symptoms of primary dysmenorrhea and prostaglandin-induced uterine contractility in labor or abortion; and an increased level of prostaglandin in the menstrual fluid of women with primary dysmenorrhea.[11] Studies have also reported a significant difference in the mean levels of PGF2 between the moderate primary dysmenorrhea group and the severe primary dysmenorrhea group. It has been demonstrated that the PGF2α level was higher in the severe primary dysmenorrhea patient group than the moderate primary dysmenorrhea group with a significant relationship between the level of PGF2α and the intensity of pain in primary dysmenorrhea ($p = 0.000$).[15]

It has been observed that during normal ovulatory menstruation, both PGE2 and PGF2α have low levels in the proliferative phase, slightly increase during the early luteal phase and then increases to fourfold in the late luteal phase and sixfold during the menstrual phase.[16]

The current evidence suggests that women with primary dysmenorrhea have 2 to 7 times higher PGF2α than in women without primary dysmenorrhea.[17] Prostaglandins are formed through arachidonic acid, which is present in cell membrane phospholipids. Its production is triggered via the cyclic adenosine monophosphate (cAMP) pathway by adrenaline, peptide and steroid hormones, mechanical stimuli and tissue trauma (Fig. 2).[18] Figure 2 shows the pathway producing pain in dysmenorrhea.

It has been established that the increased formation of arachidonic acid, intracellular destruction and tissue trauma during menstruation is responsible for enhancing prostaglandin production.[11,18] With an increasing prostaglandin concentration, the severity of menstrual pain and associated symptoms also increases.[18]

Other Mediators in Dysmenorrhea

We have seen dysmenorrhea is considered to be an inflammatory event primarily driven by prostaglandin, however, there are several other concerning factors involved in dysmenorrhea.

While arguable, vasopressin may be involved in producing dysrhythmic uterine contractions, causing reduced uterine flow, hypoxia and eventually pain. A study has also linked nitric oxide to the uterine quiescence during pregnancy.[18,19]

Experimental studies have revealed high uterine histamine levels, mediated by estradiol, and greater uterine contractility and this may be an indication of myometrial histamine receptors (uterine H1 receptors).[20] Besides, in some women, a reduction of diamine oxidase levels is also reported and a resultant severe effect of histamine at the beginning of the menstruation, further corroborating the hypothesis that histamine is one of the significant factors causing dysmenorrhea.[20]

A study conducted among dysmenorrheic patients revealed a significant association between dysmenorrhea and increased mast cells in the uterine cervix. The release of mast cell mediators such as histamine, prostaglandin and serotonin in the uterine myometrium evokes strong contractions.[21]

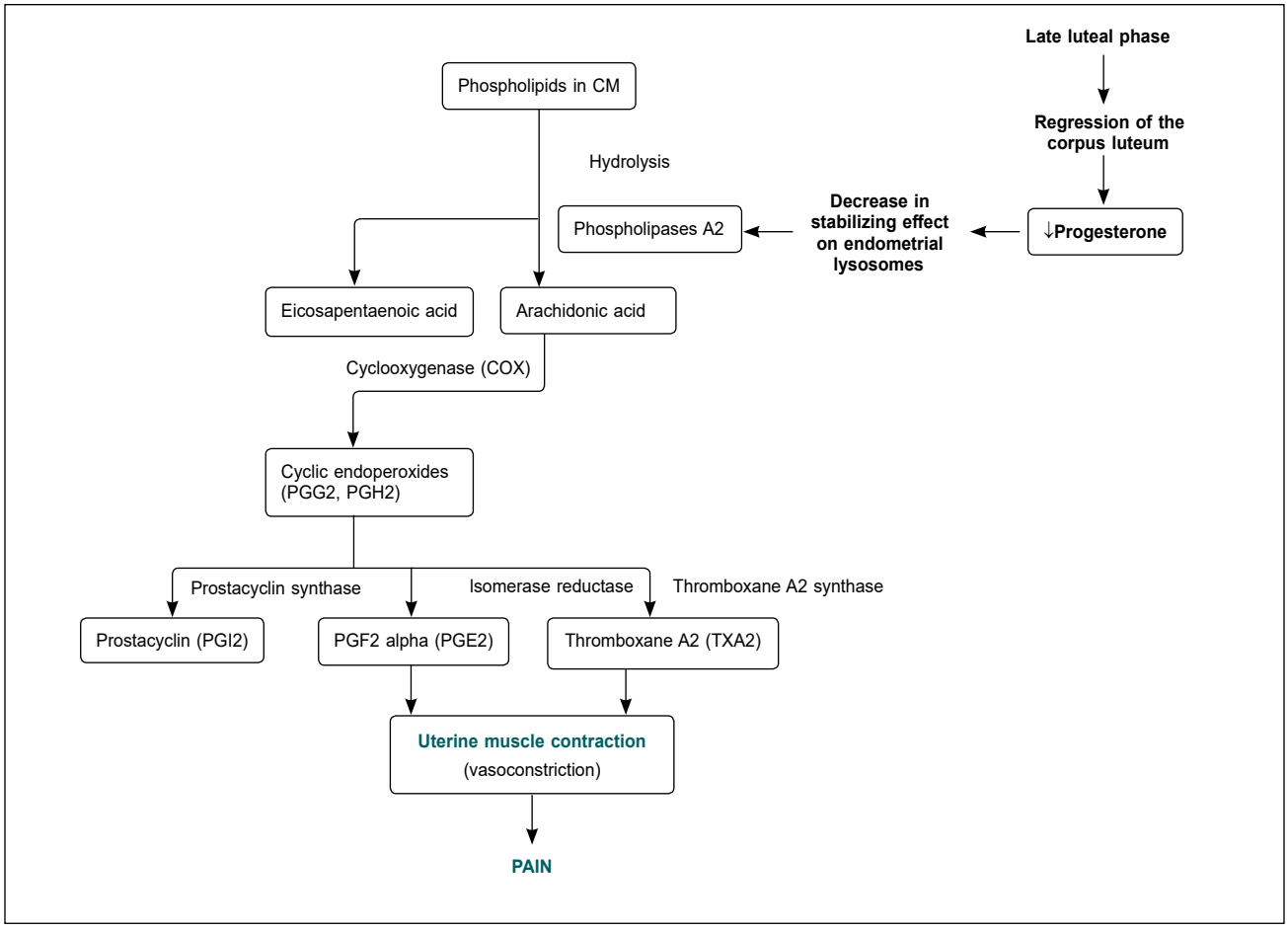

Figure 2. Prostaglandin synthesis in dysmenorrhea.

Preclinical studies have also shown that bradykinin induces uterine smooth muscle contractions via activating phospholipase C.[22,23] The pain in the pelvis results from an increased uterine activity, uterine ischemia and hypersensitization of pain fibers by the action of bradykinin and other physical stimulus.[24] It has also been shown that the response to bradykinin is dependent on the presence of prostaglandins, especially PGE2. It has been suggested that bradykinin has a self-sensitizing action and stimulates the release of PGE2.[25] In addition, we know that cholinergic nerves form moderately dense plexuses in the myometrium, cervical smooth muscles and microarterial system of the uterine horns and cervix. Acetylcholine also stimulates contraction of the myometrium[26] suggesting its role in the pathogenesis of dysmenorrhea by inducing contractions in the uterus.[27] Inflammatory cytokines also undergo changes in concentration during menstruation including tumor necrosis factor (TNF)-α, interleukin (IL)-6 which are higher in dysmenorrheic women compared to healthy women.[1]

TREATMENT OF DYSMENORRHEA

Approach to Management

The approach to managing dysmenorrhea includes nonpharmacological, pharmacological and surgical options. Nonpharmacological approaches to treat dysmenorrhea include lifestyle changes such as proper diet, exercise, smoking cessation, low alcohol consumption and use of topical heat or transcutaneous electrical nerve stimulation (TENS) to provide relief from pain and discomfort. Nonsteroidal anti-inflammatory drugs (NSAIDs) are the best-established initial therapy for dysmenorrhea,[28] and they have a direct analgesic effect through inhibition of prostaglandin synthesis, and they decrease the volume of menstrual flow.

Combined oral contraceptive is the second line of treatment, and works by decreasing menstrual volume and prostaglandin secretion, with a resultant decrease in intrauterine pressure and uterine contractility.[11] In rare cases, a surgical approach may be needed for women with severe and refractory dysmenorrhea.[29]

NSAIDs in the Treatment of Dysmenorrhea

An effective treatment of primary dysmenorrhea targets all the components of the pain causing pathways, along with focusing on suppression of uterine contraction.[24] Pharmacological agents that inhibit cyclooxygenase (COX) lead to reduced prostaglandin synthesis, and its concentration in menstrual fluid decreases uterine contractility and menstrual volume.[4]

The cramps experienced during menstruation and the intensity of pain are correlated to the high concentration of PGF2α and PGE2 in the endometrium, making NSAIDs the cornerstone in the management of dysmenorrhea.[2] The understanding of the pathogenesis of pain in primary dysmenorrhea (as explained in the previous section) provides the rationale for the use of NSAIDs for the relief of primary dysmenorrhea instead of a pharmacotherapeutic agent which only acts to block uterine contractions.[8]

NSAIDs are used as the first-line therapy in the treatment of dysmenorrhea.[30] They act by inhibiting prostaglandin production through the blockade of COX activity. The common painkiller NSAIDs used in dysmenorrhea include aspirin, naproxen, ibuprofen and mefenamic acid.[31] Clinical evidence has shown that most NSAIDs are more potent than paracetamol in managing primary dysmenorrhea. It has also been shown that NSAIDS are two times more effective than paracetamol for pain relief.[2] Out of these agents, only mefenamic acid has dual action of inhibiting prostaglandin synthesis and blocking of EP receptors, which makes it unique and more effective for treating patients with dysmenorrhea.[31] The ability of mefenamic acid to inhibit pre-existing prostaglandin causes a faster onset of uterine relaxation providing better pain relief.[16]

Mefenamic acid in Dysmenorrhea

Mefenamic acid is commonly used NSAID for the treatment of dysmenorrhea and is widely available across several regulated markets viz. European countries, USA, Canada, Australia, New Zealand, Japan, Hong Kong, India, Malaysia, Thailand and Singapore. Given in a usual oral dose of 500 mg thrice daily, it is one of the most highly prescribed medicines across the globe.[32]

Several studies provide the evidence of mefenamic acid providing adequate pain relief and also reducing the volume of blood loss in dysmenorrheic women associated with menorrhagia.[29,31]

Several studies have shown superior efficacy of mefenamic acid in reliving the pain in dysmenorrhea over placebo and other NSAIDs like ibuprofen, naproxen, indomethacin, combination of dextropropoxyphene and paracetamol.[33-35]

Mefenamic acid also acts as a bradykinin antagonist, and hence may have an extended pathway of pain relief.[33] It can also inhibit the increased uterine contractility stimulated by prostaglandin-endoperoxide analogs.[34] Mefenamic acid also reduces the high uterine resting pressure or tone, and the frequency of contractions.[35] Furthermore, it has been seen that mefenamic acid reduces the mean menstrual blood loss by 40%. It acts via an improvement of platelet aggregation and degranulation and through increased vasoconstriction.[36] This is a desirable benefit of mefenamic acid.[37] This reduction in menstrual blood loss was also seen to sustain at 6 to 9 months and at 12 to 15 months in women with menorrhagia treated with mefenamic acid during all menstrual periods for over a year. Significant sustained decrease in blood loss were observed in women with menorrhagia due to ovulatory dysfunctional bleeding and in those who had undergone tubal sterilization.[38]

In patients with dysmenorrhea, paracetamol does not work effectively as it cannot eliminate the cause of pain in dysmenorrhea, particularly, the presence of excess prostaglandins in the endometrium. A study has revealed that paracetamol was not better than a placebo in relieving primary dysmenorrhea. Usually, the paracetamol dose available for pain relief is 500 mg which is not effective as an analgesic for acute, mild-to-moderate pain. However, high-dose immediate-release paracetamol (1,000 mg), has analgesic action than lower doses for adults with mild-to-moderate acute pain. However, those suffering from pain want to achieve either a substantial reduction in their pain intensity or to achieve a low pain state, which may not be possible with suboptimal doses of paracetamol available in most marketed paracetamol preparations for pain relief.[39]

Combination Treatment

Women with primary dysmenorrhea experience four different uterine contraction-related abnormalities including increased uterine resting tone, increased active pressure, increased number of contractions and dysrhythmic uterine activity.[8]

Studies have also shown that the combined administration of NSAIDs and antispasmodics is beneficial in treatment of dysmenorrhea. Given the mechanism of prostaglandin-mediated pain, NSAIDs that inhibit COX pathway may be the ideal therapeutic path. However, owing to the more complex physiology of

Table 1. Different Spasmolytic Agents Used in Dysmenorrhea

Drug	Mechanism of action	Combination with mefenamic acid
Dicyclomine	Relieves smooth muscle spasm via dual mechanism. A specific anticholinergic effect at the acetylcholine receptor site and a direct smooth muscle antagonism of bradykinin- and histamine-induced spasms.	Symptomatic relief from menstrual pain and cramps. It is also used to treat abdominal pain by relieving spasms of the muscles in the stomach and intestines.[40]
Drotaverine	Direct spasmolytic action, selective inhibitor of phosphodiesterase-4 (PDE-4). Does not have anticholinergic effects.	Antispasmodic agent with noncholinergic action.[40]
Camylofin	Both anticholinergic action as well as direct smooth muscle action; PDE-4 inhibitor.	Pain relief, but results were not statistically significant compared with dicyclomine + mefenamic acid.[48]

dysmenorrhea, use of spasmolytic agents acting on the uterine muscle contraction becomes imperative.[40]

Studies have demonstrated the synergistic activity of mefenamic acid with dicyclomine in dysmenorrhea patients.[41] The combination emerged as a highly effective and well-tolerated option for treating spasmodic dysmenorrhea and also for additional concomitant benefits in menorrhagia. Mefenamic acid relieves primary dysmenorrhea mainly by inhibiting endometrial prostaglandin formation, restoring normal uterine activity.[42] An observational study reported that a fixed-dose combination of mefenamic acid and dicyclomine was effective in restoring the functional ability of the patients with dysmenorrhea.[43] Dicyclomine has a dual action of inhibiting muscarinic action of acetylcholine of postganglionic parasympathetic effector regions and antispasmodic action via its direct action on the uterine smooth muscles.[44,45] Their synergistic activity is also proven by the fact that dicyclomine given alone was less efficacious in moderate and severe dysmenorrhea.[46] A comparative study conducted among healthcare practitioners revealed that mefenamic acid and dicyclomine was used by 77% of the study participants for pain relief, of which 35% used it for dysmenorrhea.[47] The anticholinergic side effects of dicyclomine are not prominent in the combination owing to the lower drug dose used.

Table 1 shows different agents used along with mefenamic acid in dysmenorrhea.[40,48]

SAFETY AND EFFICACY OF MEFENAMIC ACID

Mefenamic acid is generally well-tolerated, but side effects can include headache, dizziness, somnolence, nausea, diarrhea, abdominal discomfort, heartburn, peripheral edema and hypersensitivity reactions.[49] The combination of mefenamic acid and dicyclomine is better tolerated as due to its antimuscarinic and spasmolytic action, dicyclomine reduces the gastrointestinal side effects that may be associated with mefenamic acid.[46]

There are certain concerns about the hepatotoxicity of mefenamic acid; however, in prospective studies, less than 5% of patients taking mefenamic acid experienced transient rise in serum aminotransferase levels. The abnormalities usually reduced even while the drug was continued and without dosage adjustment. There may have been rare cases of mefenamic acid-induced liver injury but mefenamic acid is not a causative agent in any large case series on drug-induced liver injury.[49]

Patients with dysmenorrhea need to take mefenamic acid irregularly, hence it has lesser chances of interfering with the COX system and presents a lower cardiovascular risk compared with other drugs such as celecoxib.[50]

CONCLUSION

Dysmenorrhea affects a significant population of women across the globe, but it continues to be a neglected health issue, with considerable underuse of medications. Even though it is not a life-threatening condition, it leads to a significant burden on the quality of life of female adolescents or women interfering with daily activities. Besides, another challenge affecting dysmenorrhea management is insufficient information or lack of awareness about primary dysmenorrhea among the younger population. NSAIDs are the first line of treatment in the treatment of dysmenorrhea and amongst the NSAIDs, mefenamic acid is a preferential COX-2 inhibitor that can effectively reduce menstrual pain with fewer side effects. Mefenamic acid is one of the most thoroughly investigated agents for the treatment of dysmenorrhea, and the results have been consistently effective in reducing subjective discomfort. One of the

first approved drugs for dysmenorrhea in the USA, mefenamic acid is very effective in improving symptoms and changing the underlying pathophysiology of the disease. Mefenamic acid has a multifactorial action in offering relief from dysmenorrhea including inhibition of prostaglandin, decrease in uterine tonicity, and bradykinin-antagonistic activity. Considering the complex pathophysiology of dysmenorrhea involving multiple pathways, combination therapies using NSAID, and other antispasmodic agents becomes imperative to treat the condition. For instance, the synergistic combination of dicyclomine and mefenamic acid is effective and safe in treating pain and discomfort related to dysmenorrhea.

In an era of women empowerment, every woman needs to be in the optimum physiological and psychological condition. Hence, it becomes all the more important to address the menstrual burden and provide effective treatment. Healthcare professionals can enhance awareness in their women patients about the problems associated with dysmenorrhea. They can provide educational literature, posters or websites such as www.painfulperiods.in where patients can get ready access to authentic information curated by the doctors.

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CASE REPORT

Scrub Typhus and Myocarditis: A Rare Complication

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ABSTRACT

Scrub typhus, also called bush typhus, is a zoonotic disease a Gram-negative bacterium. Its presentation may range from nonspecific febrile illness to severe disease, with cardiovascular, renal, hepatic and neurological involvement. Myocarditis is one of the rare complications of scrub typhus. Hence, we are reporting a case of a 50-year-old male, farmer by occupation, presenting to us in multiorgan dysfunction syndrome who developed myocarditis during second week of his illness.

Keywords: Scrub typhus, *Orientia tsutsugamushi*, myocarditis

Scrub typhus is a zoonotic disease. It is also known as bush typhus or tsutsugamushi disease. It is caused by a Gram-negative bacterium, *Orientia tsutsugamushi*, which is a member of the Rickettsiaceae family. It is transmitted to humans through the bite of larval mites, known as chiggers. They belong to the family Trombiculidae. While the disease is prevalent worldwide, most of the cases are reported from the so called "tsutsugamushi triangle", which is a wide area bounded by Pakistan, India and Nepal in the West; Siberia, China, Japan and Korea in the North and Indonesia, Philippines, Australia and the Pacific islands in the South. An estimated 1 million new scrub typhus infections are reported every year and more than 1 billion people globally are at risk. Scrub typhus presentation ranges from mild nonspecific febrile illness to severe disease with cardiovascular, renal, hepatic and neurological involvement. Cardiovascular complications like pericardial effusion, left ventricular systolic dysfunction, diastolic dysfunction, myocarditis and arrhythmias can lead to cardiogenic shock and sudden cardiac arrest. Therefore, the association of scrub typhus-induced cardiovascular disease should be investigated to provide a timely and appropriate diagnosis and to reduce the mortality in complicated scrub typhus infection. Here we are reporting a case of scrub typhus complicated with myocarditis admitted in our hospital.

CASE REPORT

A 50-year-old man with no previous comorbidity was admitted in our hospital with complaints of fever, myalgia and headache since 7 days and nausea/vomiting since 3 days. Upon physical examination, the blood pressure was 130/80 mmHg, pulse rate was 108 bpm, respiratory rate was 18 breaths/min and temperature was 36.8°C. He was alert and fully oriented. Auscultation of both lungs revealed normal vesicular breath sounds and no added sounds. Laboratory testing showed following results: complete blood count – hemoglobin [Hb] - 12.9 g/dL, total leukocyte count [TLC] - 10,680/mm^3, platelet count - 75,000/mm^3; blood urea – 106 mg/dL; creatinine - 2.21 mg/dL; and liver enzymes – serum glutamic-oxaloacetic transaminase (SGOT) - 219 U/L, serum glutamic-pyruvic transaminase (SGPT) - 182 U/L, alkaline phosphatase - 262 U/L. Chest X-ray was normal and electrocardiograph (ECG) showed sinus tachycardia. Scrub typhus immunoglobulin M (IgM) antibody test was positive (IgM capture enzyme-linked immunosorbent assay [ELISA] test). On Day 4 of admission, patient complained of chest pain and lightheadedness.

On examination, blood pressure was found to be 70/50 mmHg. ECG was suggestive of multiple

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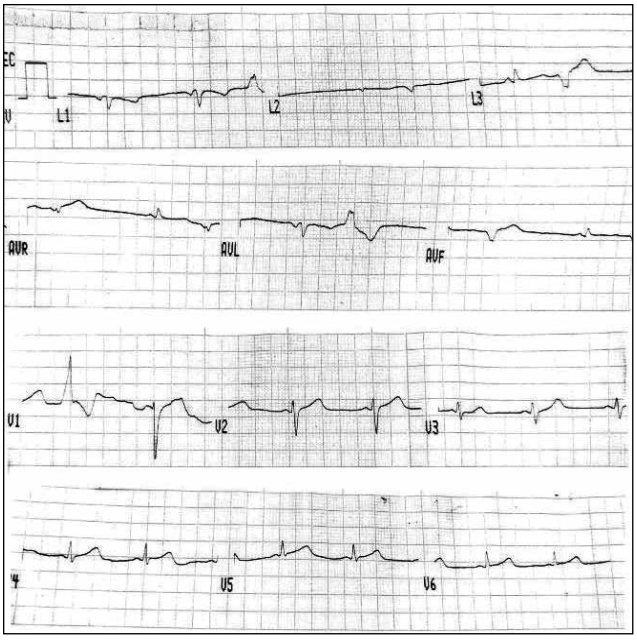

Figure 1. ECG showing multiple premature ventricular complexes with secondary ST-T changes.

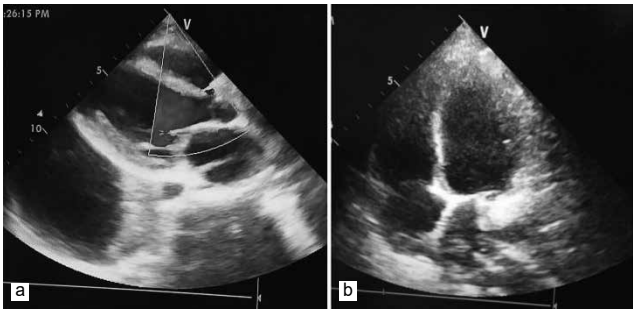

Figure 2 a and b. Echocardiographic still images showing mild mitral and tricuspid regurgitation with normal left atrial and ventricular size.

ventricular premature complexes (Fig. 1). Myocarditis secondary to scrub typhus was suspected. Cardiac enzymes were elevated (Troponin T - 0.86 ng/mL, creatine phosphokinase-MB - 68 ng/mL). Patient was started on inotropes, injection magnesium sulfate and injection hydrocortisone. A two-dimensional echocardiography (2D-Echo) was done which revealed mild mitral and tricuspid regurgitation (Fig. 2 a and b) and global hypokinesia of left ventricle with an ejection fraction (EF) of 25%.

Patient responded well to doxycycline and other supportive care; his condition improved with treatment over the next 48 hours. On Day 6, patient's blood pressure was 120/80 mmHg. He was slowly weaned off inotropic support. ECG was tracing within normal limits (Fig. 3). Review 2D-Echo was done after 2 weeks which revealed resolution of left ventricular function

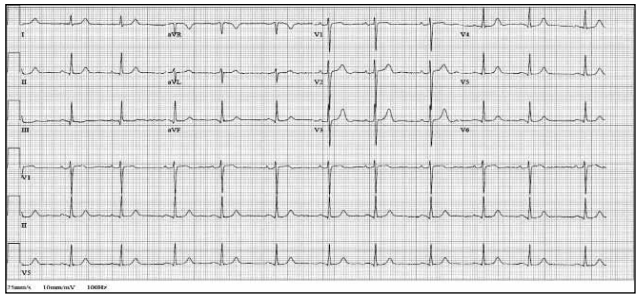

Figure 3. Tracing within normal limits.

with EF of 55%. His general condition improved and he was discharged.

DISCUSSION

Scrub typhus is a mite-borne disease predominantly seen in the Asia Pacific region. The typical presentation involves fever, headache, malaise and suffused face. In some cases, especially where early treatment is not instituted, complications may arise, such as meningitis, liver dysfunction, acute kidney injury and disseminated intravascular coagulation, which might lead to multiorgan dysfunction syndrome. The major pathologic findings in tsutsugamushi disease include systemic vasculitis and perivasculitis, which are caused by proliferation of the pathogen in endothelial cells of the microvascular system. These changes are associated within filtration of monocytes, plasma cells and lymphocytes, causing edema or necrosis in the peripheral tissues. Such microangiopathies frequently involve the heart, lungs, brain and kidneys. Various ECG abnormalities including arrhythmias, QRS axis change and ST-T changes have been reported. The heart is one of the target organs of scrub typhus disease. Levine reported that myocardial lesions were observed in around 80% of patients dying from the disease. Vasculitis and perivasculitis in the myocardium induce cellular infiltrations consisting mainly of lymphocytes, monocytes and plasma cells, along with hemorrhage and edema of the interstitial tissues. Cellular infiltrations are also frequently observed in pericardium and endocardium. Myocarditis in scrub typhus is usually subclinical and therefore many times ignored. Tsay and Chang described the serious complications of scrub typhus in 33 patients and only 1 patient (3%) developed myocarditis. A similar study was done by Bhargava et al in a tertiary care hospital in north India, who have described the clinical presentation and predictors of mortality of scrub typhus. Out of a total of 284 patients of scrub typhus, only 2 patients (8.3%) developed myocarditis without acute respiratory distress syndrome or multiorgan failure and both died.

Aggarwal et al have reported an incidence of 12% (3 out of 25 cases) for myocarditis in scrub typhus, hence emphasizing further the importance of early recognition of myocarditis.

Until our patient developed hypotension, we did not find any physical warning signs that might have helped us in making an early diagnosis of myocarditis. In our case 2D-Echo showed global hypokinesia of left ventricle with an EF of 25% and helped in making the diagnosis of myocarditis. In ECG, ST abnormalities can be seen in most patients of myocarditis at initial presentation. In our case, ECG revealed ventricular premature complexes. Cardiac biomarkers such as creatine kinase-MB and cardiac troponin-T are noninvasive and highly specific for myocarditis and if available, both can be useful in predicting myocarditis. In our case, both cardiac biomarkers were elevated. Early detection of scrub typhus myocarditis is crucial before patients develop cardiogenic shock and recovery depends on the prompt administration of hemodynamic support and the appropriate antibiotics. The mortality rate is high in severe infection; however, cardiac recovery can be good in those who survive with proper treatment.

Presence of positive serology for scrub typhus, clinical manifestations and abnormal cardiac parameters (cardiac biomarkers and echocardiogram) in our patient were strong evidences for the early diagnosis of myocarditis, which responded very well to the administration of doxycycline and other supportive treatments, resulting in the good cardiac recovery.

CONCLUSION

Myocarditis is a rare cardiovascular complication of scrub typhus. It should always be considered in a patient of scrub typhus with hypotension. The patient should be diagnosed and treated as early as possible to reduce morbidity and mortality. Thus, our case report calls attention to physicians for the possibility of myocarditis in association with scrub typhus.

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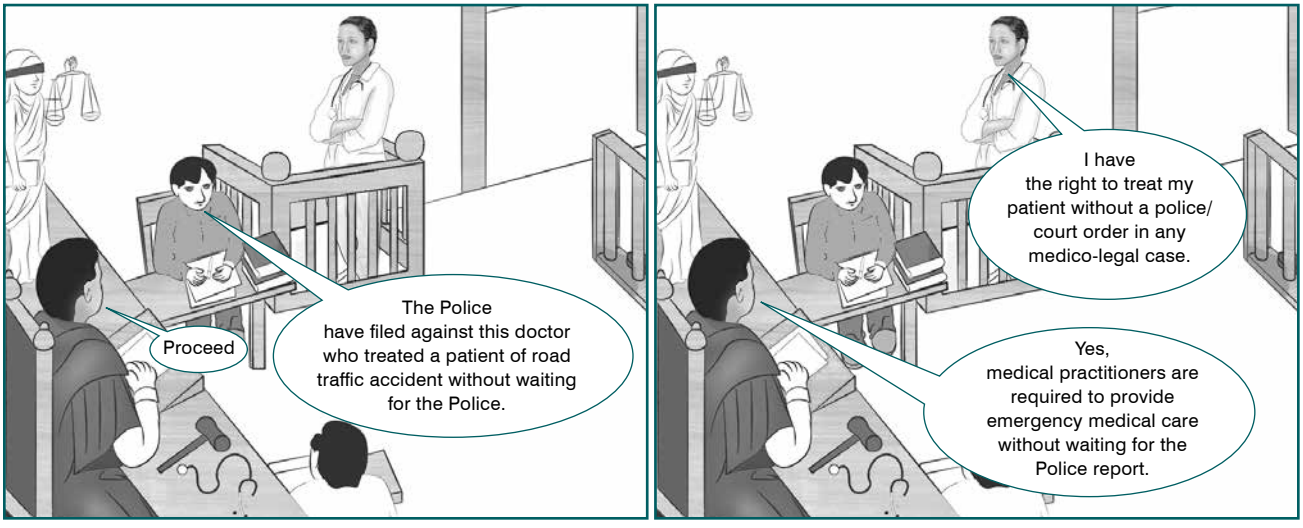
One Drink a Day can Shrink Brain Volume: Study

According to a new study, just one pint of beer or an average glass of wine a day may shrink the overall brain volume, with the damage increasing with a rise in the number of drinks daily.

The study published in the journal *Nature* noted that on average, people aged 50 years who drank a pint of beer or a 6-ounce glass of wine, which equals two alcohol units, per day over the past month had brains appearing 2 years older than people who drank just half a beer (1 unit). The brains of individuals of that age, who reported drinking three alcohol units a day, had both white and gray matter reductions which looked like 3.5 years have been added to their brain age. Consumption of four alcohol units a day led to aging of an individual's brain by over 10 years… (*CNN, March 4, 2022*)

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



Lesson: Doctors have the right to practice unencumbered in the best interest of patients even in medico-legal cases. In Pt. Parmanand Katara vs Union Of India & Ors on 28 August, 1989 AIR 2039, 1989 SCR (3) 997, the Supreme Court of India, in the context of medico-legal cases, has emphasised the need for rendering immediate medical aid to injured persons to preserve life and the obligations of the State as well as doctors in that regard. The Court observed: "Every doctor whether at a Government Hospital or otherwise has the professional obligation to extend his services with due expertise for protecting life. No law or State action can intervene to avoid/delay the discharge of the paramount obligation cast upon members of the medical profession." Regulation 13 of the Code of Medical Ethics framed by the Medical Council of India also says that the patient must not be neglected. "A physician is free to choose whom he will serve. He should, however, respond to any request for his assistance in an emergency or whenever temperate public opinion expects the service…"

CASE SUMMARY

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

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

SOME SALIENT COURT OBSERVATIONS

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

into cognisance of such cases, preparation of F.I.R. and other formalities by the Police."

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

COURT ORDER

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

1. *"Whenever any medico-legal case attends the hospital, the medical officer on duty should inform the Duty Constable, name, age, sex of the patient and place and time of occurrence of the incident, and should start the required treatment of the patient. It will be the duty of the Constable on duty to inform the concerned Police Station or higher police functionaries for further action. Full medical report should be prepared and given to the Police, as soon as examination and treatment of the patient is over. The treatment of the patient would not wait for the arrival of the Police or completing the legal formalities.*

2. *Zonalisation as has been worked out for the hospitals to deal with medico-legal cases will only apply to those cases brought by the Police. The medico-legal cases coming to hospital of their own (even if the incident has occurred in the zone of other hospital) will not be denied the treatment by the hospital where the case reports, nor the case will be referred to other hospital because the incident has occurred in the area which belongs to the zone of any other hospital. The same police formalities as given in para 1 above will be followed in these cases.*

   All Government Hospitals, Medical Institutes should be asked to provide the immediate medical aid to all the cases irrespective of the fact whether they are medico-legal cases or otherwise. The practice of certain Government institutions to refuse even the primary medical aid to the patient and referring them to other hospitals simply because they are medico-legal cases is not desirable. However, after providing the primary medical aid to the patient, patient can be referred to the hospital if the expertise facilities required for the treatment are not available in that Institution."

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HCFI Dr KK Aggarwal Research Fund

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

Topic: COVID update – Situation in various countries

Speaker: Dr Monica Vasudev, *Allergist & Clinical Immunologist, Fellow of American Academy of Asthma, Allergy and Immunology, Advocate-Aurora Health, Wisconsin, USA*

5th February, 2022 (Saturday; 9.30 am-11 am)

- Omicron sublineage BA.2, also known as the "stealth variant" was first detected in genome sequences from Philippines in November 2021. It is found in 49 countries.
- It shares many of the same mutations as its ancestor strain but with a further 28 mutations not previously seen in the original Omicron variant.
- It does not have the mutation, present in the original variant that made it easier to detect.
- BA.2 is the dominant strain in Denmark; in the US, BA.1 is still 99%.
- It may be more transmissible, but there is no evidence that it causes more severe disease.
- Those who are vaccinated and boosted are better protected.
- On February 1, Pfizer/BioNTech asked Food and Drug Administration (FDA) to approve a two-vaccine dose regimen for young children to start with.
- Children 2 to 4 years old who were given two shots were infected at a rate 57% lower than the children in the placebo group.
- Children 6 months to 2 years old who got shots were infected at a rate 50% lower than the placebo group.
- In a randomized, placebo-controlled trial published in the *NEJM*, two doses of Novavax vaccine given 21 days apart had an overall efficacy of 89.7%. The primary end point was based on the first occurrence of PCR-confirmed symptomatic coronavirus disease 2019 (COVID-19) with onset at least 7 days after the second vaccination in serologically negative adult participants at baseline.
- The Novavax vaccine has a subunit protein platform and it is formulated with an adjuvant to enhance immune response and stimulate high levels of neutralizing antibodies. The technology is the same as that used in the Flublok influenza vaccine, and is similar to other vaccines that have been around for a long time, like the hepatitis B vaccine.
- On February 3, it was accorded conditional marketing authorization by Medicines and Healthcare in UK and it has also been approved in Australia.
- Dr Pelletier on 28th January said about the Novavax vaccine, "…traditional option available for both the immunologically naïve and those hesitant to get boosted. It may provide a path forward for some who are pro-vaccine, but who drew the line at novel mRNA products…"
- The US is leading in deaths and falling behind on vaccination.
- Unvaccinated people had a greater risk of testing positive for COVID-19 and a greater risk of dying from COVID-19 than people who were fully vaccinated. Case and death rates in fully vaccinated and boosted were much lower than in the unvaccinated people.
- Unvaccinated adults aged 18 years had 13 times the risk of testing positive for COVID-19 and 68 times the risk of dying from COVID-19 in November and 5 times risk of testing positive for COVID-19 in December, compared to the fully vaccinated adults who had also taken the booster dose (CDC).
- Outpatient COVID-19 emergency use authorization (EUA) therapies are Paxlovid and Evusheld.
- In non-hospitalized patients, who have mild-to-moderate COVID-19 and are at high risk of disease progression, the therapeutic options are Paxlovid (nirmatrelvir with ritonavir), sotrovimab, remdesivir and molnupiravir.
- For those not expected to mount sufficient immune response to COVID-19 vaccine because they are on immunomodulatory therapies or those not able to receive the vaccine, there is Evusheld (tixagevimab/cilgavimab). It has been accorded EUA approval as pre-exposure prophylaxis for >12 years and >40 kg.
- Paxlovid is associated with 88% risk reduction; dose is nirmatrelvir 300 mg (2 tab) + ritonavir

100 mg twice daily within 5 days of symptoms. It is approved for ≥12 year olds. Children have to be >40 kg. Dose has to be reduced in patients with renal impairment where nirmatrelvir 300 mg (1 tab) + ritonavir 100 mg can be given.

- Sotrovimab: 85% relative risk reduction; dose is 500 mg once IV infusion within 10 days of onset of symptoms. It is approved for ≥12 years and >40 kg. It has been shown to have activity against Omicron.
- Remdesivir has 87% relative risk reduction; needs 3 consecutive doses; 200 mg IV on Day 1 then 100 mg IV on Days 2 and 3; it is to be given within 7 days of symptoms. It is approved for ≥12 years and >40 kg. Patients have to be observed for an hour after infusion.
- Molnupiravir shows 30% relative risk reduction; dose is 800 mg PO twice daily for 5 days, started within 5 days of symptoms. There are associated bone/cartilage toxicity concerns. Approved only for ≥18 years of age. It is not recommended for pregnant women due to risk of embryo-fetal toxicity. Less effective than the aforementioned medications.
- Evusheld has 69% relative risk reduction; the dose is tixagevimab 150 mg and cilgavimab 150 mg administered as two separate consecutive intramuscular injections.

Country updates

- **South Africa:** People are too relaxed. There is a common feeling that we are out of the pandemic. Schools will now be fully reopened. There has been a slight increase in cases in the last week linked to Sports Day in schools. Families are again coming with infection. But infection is mild, not alarming. Now, there is no quarantine for people exposed to the infection. New cases ranged from 3,000 to 4,500 in the last week. In the last 24 hours, there were 2,700 cases and 221 deaths. The number of people tested so far is 32 million – 3.1 million were positive. The recovery rate is 95.5%. Total deaths till now are 95,000. Hospital admissions came down to 4,800 in both public and private hospitals. Intensive care unit (ICU) admissions are also down - there are 404 cases, 180 on ventilator; the positivity rate is 8.2%.
- **Taiwan:** The country is doing well to contain the pandemic. Recently, there was a low-grade community spread of Omicron. The country has a very good hand hygiene practice and people wear masks even outdoor. We have encouraged touch and disinfect policy to prevent fomite transmission. In addition to face masks to block droplet and airborne transmission, the fomite transmission is also blocked. The booster coverage is around 80%.
- **Australia:** The Omicron wave has reached the peak, but deaths are still a concern with 30 to 40 deaths in each state per day; 85% deaths are in 60 to 70 years age group or older predominantly from nursing homes as many of the elderly are yet to get their booster dose; there is a crisis in the form of staff shortage; over 94% have received both vaccine doses; around 30% have taken the third dose. Vaccination for 5- to 11-year age group has started. Duration of quarantine has been reduced to 7 days. Positive persons but asymptomatic are asked to come back to work with masks.
- **India:** The curve is flattening with around 1.2 lakh daily cases; 169 crore vaccine doses given; 99% have received the first dose, while 85% have received both doses. Vaccination drive is going very strong in 15- to 18-year age group. Booster dose among high-risk persons is picking up. Regarding treatment, even Omicron is responding to monoclonal antibodies especially when given in early stages. Remdesivir continues to be in the treatment protocol. Molnupiravir, though authorized by drug regulator, is not included in government treatment protocol because of high side effects. Steroids, anticoagulants continue to be given. ICU admissions have come down to <1%. Despite increase in the number of cases, the mortality remained same or only marginally high. The Indian Council of Medical Research (ICMR) studies show that vaccinated persons have mild infection. COVID-appropriate behavior is stressed upon and crowd management has been given importance. Quarantine requirement for international travel has been relaxed. The budget has provision for teleconsultation for mental health problems.
- **Bangladesh:** More than 50% people have received both doses and more than 60% have taken the first dose. Hospitalization is less. Only schools are closed. But people are not following standard operating procedures (SOPs). They are also not being strictly enforced.
- **Philippines:** In the last 24 hours, there were 8,000 new cases, a declining trend was seen from mid-January to the first week of February. 1,51,000 active cases comprising 4.2%; the total number of cases is 3.3 million; total deaths are 54,214. The vaccination for 5- to 11-year-olds (14 million population), which was to start from February 4,

has been postponed for later this month. There is a decrease in cases in the national capital region, but there is a surge in cases in the provinces.

- **Pakistan:** The Omicron cases have plateaued for the last 3 days; it had reached 8,000 cases per day but now there are 6,000 to 6,500 cases per day with 30 to 40 deaths; 8.4 crore fully vaccinated, 10.8 crore are partially vaccinated, 2.7 lakh booster doses. Mortality in children is high, around 14%, which is worrisome. The positivity rate is decreasing. SOPs are not followed.

Participants - Member National Medical Associations: Dr Marthanda Pillai, India Member-World Medical Council, Advisor-CMAAO; Dr Angelique Coetzee, South Africa; Dr Akhtar Hussain, South Africa; Dr Salma Kundi, Pakistan; Dr Qaiser Sajjad, Pakistan; Dr Benito Atienza, Philippines; Dr Muh-Yong Yen, Taiwan

Invitees: Dr Russell D'Souza, Australia UNESCO Chair in Bioethics; Dr Errol Alden, USA; Dr Monica Vasudev, USA; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal

HCFI Round Table Environment Expert Zoom Meeting on "Union Budget 2022-23: What is for Environment, Sustainability and Climate Change?"

February 6, 2022 (12 noon-1 pm)

- The union budget was presented on February 1, 2022. It has promised to take the issues of sustainability and climate change seriously.
- Key features with respect to environment and sustainability are low carbon development strategy and climate change agenda.
- The main areas of focus are promoting technology, energy development and transition and climate action.
- The priorities are PM Gati Shakti, inclusive development, productivity enhancement and investment, sunrise opportunity and climate action and financing of investments.
- PM Gati Shakti, the National Master Plan for Multimodal Connectivity, is driven by seven engines: roads, railways, airports, ports, mass transport, waterways and logistics infrastructure.
- Green energy and clean mobility systems are featured as sunrise opportunities.
- Others include low carbon, climate resilient development, chemical-free natural farming, "panchamrit" the five commitments made at COP26, battery swapping policy, green bonds for green infrastructure, blended finance for sunrise sectors (such as climate action, deep-tech, digital economy, pharma and agri-tech), infrastructure strategy for data centers and energy strategy system, production-linked incentive (PLI).
- Rs. 19,500 Cr have been allocated to boost manufacturing of high efficiency solar photovoltaic modules within the country under the PLI scheme.
- The focus is also on climate adaptation.
- The Government of India has taken a very encouraging step towards electric vehicles, especially by coming up with a battery swapping policy. The team from Pondicherry (in an earlier meeting of the Round Table) had e-autorickshaws, which work on battery and they had a battery swapping policy, which is exchanging a discharged electric car battery with one which is already charged, a move that can decrease the long refuelling time, which is one of the major limitations of zero emission vehicles. This can result in huge reduction in air pollution, even water pollution, if people start following,because alternative energy is very easy for charging battery through solar power, etc. This can have a lot of positive effect on health.
- Any development done only for economic development will definitely disturb the environment. Sustainability is usually not considered.
- Two important points in this budget – One is encouragement of chemical-free farming within 5 km radius of rivers. This is a long-lasting effort, which will definitely improve water quality in rivers in long-term. Secondly, the emphasis on alternative energy; the combustion of fuel will be less. It will help in overall improvement in air quality.
- But ground water recharging should also have been highlighted and some allocation should have been made for this.
- Rs. 5,205 crore have been earmarked for manufacture of High Efficiency Solar PV Module to be implemented by the Ministry of New & Renewable Energy (MNRE).
- Sovereign green bonds will be issued for green infrastructure and proceeds will be deployed in public sector projects, which will help in reducing carbon intensity of economy.
- Energy transition, climate finance, inclusive growth – all these terms were mentioned multiple

times in the budget but the announcement (of funding) appeared to fall short in promoting clean energy in an accelerated manner.

- Amount of funding should have been more. The increased funding under the PLI scheme, the inclusion of a 'zero fossil fuel' policy, electric vehicle policy, EV battery-swapping and coal gasification policy are all good steps. At a macro level, an increase in capex will boost economic growth; however, not much additional budgetary support or tax incentives have been provided to clean energy, both grid and off-grid, including solar rooftop, storage technologies and green hydrogen- there was an expectation that support will be provided to these technologies to improve their commercial viability.
- The government should have provided a budget allocation and reduction of duties to allow deployment of roof top solar, storage, off-shore wind, green hydrogen, etc. It did not offer support for closure of inefficient fossil fuel plants. Also, it did not deal with increasing air pollution problem. While the government had made very specific allocations to tackle air pollution in the last budget, this year, there are no additional funds to specifically address the problem.
- Allocation for climate change action plan is not adequate and is only 30 crore.
- The total budget allocation for Environment ministry is 3030 crore. Out of this, only 142 crore is for environment protection, management and sustainable development.
- Rs 960 crore is allocated for centrally sponsored schemes; the budget for National Green Mission has been increased to Rs. 361 crore this year from Rs. 290 crore in the last year.
- For integrated development of wildlife habitat, the allocation is Rs. 510 crore.
- For Commission for Air Quality Management, Rs. 17 crore has been allocated.
- The allocation for the national clean air program has remained flat.
- The LPG subsidy has been reduced from 12,000 Cr to 4,000 Cr. This would affect the shift from burning of wood fuel.
- The budget for environmental education, awareness and training was also reduced from Rs. 77.13 crore in 2021-22 to Rs. 58 crore in 2022-23.
- Some allocation should have been made towards waste management.
- No sector talks of giving incentives; tax incentives should be given to the public for environmental issues, such as waste management.
- There was a lot of focus on Green hydrogen mission, but it has been ignored in the budget - only 0.1 crore has been allocated.
- The Delhi Metro Rail Corporation (DMRC) is working on multimodal integration in green mobility. A plan is being developed to allot proper space for parking of autorickshaws, which otherwise cause traffic congestion near the metro stations.
- Some targets for departments were expected to fulfil the commitments made at COP26, but no such directions have been made in the budget.
- DMRC is holding sessions for staff to create awareness about green environment. They are also being trained for this.
- The government is expanding the scope of 'Parivesh', which is a single window portal for all environmental clearances to promote ease of doing business and transparency in the process. However, this may be a risk by diluting environment safeguards.
- There is no provision for R&D to design air pollution control systems or develop technology to reduce air pollution.
- There is nothing about waste management and air pollution in this budget.
- If we want the general public to segregate waste, recycle waste, etc., there should be tax incentives/ benefits. Since, there is no encouragement, there is also no awareness or very poor awareness about environment.
- The new bill - Energy Consumption Amendment Bill 2022 will have a legal/regulatory framework for carbon trading in India.
- Budget for environment education, awareness and training has also been reduced this year.
- Manufacture and installation of solar panels in the country started from 2010 to 2011. The life of solar panels is 25 years. There is no concrete focus on their disposal. This needs to be discussed and worked out.
- Rs. 60,000 crore has been allocated to provide tap water connections under the Jal Jeevan Mission.
- Overall it's a good budget. It has focused on climate change, Atmanirbhar Bharat, Gati Shakti, renewable energy. There is need for strategic framework for India green transition.
- Public and private partnership is very important to carry forward the matter of air pollution.

Participants: Dr Anil Kumar, Mr Vivek Kumar, Mr Neeraj Tyagi, Dr SK Gupta, Mr Vikas Singhal, Mr Ankit Sethi, Dr BC Sabat, Mr Varun Singh, Ms Ira Gupta, Dr S Sharma

Coronavirus Updates

Famotidine in mild-to-moderate COVID-19

Results of a phase II trial reported in the journal *Gut* have shown that in patients with mild-to-moderate COVID-19, there was early resolution of symptoms and inflammation after treatment with famotidine without anydecrease in anti-SARS-CoV-2 immunity. Fourteen of 16 symptoms evaluated, such as loss of smell and taste, shortness of breath and abdominal pain, recovered. Fifty percent relief in symptoms was noted in 8.2 days in the famotidine-treated patients compared to 11.4 days in the placebo group. Very few patients on famotidine showed detectable plasma levels of interferon alpha… (*Source: Gut, February 10, 2022*)

Ivermectin does not stop progression of mild-to-moderate COVID-19 to severe disease

The Malaysian Ivermectin Treatment Efficacy in COVID-19 High Risk Patients (I-TECH) study, reported in *JAMA Internal Medicine,* has not shown favorable results with ivermectin for mild-to-moderate COVID-19. The study was conducted between May 31 and October 25, 2021. In these patients, ivermectin did not stop disease progression to severe disease (21.6% vs. 17.3%, respectively with relative risk of 1.25). Patients treated with ivermectin also required mechanical ventilation (1.7% vs. 4.0%) and intensive care (2.4% vs. 3.2%, respectively)… (*Source: Medscape, February 18, 2022*)

Mental health outcomes in COVID patients

COVID survivors were at a 60% higher risk of being diagnosed with a new mental health condition up to 1 year compared with those who were never infected, according to a *BMJ* study. They were 1.35 times at higher risk of developing anxiety disorder and 1.39 times the risk for depressive disorder. Stress, both acute and PTSD, adjustment disorders and sleep disorders were also prevalent in them. Mental health-related drug prescriptions also increased by 86% and they were more likely to be prescribed an antidepressant, selective serotonin reuptake inhibitors (SSRIs), benzodiazepenes, serotonin–norepinephrine reuptake inhibitors (SNRIs)… (*Source: Medpage Today, February 16, 2022*)

WHO recommends reducing quarantine period in places with huge number of cases

The World Health Organization (WHO) has recommended reducing the quarantine period in countries with high number of cases that are overwhelming the resources in its interim guidance. It suggests shortening the quarantine period from 14 days to 10 days without a test and to 7 days with a negative test, if the person should not develop any symptoms. If testing is not possible, then absence of symptoms could be used as a marker in place of testing…(*Source: Medscape, February 18, 2022*)

Booster effectiveness decreases after 4 months

CDC's report in *Morbidity and Mortality Weekly Report (MMWR)* states that the effectiveness of the booster dose against COVID-19–associated emergency department/urgent care visits and hospitalizations was higher after the third dose than after the second dose but the effectiveness declined after some time. During the Omicron-predominant period, the vaccine effectiveness against COVID-19–associated ED/UC visits was 87% during the first 2 months after the booster but declined to 66% after the fourth month. Similarly, vaccine effectiveness against hospitalizations, which was 91% initially decreased to 78% by the fourth month after a third dose. These findings call for being up to date with the recommended vaccination program in respective countries…(*Source: MMWR, February 18, 2022*).

Study finds vagus nerve dysfunction as the cause of post-COVID symptoms

Research from Spain has suggested that many symptoms of long COVID could be due to the effect of SARS-CoV-2 on the vagus nerve, which performs several functions in the body. Nearly 66% of the 348 patients had at least one symptom suggesting dysfunction of the vagus nerve, such as diarrhea, low blood pressure, tachycardia, dizziness, dysphagia and voice problems. Six patients showed vagus nerve thickening and increased echogenicity on ultrasound, indicative of inflammation. Many of these patients had "structural and/or functional alterations in their vagus nerve, including nerve thickening, trouble swallowing and symptoms of impaired breathing" which point to "vagus nerve dysfunction as a central pathophysiological feature of long COVID", state the authors… (*Source: Medscape, February 15, 2022*).

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79th AIOC 2021: All India Ophthalmological Society

PHACOEMULSIFICATION IN CHALLENGING SITUATIONS: MANAGEMENT OF POSTERIOR POLAR CATARACTS

Dr Angshuman Goswami, Kolkata

In his presentation, Dr Angshuman discussed the general features of posterior polar cataract and mentioned that it is congenital and a dominantly inherited disorder with variable expressivity. It can be sporadic, with a positive family history in 40-55% of the cases.

The symptoms include light scattering, increasing glare, difficulty in reading fine prints, difficulty in vision in bright light. Dr Angshuman discussed the significance of posterior polar cataract and said that it is located at a point where it affects a person's vision earlier than in other types of cataract. There is strong adherence of the opacity to the weak posterior capsule. Additionally, there is a high rate of intraoperative PC rupture, he emphasized. He discussed the preoperative examination which includes usual cataract work up, slit lamp biomicroscopy, ultrasound biomicroscopy (UBM), anterior segment optical coherence tomography (OCT), and Pentacam. While discussing the preoperative counseling, he stated that there is a possibility of the nucleus dropping intraoperatively due to a posterior capsule rupture. It has a long operative time and the visual recovery is delayed. He also discussed the surgical techniques, and explained the inside out technique of Vasavada with transverse trenching. He also elaborated on the important surgical dos and don'ts.

EPITHELIAL TO MESENCHYMAL TRANSITION IN RETINOBLASTOMA TUMOR: A NEW INTERVENTION TARGET

Dr Gagan Dudeja, Bengaluru

Presenting a study, Dr Gagan Dudeja said that the findings of the study demonstrated for the first time the role of ZEB1 and ABCB1 in epithelial mesenchymal transition (EMT) and drug resistance in retinoblastoma tumorigenesis. EMT suppression can halt metastasis propensity and reverse chemoresistance in retinoblastoma. He said that it is a new therapeutic intervention target since antifibrotics are already clinically available. There is a role of ZEB1 transcription factor and Wnt signalling pathway in driving EMT in retinoblastoma. The currently available drugs and small molecules can be repurposed for blocking EMT, he further said.

EMT is associated with tumor metastasis and drug resistance in cancers. Dr Dudeja undertook a study, co-authored by Dr Thirumalesh MB, to evaluate the EMT markers in retinoblastoma and *in vitro* model and understand the signalling mechanism associated with retinoblastoma metastasis.

MANAGEMENT OF SEVERE CORNEAL THINNING AND PERFORATIONS IN ADVANCED PUK PATIENTS USING BANANA GRAFTS

Dr Amit Gupta, Chandigarh

Dr Amit Gupta spoke about peripheral ulcerative keratitis (PUK), which is a corneal disorder of grave concern. He said that PUK often progresses circumferentially and may progress to severe corneal thinning or melt leading to perforation and cause considerable ocular morbidity. Larger peripheral melts and perforations are much more challenging, while smaller perforations are easier to manage surgically.

Recurrences are commoner compared to scleritis alone and also occur earlier (within 2 years). Most patients require surgical intervention. He mentioned various available surgical options for PUK such as conjunctival resection/peritectomy, cyanoacrylate adhesive, conjunctival flaps, amniotic membrane grafts, tectonic lamellar graft, penetrating corneal grafts and patch grafting. He further said that sutureless (fibrin glue-assisted) semi-annular tectonic lamellar grafts are effective and they are also relatively simple to perform and have excellent long-term outcomes.

PATTERN ERG

Dr Bibbhuti Kashyap, Ranchi

Dr Kashyap discussed about pattern ERG (pERG) during his presentation. He stated that pERG assesses the central retinal response to a structured nonluminance stimulus. It provides useful information in the distinction between macular dysfunction and optic nerve dysfunction.

He explained that the net retinal illumination remains constant and only a redistribution of the pattern of light and dark areas is made. He discussed the types of pERG, namely transient pERG and steady state pERG. He detailed the requirements for ERG as: positioning

of patient at 100 cm, light adapted patients, nondilated pupils, fixation (excessive blinking to be avoided), appropriate optical correction for 100 cm viewing distance, and 100-300 artefact free sweeps.

He discussed in detail about different electrodes. In terms of reporting, he emphasized that it would be ideal if each laboratory has its set of normal values for its own equipment and population. He mentioned that pERG is detectable in NPL eyes and helps distinguish central macular dysfunction from peripheral macular dysfunction. Other uses include early glaucoma detection, ocular hypertension, monitoring drug toxicity and monitoring therapeutic success.

THERAPEUTIC CARE AFTER CATARACT SURGERY

Dr Shreyas Ramamurthy, Coimbatore

During his presentation, Dr Shreyas discussed about the ESCRS study which showed a 5- to 7-fold decrease in endophthalmitis rates. However, a major criticism of the study has been a high incidence of endophthalmitis in the control group (0.35%). He mentioned that a study by Sharma et al (2015) evaluating intracameral (IC) cefuroxime found no difference in the incidence of endophthalmitis after cataract surgery.

Dr Shreyas mentioned that IC moxifloxacin is a fourth-generation quinolone with a wide-spectrum of activity against Gram-positive and Gram-negative organisms. It is preservative free and is commercially available in India.

He discussed a study by Haripriya and colleagues (2016) stating that there were 0.08% cases of postoperative endophthalmitis in the group that did not receive IC moxifloxacin (charity), 0.02% cases in the group that received IC moxifloxacin (charity) and 0.07% cases in the private patients' group that did not receive IC moxifloxacin. He detailed another study by Haripriya et al (2017) which noted that without IC moxifloxacin, PCR increased the endophthalmitis rate to 0.48%, while IC moxifloxacin reduced the endophthalmitis rate with PCR to 0.21%.

Comparing moxifloxacin with cefuroxime, Dr Shreyas said that 1 mg/0.1 mL cefuroxime is insufficient to kill sensitive *Staphylococcus aureus*. 0.5 mg moxifloxacin is sufficient to kill resistant *S. aureus*.

Dr Shreyas outlined the complications of postoperative inflammation after cataract surgery stating that the early complications include posterior synechiae, pupillary block and acute rise of IOP, while late complications include posterior capillary opacity and cystoid macular edema.

He mentioned that 0.1% dexamethasone is one of the strongest anti-inflammatory agents. Discussing about the combination of moxifloxacin and dexamethasone, he said that using combination therapy has several advantages, including improved patient compliance, reduced medication cost, decreased complexity of dosing, increased likelihood of receiving proper dosage and positive impact on clinical outcomes.

PIGMENTED FUNDUS LESIONS

Prof Bertil Damato, UK

Early treatment of choroidal melanoma enhances any opportunities for conserving vision, the eye and life itself, but it can be difficult to distinguish small melanomas from nevi. Delivering a talk at the ongoing AIOC, Prof Bertil Damato said that the likelihood of malignancy in melanocytic choroidal tumors can be estimated according to: Mushroom shape, Orange pigment, Large size, Enlargement and Subretinal fluid (MOLES). Each of these features is scored between 0 and 2 and tumors are categorized as common nevus, low-risk nevus, high-risk nevus and probable melanoma according to whether the sum total of the 5 scores is 0, 1, 2 or 3 or more, respectively.

He further recommended that the MOLES acronym and scoring system should avoid patients with benign nevi from undergoing unnecessary care while preventing delays in the diagnosis and treatment of patients with malignant melanoma.

AJCC STAGING FOR RETINOBLASTOMA: ONE SYSTEM PREDICTS BOTH GLOVE SALVAGE AND PATIENT MORTALITY

Dr Paul T Finger, Ankit Tomar, USA, AJCC Ophthalmic Oncology Task Force

The American Joint Committee on Cancer (AJCC) is the only classification validated to predict both metastasis and globe salvage, emphasized Dr Paul T Finger in his presentation. It accounts for the extent of both intraocular and extraocular retinoblastoma, he said. AJCC includes TNMH - characteristics of the Tumor, lymph Nodes, Metastasis and Heritable trait. AJCC is periodically updated to include the latest medical evidence. This staging system is accepted by both the AJCC and the Union for International Cancer Control (UICC), joining ophthalmic oncology into the world of general oncology, he added.

News and Views

COVID-19 Vaccine Protection Better Maintained Against Severe Disease: Study

The protection induced by vaccines against coronavirus disease 2019 (COVID-19) infection seems to fade within a few months; however, the protection against severe disease appears to be better maintained, suggests a study published in *The Lancet.*

The study reported that protection wanes at different speeds, based on the type of vaccine. The nationwide, observational study, based on registry-data from the Public Health Agency of Sweden, the National Board of Health and Welfare, and Statistics Sweden, included around 1.7 million people in the main analysis, and the results were confirmed in a larger population of close to 4 million people. Investigators noted that protection against infection of any severity diminished after the peak reached 1 month after the second dose. Six months following immunization, the remaining protection against infection was 29% with two doses of Pfizer vaccine and 59% with two doses of Moderna vaccine. With the AstraZeneca jab, there appeared to be no remaining protection from a month and onwards.

Protection against severe illness was reported to be 89% after 1 month and 64% from 4 months and onwards over the remaining maximum follow-up period of 9 months… (*ET Healthworld – PTI, February 8, 2022*)

Vitamin D Deficiency Tied to Severe COVID-19: Study

A new study suggests that individuals with vitamin D deficiency are more prone to develop a severe or critical case of COVID-19.

Investigators in Israel assessed vitamin D levels in over 250 patients hospitalized at the Galilee Medical Center with a positive COVID-19 test from April 2020 through February 2021. The vitamin D levels were obtained from tests conducted prior to hospitalization, as part of routine examination or for vitamin D deficiency, ranging between 14 and 730 days before the positive COVID test. Patients with vitamin D deficiency were found to have a 14-fold higher likelihood of having a severe or critical case of COVID-19. Additionally, the mortality rate for those with insufficient vitamin D levels was 25.6%, while it was 2.3% among individuals with adequate vitamin D levels.

The results are published in the journal *PLOS ONE…* (*Medscape, February 8, 2022*)

Changing Diet could Add Years to Life: Study

According to a new study published in the journal *PLOS Medicine*, changing what we eat could add up to 13 years to our life, particularly if we start at a young age.

Investigators used available meta-analyses and data from the Global Burden of Disease study. They developed a model for what could happen to an individual's longevity if a typical Western diet is replaced with an optimized diet, with focus on less red and processed meat and more fruits, vegetables, whole grains, legumes and nuts. The study revealed that if a woman started eating optimally at 20 years of age, she could increase her lifespan by a little over 10 years. A man starting to eat a healthier diet from age 20 could add 13 years to his life.

When starting at age 60, a woman could add 8 years to her life, while men starting a healthier diet at age 60 may add about 9 years to their lifespan… (*CNN, February 8, 2022*)

Blood Pressure Risk with Long-term Paracetamol Use

According to a new study, published in the journal *Circulation*, individuals with high blood pressure (BP) who take prescription paracetamol could have an increased risk for heart attacks and strokes.

The study looked at 110 volunteers, with two-thirds of them taking drugs for high BP. The randomized trial allocated them to take 1 g of paracetamol 4 times a day or placebo for 2 weeks, followed by a 2-week washout period and then crossing over to the alternate treatment.

Paracetamol was shown to increase the BP of study participants. Regular intake of 4 g paracetamol increased systolic BP in people with hypertension by ≈5 mmHg in comparison with placebo.

The investigators advised that patients with chronic pain should be started on as low a dose of paracetamol as possible and patients with high BP and at risk of heart disease should be closely monitored… (*BBC, February 8, 2022; Circulation February 7, 2022*)

Effectiveness of Previous Infection in Preventing Reinfection with SARS-CoV-2 Variants

A previous COVID infection protects against symptomatic reinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants, according to a study from Qatar published February 9, 2022 in the *New England Journal of Medicine*.[1]

This study conducted in the resident population of Qatar evaluated the effectiveness of previous COVID-19 infection in preventing reinfection with the different variants. Data was sourced from the national databases of test results, disease course and vaccinations. Cases detected between March 23, 2021 and November 18, 2021 were examined. A test-negative, case-control study design was used for this purpose. Only those cases where the cycle threshold (Ct) value was ≤30 and persons suspected to have symptoms compatible with COVID-19 were included. Vaccinated persons were excluded from the study. The median age of the participants ranged from 31 to 35 years. Previous infection was defined as positive reverse transcription-polymerase chain reaction (RT-PCR) at least 90 days before another positive test.

Analysis of data showed 90.2% effectiveness of previous infection in preventing reinfection with Alpha variant; the effectiveness against the Beta variant was 85.7%; against Delta variant, the effectiveness was 92.0%; while the effectiveness against the Omicron variant was found to be 56.0%.

Among the patients with reinfection, severe disease occurred in only 1 patient with the Alpha variant, two patients each with the Beta variant and the Omicron variant, while no patient with Delta variant progressed to severe disease.

There were no critical cases or deaths among patients with reinfection. The effectiveness against severe, critical or fatal disease was estimated to be 69.4% against Alpha, 88.0% against Beta, 100% against Delta and 87.8% against Omicron.

This study has demonstrated that previous infection provides robust protection against reinfection with the Alpha, Beta and Delta variants of SARS-CoV-2. Although comparatively the degree of protection against reinfection with the Omicron variant was lower, it was still significant at roughly 60%.

Reference: [1]Altarawneh HN, et al. Protection against the Omicron variant from previous SARS-CoV-2 infection. N Engl J Med. 2022 Feb 9:NEJMc2200133.

Risk of New Cardiovascular Problems Increases after COVID-19 Infection

According to a new study, long after recovery from COVID-19 infection, people have a significantly higher risk for developing new cardiovascular problems.

Investigators at the US Department of Veterans Affairs compared the rates of new cardiovascular problems among 1,53,760 people infected with COVID-19 before vaccines were available, 5.6 million individuals who did not contract the infection, and 5.9 million individuals whose data was obtained prior to the pandemic.

After an average of 1 year following recovery from the acute phase of infection, COVID-19 survivors appeared to have a 63% higher risk for heart attack, 69% higher risk for irregular heart rhythm, 52% higher risk for stroke, 72% higher risk for heart failure and about threefold higher risk of potentially fatal blood clot in the lungs, when compared with the other two groups. The increased risks noted in COVID survivors were observed in young and old, Blacks and Whites, males and females, those with and without diabetes, those with and without kidney disease, and among those who smoked and nonsmokers, noted researchers.

The findings are published in *Nature Medicine…* (*Reuters, February 10, 2022*)

Non-COVID Respiratory Infections Bounce Back Once Pandemic Restrictions are Relaxed

A recent study from Israel has reported an increase in the incidence of non-COVID respiratory infections in the first 3 months in all age groups after the COVID-19 restrictions were relaxed. Published in the journal *JAMA Network Open*, the study cautions about similar scenarios in other countries after restrictions are relaxed, which may pose a challenge to the healthcare system in concurrence with the threat of emergence of new SARS-CoV-2 variants.

Researchers evaluated 3,86,711 patients who attended 209 community clinics from January 2017 through June 2021 with complaints of respiratory and gastrointestinal illnesses in this cross-sectional study. There were more than 1.2 million clinic visits. The mean age of the participants was 27 years and men comprised just over half of the study population (52.3%). Visits that led to symptomatic diagnoses, such as fever, cough or diarrhea, recurrent diagnoses within 7 days, and diagnoses of confirmed COVID-19 were not included in the study group. The study sought to investigate the incidence rates (IRs) of infectious diseases from April to June 2021 when the COVID restrictions were lifted.

The rates of non-SARS-CoV-2 respiratory and gastrointestinal infection were found to be significantly high in children aged ≤3 years (IR ratio 2.64) in the 3 months after lifting of restrictions. And, all age groups included in the study showed a very high incidence of non-COVID respiratory infections (IR ratio 1.74).

Older adults, aged ≥80 years, reported more of non-SARS-CoV-2 upper respiratory tract infections (IR ratio 1.20) and lower respiratory tract infections (IR ratio 1.38), but less gastrointestinal infections (IR ratio 0.90).

This study highlights that the restrictions imposed on account of the pandemic also reduced the incidence of non-COVID infectious diseases, such as flu, but relaxation of the restrictions saw a rise in their incidence. This was particularly evident in children younger than 3 years of age. Less adherence to personal protective behaviors, such as physical distancing, mask wearing and hand washing, may account for this rebound in infections.

Reference: [1]Amar S, et al. Prevalence of common infectious diseases after COVID-19 vaccination and easing of pandemic restrictions in Israel. *JAMA Netw Open*. 2022;5(2):e2146175.

One in Three Elderly Develop New Conditions after COVID-19: Study

A new observational study published in the *BMJ* suggests that around one-third of older adults infected with COVID-19 in the year 2020 developed at least one new health condition that called for medical attention in the months after initial infection.

Investigators in the US noted that the conditions involved several major organs and systems, including the heart, kidneys, lungs and liver, and mental health complications.

Health insurance plan records were used to identify 1,33,366 individuals aged 65 years or older in 2020, diagnosed with COVID-19 prior to April 1, 2020. They were matched to three non-COVID comparison groups from 2020, 2019 and a group with viral lower respiratory tract disease. Any persistent or new conditions or sequelae beginning 21 days following a diagnosis of COVID-19 were noted. The investigators determined the excess risk for conditions fuelled by the disease over several months on the basis of age, race, sex and whether the patients were hospitalized for COVID-19. Among the people diagnosed with COVID in 2020, around 32% needed medical attention in the post-acute period for one or more new or persistent conditions. This figure was 11% higher than the comparison group from 2020… (*NDTV – PTI, February 10, 2022*)

History of Pancreatitis Tied to Severe COVID-19 Outcomes

According to a retrospective study published in the journal *Gastroenterology*, history of pancreatitis was associated with a higher risk for severe outcomes after a COVID-19 diagnosis. The study included more than 3,25,000 patients with COVID-19. According to adjusted analyses, patients with pre-existing pancreatitis appeared to have a higher risk for COVID-related hospital admission (odds ratio [OR] 1.23) and mortality (hazard ratio [HR] 1.16), in comparison with those without pancreatitis.

Additionally, as pancreatitis progressed, the risk of COVID-related hospitalization increased (OR 1.16 for single episode acute, 1.28 for recurrent acute and 1.50 for chronic pancreatitis). Among patients with acute pancreatitis, the higher risk for hospitalization and death were observed only among those who had an episode within the previous 5 years (OR 1.27 for hospitalization; OR 1.25 for death)… (*Medpage Today, February 10, 2022*)

Novel Stroke Risk Score for COVID-19 Patients

A quick and easy scoring system has been developed to predict which hospitalized COVID-19 patients have a greater risk for stroke.

The new system, presented at the 2022 International Stroke Conference (ISC), will help clinicians stratify the patients and assist with closer monitoring of those who have the highest risk for stroke. Investigators used the American Heart Association (AHA) Get with the Guidelines COVID-19 cardiovascular disease registry for the analysis. A total of 21,420 adult patients (mean age 61 years), who were hospitalized with COVID-19 at 122 centers between March 2020 and March 2021 were assessed. Among the hospitalized COVID-19 patients, 312 (1.5%) had a cerebrovascular event.

Researchers used standard statistical models to identify the risk factors most associated with the development of stroke and six such factors were identified, including history of stroke, no fever at the time of hospital admission, no history of pulmonary disease, elevated white blood cell count, history of hypertension and raised systolic BP at the time of hospital admission.

The scoring system assigns points for each variable, with more points pointing to a higher risk of stroke. Researchers also used a machine-learning approach wherein a computer takes all the variables and determines the best algorithm to predict stroke. The machine-learning algorithm was reported to be as good as the standard model… (*Medscape, February 10, 2022*)

Pfizer, Moderna Booster Dose Efficacy Declines after 4 Months: Study

According to a new study by the US Centers of Disease Control and Prevention (CDC), the efficacy of a third dose of the Pfizer and Moderna COVID-19 vaccines declines considerably by the 4th month following administration.

The results of the study are based on over 2,41,204 visits to the emergency department or an urgent care clinic, and 93,408 hospital admissions, which were more serious, among adults with COVID-like illness, between August 26, last year and January 22, this year.

Investigators determined vaccine efficacy by comparing the likelihood of a positive COVID-19 test between vaccinated and unvaccinated patients. During the period when Omicron variant was predominant, vaccine efficacy against COVID-related emergency department or urgent care visits was 87% in the 2 months after a third jab, while it declined to 66% by the 4th month. Efficacy against hospitalization was 91% in the first 2 months, and dropped to 78% by the 4th month after the third shot… (*NDTV – AFP, February 12, 2022*)

Body Fat Associated with Lower Bone Density, Especially in Men

Higher body fat is linked to lower bone mineral density (BMD), especially in men, suggests an analysis of data from a large, nationally representative sample, published in the *Journal of Clinical Endocrinology & Metabolism.*

Investigators assessed the relationship between BMD and body composition in 10,814 men and women, 20 to 59 years of age, from the National Health and Nutrition Examination Survey (NHANES) 2011 to 2018. Lean mass was found to have a strong positive correlation with bone density, while fat mass had a moderate negative effect. An added kg/m^2 of fat mass index (FMI) was linked to a 0.10 lower T-score, the number of standard deviations from the likely bone density in a young adult. The negative effect appeared to be greater among men, with a 0.13 lower T-score for each additional 1 kg/m^2 of FMI, in comparison with 0.08 lower T-score among women. Additionally, the effect was most marked in individuals in the highest FMI quartile… (*Medscape, February 11, 2022*)

DASH and Mediterranean Diet may Reduce Risk for NAFLD, Especially in Women

According to a study conducted in Iran, the Mediterranean diet (MeD) and the Dietary Approach to Stop Hypertension (DASH) seem to have an inverse correlation with the development of nonalcoholic fatty liver disease (NAFLD), especially among women.

The analysis included 3,220 adults from 2016 to 2017 and noted that those who followed DASH and MeD with the highest tertiles of adherence had the lowest risk for NAFLD with an OR of 0.80 for DASH and 0.64 for MeD. According to stratified analyses, there was a stronger association among women (OR 0.42 for MeD; OR 0.72 for DASH), while the association was not significant among men, noted the researchers.

The findings are published in *Nature Scientific Reports*… (*Medpage Today, February 11, 2022*)

CDC Updated Guidance Reduces Booster Interval for Immunocompromised Persons

The CDC recommends a 3-dose primary mRNA COVID-19 vaccine for primary vaccination for the moderately or severely immunocompromised persons aged ≥5 years; the third dose is given at a gap of at least 1 month after the second dose. This is followed by a booster dose for those aged ≥12 years.

In its updated guidance, the CDC has shortened the duration for booster dose following primary vaccination for immunocompromised persons.

The moderately or severely immunocompromised persons who have taken an mRNA COVID-19 vaccine for the primary series are now advised to take a booster dose 3 months after the third dose for a total of four doses. The earlier recommended interval was 5 months. These recommendations apply to those who took the Moderna vaccine (≥18 years) as well as those who received the Pfizer-BioNTech vaccine (≥12 years).

Immunocompromised people who have received Johnson & Johnson's (J&J) COVID-19 vaccine should preferably take an mRNA vaccine for the booster dose. A single booster dose is recommended at least 2 months after the second (additional) dose, for a total of 3 doses, i.e., one J&J vaccine dose followed by one additional mRNA vaccine dose at least 4 weeks later and then one booster dose.

Moderna vaccine should be used in a dose of 50 μg (0.25 mL) for the booster shot.

Source: Interim Clinical Considerations for Use of COVID-19 Vaccines Currently Approved or Authorized in the United States, CDC. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#vaccination-people-immunocompromised

The Science of Power

Power is the potential to impact others to get a work done the way you want it.

There has been an evolution in the way power works. There was an era when Brahmins ruled using the power of knowledge. Then Kshatriyas ruled using their physical power. Then came the era of Vaishyas ruling with the power of money and a time will come when Shudras will rule with the power of their work.

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

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

Everyone has these four inherent powers. The physical power is based on fear, tamas and rajas. The economical and the power of chair are associated with one's ego and rajas. The power of human resource is linked to the soul, consciousness and Satva. The physical power is at the level of body, economic power is at the level of mind, the power of chair is at the level of intellect and ego, while the power of human resources is at the level of soul. The power of human resource is based on Dharma and is universally accepted by all religions.

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

In Vedic sciences, these powers are also defined as *Ichhashakti* (the power of desires to be with the consciousness), *Kriyashakti* (the power to do selfless work), *Gyanshakti* (the power to learn about consciousness), *Chittashakti* (the power to take consciousness-based decisions) and *Anandshakti* (the power of inner happiness).

The power of human resources is focused on nurturing relationships. It is not based on the principles of survival of the fittest, which is an animal behavior. The power of human resource addresses training and developing everyone to survive and become the fittest of the fit.

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Link Between Periodontal Treatment and CV Events in Stroke Patients

The first randomized study that looked into the effect of periodontal treatment on future risk of cardiovascular events or stroke finds some promising results.

The PREMIERS study was conducted among patients with a recent stroke or transient ischemic attack (TIA) who also had gum disease. The study found no statistically significant difference between intensive periodontal treatment and standard treatment in the rate of recurrent stroke, myocardial infarction (MI) or death in the 1-year follow-up. However, there was a strong trend towards benefit in the intensive group. Both the groups were found to have a considerably lower event rate compared with a historical control group comprising of similar patients. The number of dental visits had a significant correlation with a reduction in the composite event rate.

In the study, investigators randomized 280 patients from the Stroke Belt area (south-eastern part of the United States) with a recent stroke or TIA and periodontal disease to receive standard or intensive periodontal treatment and followed them for 1 year. Standard treatment included regular (every 3 months) supragingival removal of plaque and calculus, and patients were given a regular toothbrush and advice about dental care. Intensive treatment included supragingival and subgingival removal of plaque and calculus (every 3 months), extraction of hopeless teeth, local antibiotics, an electric toothbrush, mouthwash and air flosser for dental care. All patients also received conventional stroke risk factor treatment. After 1 year of follow-up, the primary outcome (stroke/MI/death) was noted in 7.7% of the intensive treatment group compared to 12.3% of the standard care group, with a HR of 0.65… (*Medscape, February 11, 2022*)

INSPIRATIONAL STORY

A Great Story

A woman clad in the best of clothes walked up to a man sitting on the ground. "Good morning," she politely greeted him. The man slowly looked up. He thought that she wanted to make fun of him, like many others and just asked her to leave him alone.

The woman continued standing and asked the man if he was hungry. The man sarcastically said 'No'. He said that he had just had a meal with the President. Furious, he told her to go away. The woman smiled and held him from his arm to help him get up. The man resisted.

Just then a policeman came up and asked the lady if there was a problem. She asked the officer to help her get the man to his feet.

The officer wondered what business she had with him. The woman told the officer that she wished to get the man some food at the cafeteria nearby.

The homeless man resisted. But by then, he was brought to his feet by the officer.

The woman and the police officer got the homeless man into the cafeteria and sat him at a table in a corner. It was the middle of the morning, so most of the breakfast crowd had already left and there was still time for lunch.

The manager came to the table and asked the officer what was going on. The officer told him that the lady had brought this man in to be fed.

The manager replied angrily that it was not possible in that cafeteria. The homeless man smiled and told the lady that he knew this would happen. He got up and wished to leave.

The woman turned to the cafeteria manager, smiled and asked him if he was familiar with Eddy and Associates, the banking firm.

The manager said that he was. He told her that they hosted their weekly meetings in one of their banquet rooms. The woman went on to ask that they must be making a huge amount of money providing food at these weekly meetings. The manager was curious by now.

She went on to tell him that she was the President and CEO of the company. The manager was taken aback.

The woman smiled again. The officer was also giggling by now.

The woman offered the officer a cup of coffee. He gladly agreed. The cafeteria manager rushed to get his coffee.

The woman sat down at the table across from her guest. She stared at him and asked him if he remembered her. He looked closely at her and said that she looked familiar.

She said that she was a little older now from when she last met him when he worked at the same cafeteria. She told him that she came through that very door, cold and hungry on day.

She had come to the city looking for a job, but couldn't find anything. She was completely out of money and had been kicked out of her apartment. It was very cold and she was nearly starving. That's when she had walked into the cafeteria to try her luck and see if she could get something to eat.

The homeless man lit up with a smile. He recognized the woman. He remembered that she had come once and asked him if she could work for something to eat. The woman then said that he made her the biggest roast beef sandwich that she had ever seen, gave her a cup of coffee, and told her to go over to a corner table and enjoy it. She saw him put the price of her food in the cash register.

She went on to tell them that she got a job that very afternoon and worked her way up. She opened her purse, pulled out a business card and gave it to the homeless man. She told him to visit the personnel director of her company.

There were tears in the old man's eyes. He said that he could never thank her enough. She told him to thank God, because He led her to him.

As they walked out the cafeteria, the officer told the lady that he had seen a miracle, something that he will never forget.

God closes doors no man can open and opens doors no man can close.

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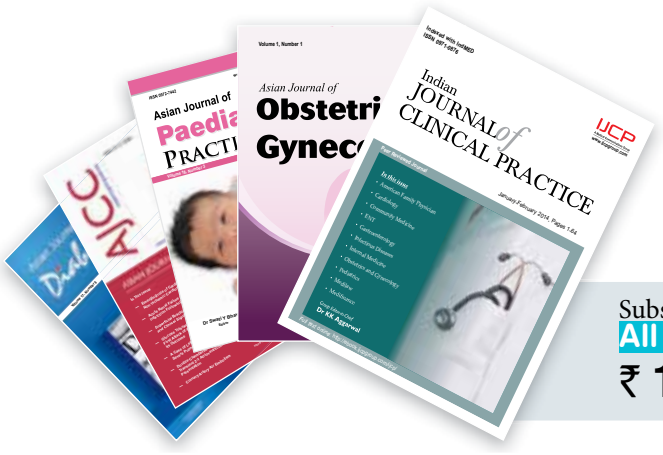

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Lighter Side of Medicine

HUMOR

WHAT IF I HAVE A BATH?

Mum: If you wash your face, Sammy, you can have one slice of chocolate cake. But if you wash your neck, too, you can have two slices.

Sammy: What if I have a bath?

DREAM OF A NECKLACE

After she woke up, a woman told her husband, "I just dreamed that you gave me a pearl necklace for our anniversary. What do you think it means?"

"You'll know tonight." he said.

That evening, the man came home with a small package and gave it to his wife.

Delighted, she opened it to find a book entitled "The Meaning of Dreams."

ABSENT-MINDED PROFESSOR

One of the world's greatest scientists was also recognized as the original absent-minded professor. One day, on board a train, he was unable to find his ticket. The conductor said, "Take it easy. You'll find it."

When the conductor returned, the professor still couldn't find the ticket. The conductor, recognizing the famous scientist, said, "I'm sure you bought a ticket. Forget about it."

"You're very kind," the professor said, "but I must find it, otherwise I won't know where to get off."

A TEXAS MILLIONAIRE

A Texas millionaire had fallen ill. The doctors consulted did not seem to understand what ailed him. The millionaire let it be known that any doctor who could heal him could have whatever he desired.

A country doctor was finally able to cure him, and as the doctor was leaving after a week's stay, the Texan said, "Doc! I am a man of my word. You name it, and if it is humanly possible I'll get it for you." "Well," said the doctor, "I love to play golf, so if I could have a matching set of golf clubs, that would be fine." With that the physician left.

The doctor didn't hear from the Texan millionaire for some months. Then, one day, he got a phone call from the millionaire.

"Doc, I bet you thought that I had gone back on my word. I have your matching set of golf clubs. The reason it took so long is that two of them didn't have swimming pools, and I didn't think they were good enough for ya. So, I had pools installed and they're all ready for you now!"

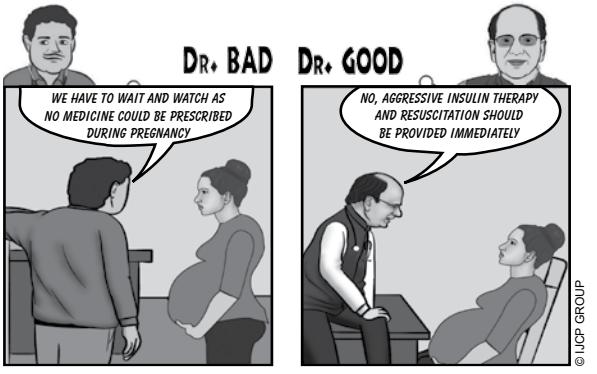
DAUGHTER IN COLLEGE

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

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

Dr. Good and Dr. Bad

SITUATION: A pregnant lady who had diabetic ketoacidosis presented with complaints of nausea and vomiting.



LESSON: Hyperglycemia and acidosis can be improved with aggressive insulin therapy and resuscitation during pregnancy.

J Neonatal Perinatal Med. 2017;10(1):17-23.

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- It should not contain abbreviations, footnotes or references.

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- The introduction should state why the study was carried out and what were its specific aims/objectives.

Methods

- These should be described in sufficient detail to permit evaluation and duplication of the work by others.
- Ethical guidelines followed by the investigations should be described.

Statistics

The following information should be given:

- The statistical universe i.e., the population from which the sample for the study is selected.
- Method of selecting the sample (cases, subjects, etc. from the statistical universe).
- Method of allocating the subjects into different groups.
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- These should be concise and include only the tables and figures necessary to enhance the understanding of the text.

Discussion

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References

These should conform to the Vancouver style. References should be numbered in the order in which they appear in the texts and these numbers should be inserted above the lines on each occasion the author is cited (Sinha[12] confirmed other reports[13,14]...). References cited only in tables or in legends to figures should be numbered in the text of the particular table or illustration. Include among the references papers accepted but not yet published; designate the journal and add 'in press' (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as 'unpublished observations' (in parentheses). At the end of the article the full list of references should include the names of all authors if there are fewer than seven or if there are more, the first six followed by et al., the full title of the journal article or book chapters; the title of journals abbreviated according to the style of the Index Medicus and the first and final page numbers of the article or chapter. The authors should check that the references are accurate. If they are not this may result in the rejection of an otherwise adequate contribution.
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Articles

Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

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Figures

– Two complete sets of glossy prints of high quality should be submitted. The labelling must be clear and neat.

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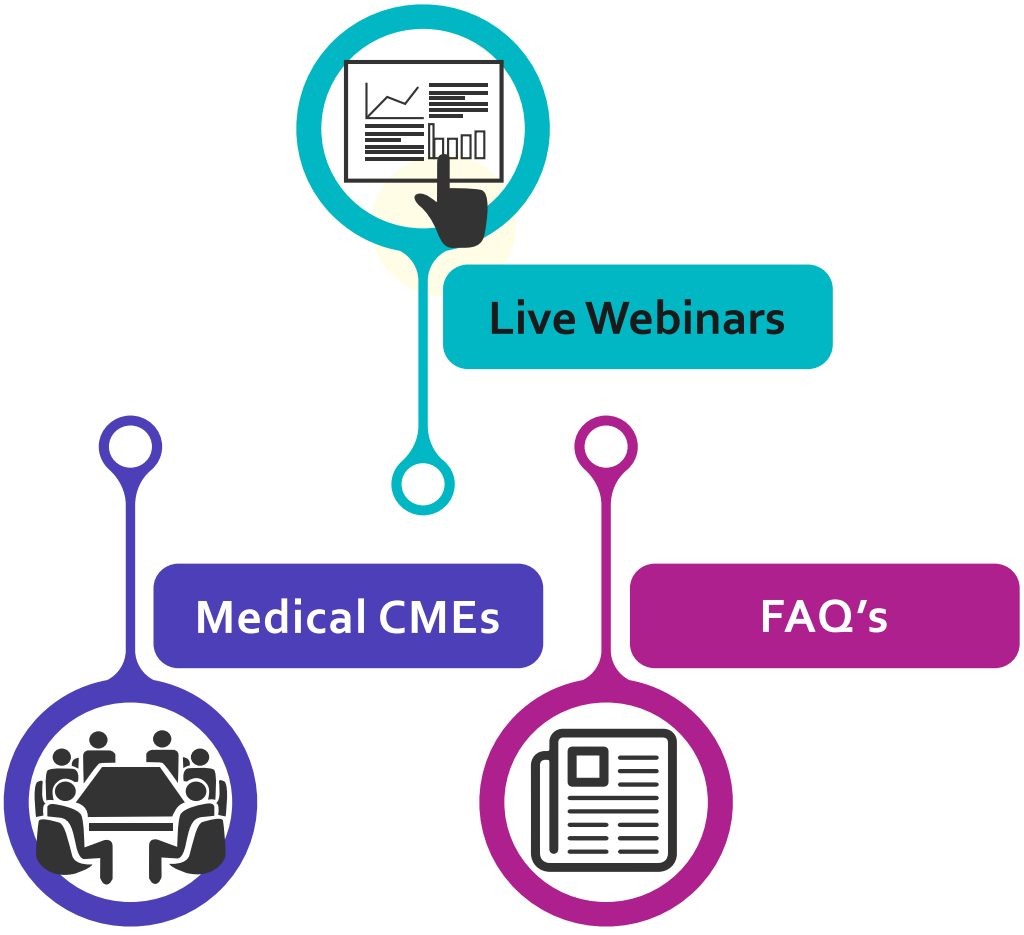

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