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# Update on COVID-19 Vaccine/Booster Dose and COVID-19 Update by National Medical Associations

- The US is going through its fifth wave and currently it is growing exponentially with 1,22,000 cases today. The seven-day average is now greater than 50k hospitalizations and 1,900+ deaths.
- The US Food and Drug Administration (FDA) has authorized emergency use of Pfizer-BioNTech vaccine for children aged 5 to 11 years. Immune responses in children were comparable to those aged 16 to 25 years. The vaccine was found to be 90.7% effective in preventing COVID in children. No serious side effects were observed in the ongoing study.
- An editorial in *Science* magazine has highlighted the importance of vaccinating children. COVID-19 is among the top 10 causes of death in children. No child has died of vaccination. The vaccine associated myocarditis is mild and self-limited; the incidence is less in 12- to 15-year age group than in the 16- to 25-year age group. Vaccinating children may be the most impactful public health efforts the US has seen in decades. And, it is one of the most important health decisions a parent will make.
- A *Lancet* study evaluating the effectiveness of a third dose of the Pfizer vaccine has shown that the risk of hospitalization and COVID-related mortality was higher in those who had received only two doses at least 5 months ago.
- Phase III trial data has shown high efficacy of a booster dose of the Pfizer-BioNTech vaccine. There were 5 cases of COVID in those who received the booster compared with 109 who were given a placebo. The booster trial showed a relative vaccine efficacy of 95.6% against disease during a period when Delta was the prevalent strain.
- The Centers for Disease Control and Prevention (CDC) has recommended for booster shots to include all adults ≥18 years, who received a Pfizer/Moderna vaccine at least 6 months after their second dose.
- The CDC reports that 195.9 million people are fully vaccinated and 33.5 million have received a booster dose. About 1,108,533,298 have taken the Pfizer vaccine; 71,543,150 have taken the Moderna vaccine, while 15,719,927 have taken the single dose J&J vaccine. Regarding booster dose, 19,477,683 have taken the Pfizer booster dose; 13,555,019 have taken the Moderna booster and 4,12,992 have taken the J&J booster.
- The main vaccine platforms are the mRNA vaccines (Pfizer, Moderna) and the viral vector vaccines (AstraZeneca, J&J). There are inactivated vaccines (Sinopharm, Sinovac), subunit vaccine (Novavax). Mixing and matching should be based on vaccine platform rather than individual vaccine.
- Persons who originally received the single dose J&J vaccine and then a Moderna booster had a 76-fold increase in antibodies 15 days after receiving the booster compared to before.
- Molnupiravir is the new oral antiviral drug. The 5-day course of the drug has halved the risk of hospitalization in people with mild or moderate infection. Earlier this month, UK became the first country to approve molnupiravir. It inserts a defective RNA building block when the virus uses an enzyme known as polymerase to copy its genome. Experiments suggest that it can cause mutations in human DNA as well.
- Paxlovid, the antiviral drug from Pfizer also reduced hospitalization by 89%. It inhibits the main protease

that creates other essential proteins. There should be a gap of 6 months between the second dose and the booster dose. Taking the booster dose closer to the flu season will better protect from virus if its COVID infection.

- A patient who has had COVID is likely to have some long COVID symptoms. There is some data to suggest that immunization with vaccine/booster may improve symptoms of long COVID. A person who has recovered from COVID should take the vaccine and the booster, if there are no contraindications. High-risk persons should not hesitate about taking the booster dose.
- Persons who have had AstraZeneca as the primary vaccine have done very well with Pfizer booster. A preliminary study has shown that mixing Pfizer and AstraZeneca vaccines provide strong protection. In patients with long COVID symptoms, the virus is trapped in the microthrombi, which prolong the inflammatory process in the body. Vaccination may improve symptoms by generating the B-cell and T-cell response, which attack the virus trapped in the microthrombi.
- The Moderna booster dose is half of the original dose, while the Pfizer booster dose is the regular dose. The recommended doses are three so far. There is no data yet on fourth dose or more than that.
- A person who has taken only the first dose of the vaccine should complete the initial immunization (as recommended) and then take the booster dose (mix and match). Having a variety of vaccines is much better than every citizen getting the same vaccine at the same time. Heterogeneity in the persons receiving the vaccine, the vaccine schedule and the vaccine themselves.
- Booster protection is better than natural infection. It should not be precluded because of the infection and should be timed according to the risk.

## COUNTRY UPDATES

**Singapore Update:** Singapore is undergoing a decline in its most recent surge. The number of cases from a peak of 3,000 to 5,000 cases per day is coming down. There are 1,700 cases today; 1,003 are in hospital, 200 require oxygen supplementation, 46 in ICU, 64 patients are critically ill in the ICU. The overall ICU utilization rate is 57%.

**India Update:** The vaccination is proceeding at a rapid pace; 110 crore people have been vaccinated; 40-50% population has been vaccinated with both doses and around 70% population has received one dose. Door-to-door vaccination is taking place. The numbers of new infections have come down from 4 lakhs per day to around 10k per day. Now pockets of infection are present. A third wave is not expected. The Delta variant has become little less hostile as severe infections and hospitalizations have reduced considerably. The hospitalization rate is 0.8%. The monoclonal antibody cocktail is being given as an outpatient treatment. Treatment protocols have changed in that even injectables are being given as day care.

**Malaysia Update:** The number of daily cases is hovering between 5000 to 6000 per day for the last 1 week. Daily deaths have also declined from 200-300 to around 50-60. Ninety-four percent population has been given two doses of vaccine; 70% of adolescents have been given two doses. Booster dose with Pfizer vaccine is being administered starting with the front liners and persons older/younger than 60 years with comorbidities. People who have taken Sinovac are apprehensive about taking the Pfizer booster, so many do not turn up for their booster dose. It is compulsory to wear face mask. MySejahtera App is used to monitor COVID-19 cases and vaccination status.

**South Africa Update:** The infectivity rate for the last few weeks had been less than 1%. But in the last week, the infectivity rate increased to 2.6% and there has been a surge in the number of cases. This is of concern as the festive season is starting soon.

**Pakistan Update:** The number of new cases is decreasing. Yesterday, there were 400 cases; 45% people have received single vaccine dose; 28% have received two doses.

**Australia Update:** The situation is stabilizing. In Victoria, 90% of population above 12 years has been vaccinated. NSW has vaccinated 94% of its population. These two states have opened up for those who are vaccinated. The 7-day hospital quarantine has been now dropped. Vaccination for 5- to 11-year age group may start from January. Booster dose has started.

**Participants - Member National Medical Associations:** Dr Yeh Woei Chong, Singapore, Chair-CMAAO; Dr Ravi Naidu, Malaysia, Immediate Past President-CMAAO; Dr Marthanda Pillai, India Member-World Medical Council, Advisor-CMAAO; Dr Wasiq Qazi, Pakistan, President Elect-CMAAO; Dr Angelique Coetzee, South Africa; Dr Akhtar Hussain, South Africa; Dr Salma Kundi, Pakistan

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

**Moderator:** Mr Saurabh Aggarwal

***Source:*** *Minutes of an International Weekly Meeting on COVID-19 Held by the HCFI Dr KK Aggarwal Research Fund (20th November, 2021, Saturday, 9.30 am-11 am)*

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# Pharmacists' Role in Reducing Pharmaceutical Waste

RASHMI ZALPURI*, VISHAL KAMRA†, JK SHARMA‡, ASTHA ZALPURI#


## ABSTRACT

The disposal of leftover/unused medicines is an area of concern in several countries as their improper disposal can impact the environment, which in turn, will affect the health of humans and animals. The main objective of this study is to know the opinion of pharmacists related to the disposal methodologies of unused medications. Several pharmacists were studied in Northern India to evaluate the opinion and the practice towards safe disposal of unused/unwanted medicines. Random interview studies were carried out in North India using a questionnaire. The questionnaire was based on reason, i.e., unused medicine disposal practices opinion of pharmacist as appropriateness of the disposal methodology and awareness of hazard effects of improper disposal. The data was collected from various categories of individuals and interpreted. A total of 135 registered pharmacists participated in this study. The main method that was adopted by the respondents was to dispose the unwanted medications in trash and flush down the sink, which accounted for nearly 42% and 11% of the respondents, and 6% were in the practice of burning/throwing in household waste. Fifty-three percent agreed that they were not aware of the environmental hazards due to this practice and 11% said community take-back programs could help to solve the problem. About 30% of the pharmacists accepted that their pharmacy has collecting point of unwanted medicines. Regulatory authorities should implement and execute policies for proper and safe disposal of unused medicines.


**Keywords:** Unwanted medications, unused medications, disposal of unused medicines, expired medicines, pharmaceutical waste

The disposal of unused/unwanted medicines from household and healthcare sector is becoming an emerging problem for local and national health and environmental departments. The concerns regarding inappropriate medicine disposal by throwing them in dustbin, flushing down the sink and disposing without proper precautions have been growing and now they are receiving attention.[1] Expired, unused, damaged and contaminated substances from households and healthcare activities all come under the category of unwanted medicines. So, it is not uncommon to find them, but whenever such situations arise, there should be clear guidance and methods on how to dispose them.

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There have been several ways, such as educational materials and regulations, which are available for the same, but the extent to which they are implemented is not clear.[2] Not just one, but many problems have been encountered regarding improper disposal of medicines. Some of them are not just limited to humans but animals also.

Keeping unused medicines at home may end up in accidental poisoning in children.[3] Pharmaceuticals have a chance of entering drinking water as well and they may affect populations like pregnant women, which emphasizes the need for awareness and practices for safe disposal.[4]

The fate of the improperly disposed medicines in water is unknown because unfortunately, current water treatment systems do not remove many pharmaceuticals from drinking water.[5] Usually the concentration of these medications is negligible; however, long-term exposure to even low levels of multiple medications could be hazardous.[6-8]

If medicine disposal is improper, the health of the exposed population is at risk. The drains often percolate to the soil, which in turn, contaminates the mass of

land and it passes to the food chain. Ineffective treatment of wastewater pollutes freshwater, thus polluting the environment.[9] Many types of chemicals were found in 80% sampling of 139 streams of US and the most common were detergents, hormones, prescription/nonprescription drugs, pesticides and antibiotics.[10] Some pharmaceuticals have been found in cow, goat and human milk.[11]

It is a common myth that the expired or unused medicines may be resupplied/repacked by changing their expiry period. While there is no evidence, many people continue to have this opinion.

To cope up with the current market, the increase in manufacturing of pharmaceuticals has led to increase in pharmaceutical waste. The recommendation comes from the World Health Organization (WHO) that unusable medicines should be considered as a pharmaceutical waste, which need to be disposed appropriately, as unsafe disposal of these unwanted or expired drugs often creates a major problem.[12] Some medicines should be crushed and mixed with cat litter or coffee grounds and disposed in trash in a leak proof sealed container, which will eventually decrease the chances of poisoning.[13-15]

However, several other safer methods are also used, such as reverse distribution and drug take-back programs, in which unused/left out medicines are collected by nearby local pharmacies or government/private agencies. In many countries, it has been found to be the best method. The main aim of this medicine collection program is to avoid the unwanted medicine pollution, thus reducing the amount of drugs available for accidental poisoning or theft. Further, such programs provide full support to the public to return unwanted medicines so that they can be disposed of safely.[16] Medicines take-back programs that collect medicines from a central location for safe disposal are the most environmentally safe disposal method.[17]

Considering the fact that pharmacists can have a role in safe disposal of medicines, we conducted a study among pharmacists to determine their awareness, behavior, opinion and practice towards safe disposal of unwanted medicines.

## METHODOLOGY

North India (mainly Delhi and NCR) was selected for the study. Pharmacists were selected at random and the study was conducted from July to November 2019. All the selected pharmacists were visited with a questionnaire.

The questionnaire was prepared in English language. Before the survey was conducted, its purpose was well informed to the participants and they were assured that their information would remain confidential, and that only the researchers would have access to the information. For the conclusion and completion of the study, few points were taken care of:

- Socio-demographic characteristic of the respondent (male/female), including their age, marital status, educational qualification (Table 1).
- Reason mentioned for having unused medicine with consumers including subsiding condition, carelessness, forgetfulness, excess purchase, intolerable side effects, treatment changed, unpleasant taste, expiry date.
- Unused medicine disposal practices, including throwing them in waste bins, flushing into toilet, burning, return to pharmacy, buried in ground, given to needy persons.

By using appropriate statistics, the collected data was analyzed.

## RESULTS

A total of 135 government and private pharmacists participated in the study and had work experience of 10 to 30 years. Male participants were more than female participants.

**Table 1.** Socio-demographic Data

| Demographic Data | Variables | No. of participants | Percentage (%) |
|---|---|---|---|
| Gender | Male | 110 | 81.4 |
| | Female | 25 | 18.5 |
| Qualification | Graduate in Pharmacy | 45 | 33.3 |
| | Diploma in Pharmacy | 35 | 25.9 |
| | Others | 55 | 40.7 |
| Age | 25-30 | 42 | 31.1 |
| | 31-40 | 48 | 35.5 |
| | 41-50 | 45 | 33.3 |
| Experience | Less than 10 | 37 | 27.4 |
| | 10-20 | 53 | 39.2 |
| | 21-30 | 45 | 33.3 |

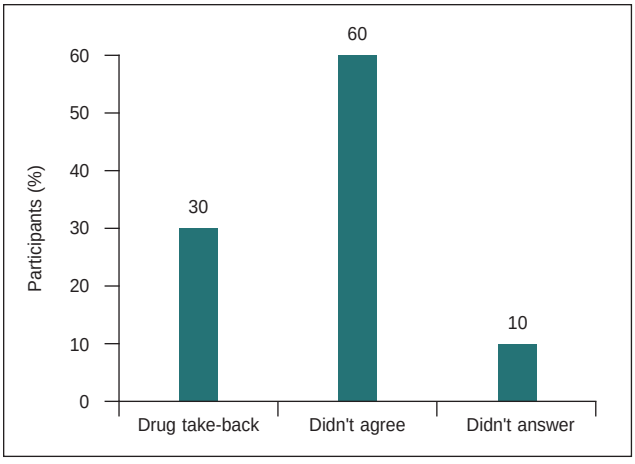


**Figure 1.** Participants' opinion on drug take-back.

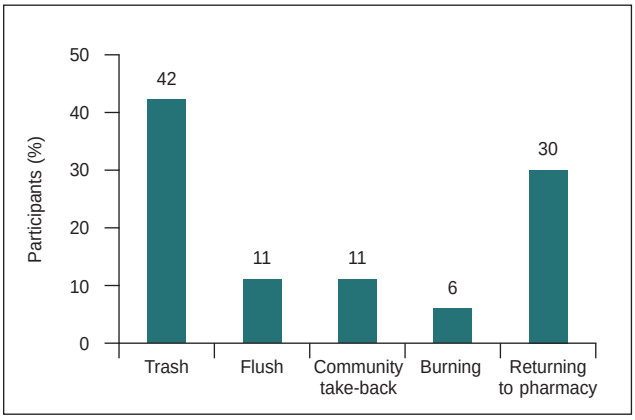


**Figure 2.** Participants' opinion and practice towards disposal of medicines.

Figure 1 represents the participants' opinion on drug take-back. About 30% of the respondents accepted take-back of unwanted medicines and agreed to keep their pharmacy as a drug take-back center while 60% of the respondents did not agree. About 10% didn't answer.

Figure 2 shows participant's opinion and practice towards disposal of medicines. Among these, 42% of the respondents stated that they were throwing the unwanted/left out medicines into trash, 11% were flushing it down the sink/toilet, 30% stated giving back to pharmacy was the best option, 11% said community take-back programs could help to solve the problem and 6% were following other methods like household waste or burning the unwanted pharmaceuticals.

Figure 3 represents the knowledge and awareness of safe disposal methods and hazards of improper disposal. Among the respondents, 53% stated that they were not aware of the consequences due to improper disposal of medicines on humans and environment, 45% were aware of the hazardous effects while 2% didn't answer.

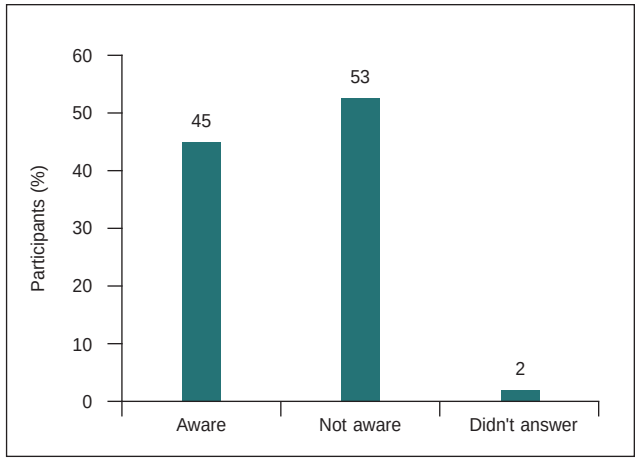


**Figure 3.** Participants' knowledge and awareness of safe disposal methods and hazards of improper disposal.

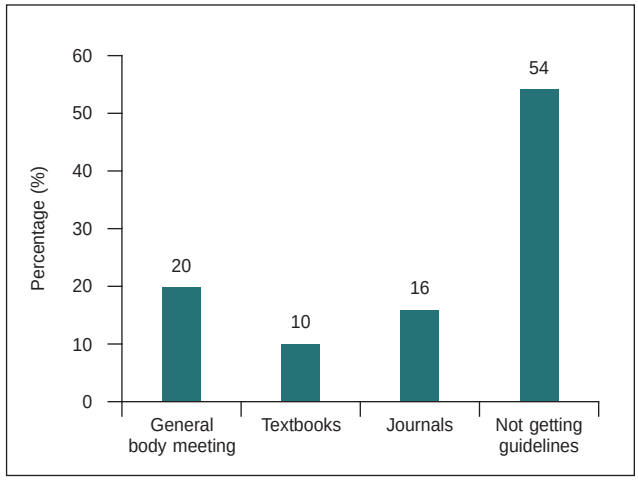


**Figure 4.** Receipt of instruction or guidelines for safe disposal.

Figure 4 represents receipt of instruction or guidelines for the safe disposal methods. Fifty-four percent of the participants said that they couldn't get any guidelines regarding the safe disposal procedures while 46% were getting guidelines for safe disposal from different sources, including 20% from general body meeting, 10% from textbooks and 16% from journals. It was also stated by the participants that national and local government agencies, social media, and drug manufacturing companies have to take a step forward in creating awareness and giving guidelines for environment friendly disposal methods. Most of the participants expressed that there is much less awareness of the issue.

## DISCUSSION AND CONCLUSION

There is high occurrence of pharmaceutical and personal care products in drains, sewerages and rivers and they are signaled to be a future disaster. One of the

important effects due to presence of pharmaceuticals in environment is occurrence of antibiotic resistance.

Improper disposal of unused medication is a global problem, both in developed and developing countries. In developing countries, this is more problematic as it often leads to health risks and environmental hazards.

Although there are options for disposing medications, consumers keep the unused leftover as they don't want to let their money go waste, while they don't know the risk of keeping unused medication. The leftover medication at home possesses several risks, such as deterioration of potency, accidental overdose and consumption of expired medicine. Therefore, one has to dispose of these medicines timely, but the disposal shall be done keeping in view the community and environment.

A major hand behind safe disposal of medicines is that of medical professionals since they are directly in contact with the consumers. Pharmacists can influence safe disposal of medicines.

One of the best methods encountered for the safe disposal of unwanted medicines is the drug take-back programs; however, it is less popular, less practiced and leaves people with fewer options. Among the participants in the study, a pharmacist with years of experience said, "We are ready to accept the unused medicines from the patients if they come along with their payment slip and the prescription within couple of months of the purchase of the medicines. Another pharmacist with work experience of years said, "We give back the expired medicines within 3 months back to the distributor/manufacturer, in return we get credits from them, it's a kind of redistribution and an environmentally friendly habit by avoiding unsafe disposal of drugs, especially of antibiotics and cytotoxic drugs.

Usage of medicines from soon to expire stock and avoiding unnecessary prescribing are practices that may contribute to decreased medicinal waste.

This study provided the current scenario of knowledge and practice towards the disposal of medicines by pharmacists. The awareness regarding impact of improper disposal of pharmaceutical waste is still an issue, which needs immediate attention. The current practices are not optimal for collection and disposal for the pharmacist. Pharmacists have the potential to be on the forefront of this movement, but it is essential that their knowledge of proper medication disposal should be complete and accurate.

Teaching of proper disposal of pharmaceuticals in medical, dental, nursing, veterinary or pharmacy curriculum is needed. From this study, it can be said that there is an urgent need for raising awareness and education on medicines take-back program to avoid environmental pollution. There should be national guidelines on the appropriate disposal of unused and expired medicines to minimize the impact on environment and best ways to educate about proper disposal, which may be started through school, religious places, community meetings and at pharmacies.

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■■■■

### New Type 2 Diabetes Treatment Appears Promising in First Human Study

Patients with type 2 diabetes who were given daily treatment with sodium phenylbutyrate for 2 weeks were found to have significant improvements in peripheral insulin sensitivity and glucose oxidation, reported a single-center, randomized, double-blind, placebo-controlled, crossover study.

Patients received their glucose-lowering medications and 4.8 g/m$^2$/day sodium phenylbutyrate or placebo divided in three doses, for a duration of 2 weeks. This was followed by a 6- to 8-week washout period, and 2 weeks on the alternative treatment. Peripheral insulin sensitivity improved after 2 weeks on sodium phenylbutyrate by 27% in comparison with placebo ($p = 0.0155$). Sodium phenylbutyrate also improved carbohydrate-driven muscle mitochondrial oxidative capacity, whole-body insulin-stimulated carbohydrate oxidation and decreased plasma branched-chain fatty acid levels. The treatment was found to be safe. The findings suggest that targeting branched-chain amino acids may serve as a novel treatment strategy for patients with type 2 diabetes… (*Source: Medscape*)

### FDA Clears Pembrolizumab for Adjuvant Treatment of Kidney Cancer

The US Food and Drug Administration (FDA) has granted approval to pembrolizumab for the adjuvant treatment of renal cell carcinoma (RCC) for those patients who have an intermediate-high or high risk of recurrence after nephrectomy, or after nephrectomy and metastatic lesion resection.

The approval has come after the KEYNOTE-564 trial showed that adjuvant treatment with pembrolizumab after nephrectomy led to a significant improvement in disease-free survival (DFS). About 22% of patients receiving immunotherapy had events of recurrence or death compared to 30% of patients in the placebo group (HR 0.68). This was a multicenter, randomized, double-blind, placebo-controlled trial that included 994 patients with intermediate-high or high risk of RCC recurrence, or stage M1 with no disease evidence… (*Source: Medpage Today*)

### COVID-19 Booster Shots Increase Protection among Cancer Patients

According to a new study published in *Cancer Cell*, booster shots of COVID-19 vaccines evoked immune responses in cancer patients who did not have any detectable antibodies after the primary vaccination.

It was noted that in seronegative patients, a third vaccine dose led to a seroconversion rate of 56%. Investigators evaluated the anti-COVID immunity before and after a booster dose in 88 patients with cancer (31 with solid tumors and 57 with hematologic malignancies). About 73% of these were on active treatment at the time of receiving a booster shot. Nearly 64% of the patients were seropositive before the booster shot, while 36% were seronegative and all seronegative patients, except one, had hematologic malignancies. Four weeks following the booster jab, 70 of the 88 patients (80%) were found to have antibody levels higher than the levels prior to receiving the booster… (*Source: Medpage Today*)

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CLINICAL STUDY

# Comparative Study of Obstetrics Outcome Between Scarred and Unscarred Uterus in Placenta Previa Cases

GAYATRI MATHURIYA*, PALLAVI LOKHANDE†

## ABSTRACT

**Objective(s):** To compare the incidence of placenta previa, associated factors, complications, placental position, mode of delivery and fetal and maternal outcome in scarred (Group A) and unscarred uterus (Group B) in 20 months of hospital-based study. **Material and methods:** In a prospective study, 140 cases of pregnancies beyond 28 weeks of gestation complicated by placenta previa were identified. These cases were divided into two groups, scarred uterus (Group A, n = 34) and unscarred uterus (Group B, n = 106). Total number of deliveries were 16,784 out of which 2,354 patients had cesarean section and 140 patients had placenta previa. **Results:** The incidence of placenta previa in scarred cases is significantly higher (1.2%) than overall incidence (0.6%). Majority of scarred cases had anterior placenta (85.2%) and majority of unscarred cases had posterior placenta (63.2%) (p = 0.00, HS). The number of unbooked cases in both Groups A and B was high (p = 0.404, NS). A significant association of placenta previa following curretage in Group B was observed (p = 0.002, S). There was only one maternal mortality in Group B and none in Group A. Results showed a favorable fetal outcome in both groups. (Group A-70.6%, Group B-64.2%, p = 0.08, NS). **Conclusion(s):** An increase in the incidence of prior cesarean section and advanced maternal age probably contribute to a rise in the number of pregnancies complicated with placenta previa and its association with adverse maternal and perinatal outcome.

**Keywords:** Placenta previa, incidence, maternal outcome, fetal outcome

Placenta previa is an obstetric complication in which the placenta is inserted partially or wholly in lower uterine segment.[1] It can sometimes occur in later part of the first trimester, but usually occurs during the second or third. It is a leading cause of antepartum hemorrhage (vaginal bleeding). It affects approximately 0.4-0.5% of all labors.[2] Exact etiology of placenta previa is unknown. It is hypothesized to be related to abnormal vascularization of the endometrium caused by scarring or atrophy from previous trauma, surgery or infection. These factors may reduce differential growth of lower segment, resulting in less upward shift in placental position as pregnancy advances.[3]

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The traditional classification of placenta previa describes the degree to which the placenta encroaches upon the cervix in labor and is divided into low-lying, marginal, partial or complete placenta previa.[4] In recent years, due to the increased value of transvaginal ultrasound in diagnosis of placenta previa, the traditional classification is rendered obsolete.[4] Diagnosis is made on history, clinical examination and few investigations that include ultrasound (transabdominal, transvaginal) and megnetic resonance imaging (MRI).[5]

Although the etiology the placenta previa remains speculative, several risk factors associated with this condition have been established. These include advanced maternal age, multiparity, multiple gestation, previous abortion, previous cesarean section and placenta previa in previous pregnancy.[6] Myometrial damage due to cesarean section and dilation curettage are main predisposing factors.[7] Also, risk factors are previous cesarean section, history of abortion and complete previa.[8]

Most obstetricians have concerns about massive hemorrhage not only when complete previa exists but also when placenta is located on the anterior position of the uterus, beneath the cesarean incision site.[9,10]

Patients with placenta previa are at increased risk of spontaneous abortion, fetal malpresentation, cesarean section, increased loss of blood, peripartum hysterectomy and prolonged hospitalization.

The infants of these patients are also at increased risk of premature deliveries, increased perinatal mortality than in general population. The frequency of this condition may be on the rise, so we need to identify and target preventive interventions among women at increased risk of placenta previa.

## MATERIAL AND METHODS

This study was conducted in the Dept. of Obstetrics and Gynecology, MGM Medical and MY Hospital, Indore, from May 2011 to December 2012.

A total number of 140 patients beyond 28 weeks gestation, complicated by placenta previa alone or with previous myomectomy, cesarean section and uterine repair were identified. All types of placenta previa were included. The subjects were divided into two groups: Group A in which placenta previa occurred in scarred uterus and Group B in which placenta previa occurred in unscarred uterus. Transabdominal sonography was done for obstetrical reasons as well as for exact location of placenta.

The following potential risk factors such as maternal age, parity, previous abortion, prior cesarean section and multiple pregnancies were examined in both the groups and were compared.

The association of placenta previa with fetal malpresentation, abruptio placenta, postpartum hemorrhage and maternal-fetal outcome were also evaluated in both the groups and compared.

Chi-square test and chi-square test with Yate's correction was used to compare different quantitative data variable.

## RESULTS

Maternal characteristics of the two groups are given in Table 1. Majority of the patients in the study were between the age range of 26-30 years in Group A (67.6%) and 20-25 years in Group B (65%) (p = 0.00, HS). Primipara with placenta previa were 0 in Group A and 31 (29.2%) in Group B (p = 0.002, S). A definite association of placenta previa following curretage was observed (Group A-20.58%, Group B-3.8%, p = 0.002, S).

Table 2 shows that majority of cases had Grade I or low-lying placenta, which is 47.2% in unscarred and 67.8% in scarred cases (p = 0.17, NS). Majority of patients with scarred uterus had anterior placenta, that is 85.3% and majority of patients with unscarred cases had posterior placenta, that is 63.2% (p = 0.00, HS).

Table 3 compares the related complications between the two groups. There was only one maternal mortality in Group B and none in Group A (p = 0.001, S). Results showed a favorable fetal outcome in both groups (Group A-70.6%, Group B-64.2%, p = 0.08, NS) (Table 4). Both Groups A and B had a high number of unbooked patients (A-94.11%, B-97.2%, p = 0.404, NS) (Table 5).

**Table 1.** Maternal Characteristics

| | Scarred uterus (Group A) | | Unscarred uterus (Group B) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| **Age in years** | | | | | |
| 20-25 | 8 | 23.6 | 69 | 65.0 | 0.00 (HS) |
| 26-30 | 23 | 67.6 | 24 | 22.6 | |
| >30 | 3 | 8.8 | 13 | 12.4 | |
| **Parity** | | | | | |
| 0 | 0 | 0 | 33 | 31 | 0.002 (S) |
| 1 | 15 | 44 | 33 | 31 | |
| 2 | 16 | 47 | 23 | 21.6 | |
| 3 | 2 | 5.8 | 7 | 6.6 | |
| ≥4 | 1 | 3 | 8 | 7.6 | |
| **History of curettage** | 7 | 20.58 | 4 | 3.8 | 0.002 (S) |
| **Gestational age (weeks)** | | | | | |
| <37 | 20 | 58 | 50 | 47 | 0.23 (NS) |
| >37 | 14 | 42 | 56 | 53 | |

**Table 2.** Relative Frequency

| | Scarred uterus (Group A) | | Unscarred uterus (Group B) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| **Grading** | | | | | |
| I | 23 | 67.8 | 50 | 47.2 | 0.17 (NS) |
| II | 6 | 17.6 | 35 | 33.0 | |
| III | 2 | 5.8 | 12 | 11.4 | |
| IV | 3 | 8.8 | 9 | 8.4 | |
| **Type** | | | | | |
| Anterior | 29 | 85.3 | 39 | 36.8 | 0.00 (HS) |
| Posterior | 6 | 17.7 | 67 | 63.2 | |

**Table 3.** Related Complication

| Complications | Scarred uterus (Group A) | | Unscarred uterus (Group B) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Fetal malpresentation | 4 | 11 | 9 | 8.4 | 0.001 |
| Postpartum hemorrhage | 16 | 47.05 | 76 | 71.6 | (S) |
| Cesarean section with uterine artery ligation | 7 | 20.5 | 6 | 5.6 | |
| Cesarean section with internal iliac artery ligation | 0 | 0 | 1 | 0.94 | |
| Cesarean hysterectomy | 3 | 8.8 | 0 | 0 | |
| Placenta accreta | 1 | 2.9 | 0 | 0 | |
| Placenta percreta | 1 | 2.9 | 0 | 0 | |
| Maternal mortality | 0 | 0 | 1 | 0.94 | |
| Blood transfusion | 29 | 85 | 76 | 71.6 | |

**Table 4.** Fetal Outcome

| | Scarred uterus (Group A) | | Unscarred uterus (Group B) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Alive | 24 | 70.6 | 68 | 64.2 | 0.08 |
| Stillbirth | 3 | 9 | 26 | 24.4 | (NS) |
| Neonatal death | 7 | 20.4 | 12 | 11.4 | |

**Table 5.** Booking Status

| Status | Scarred uterus (Group A) | | Unscarred uterus (Group B) | | P value |
|---|---|---|---|---|---|
| | No. | % | No. | % | |
| Booked | 2 | 5.88 | 3 | 2.8 | 0.404 |
| Emergency | 32 | 94.11 | 103 | 97.2 | (NS) |

## DISCUSSION

The incidence of placenta previa in present study is 0.62%, which is comparable to study of Hemmadi et al[11] and Reddy et al,[12] which is 0.4% and 0.5%, respectively. Incidence of placenta previa is significantly higher in patients with previous cesarean section (1.2%) than overall incidence of 0.6% (Table 6).

**Table 6.** Relative Incidence

| Overall incidence of placenta previa | Incidence in scarred cases | Incidence in unscarred cases |
|---|---|---|
| 0.6% | 1.2% | 0.47% |

Placenta previa is more common among increasing age group, which is 68% in 26-30 years in scarred cases and in unscarred cases 65% in the age group 20-25 years, as comparable to Reddy et al[12] who reported 73% incidence in 20-29 years age group and also comparable to Rasmussen[13] who showed increase incidence with increasing maternal age (20-29 years).

Our study shows increasing parity increases with risk of placenta previa, Para 3 in scarred uterus, which is 45% and in unscarred cases increased incidence is found in Para 2 cases, which is 30%. The results are consistent with Reddy et al[12] in which 69% were multiparous. In our study, we found 7.8% association of placenta previa with previous history of curettage, comparable to study of Taylor et al[14] who found that women with one or more spontaneous abortion or induced abortion are 30% more likely to have placenta previa in subsequent pregnancy.

Incidence of placenta accreta is greater in patients with prior cesarean section than in unscarred uterus. In our study, 5.8% out of the scarred uterus constitute placenta accreta and percreta, which is consistent with the study of Clark et al[15] who concluded that probability of placenta accreta is greater in patients with prior cesarean section.

In evaluation of the related complications, we found that women with placenta previa were more likely to have postpartum hemorrhage, cesarean hysterectomy as diminished muscle content in lower uterine segment causes less effective contraction to control bleeding. The associated malpresentation with placenta previa increases the number of cesarean section, deliveries even in cases where placenta previa is marginal.

Anterior previa is more common in patients with prior cesarean section compared to no prior cesarean section and it is more dangerous than posterior previa in view of increasing maternal morbidity such as excessive blood loss, massive transfusion, placenta accreta and hysterectomy.[16] In our study, also 85.3% cases have anterior previa in scarred uterus and only 36.8% cases in unscarred uterus (p = 0.00 HS).

Prematurity due to placenta previa accounts for 60% of perinatal morbidity.[17] In our study, 50% of cases delivered premature babies.

## CONCLUSION

This study concludes that efforts should be made to reduce the rates of operative deliveries because there is greater likelihood of placenta previa in scarred uterus in subsequent pregnancies.

Sonographic detection of anterior placenta is very important to predict maternal outcome in placenta previa and in such cases obstetricians should be aware of maternal massive hemorrhage. The family planning services should be further improved to attain a decline in the number of women of high parity. The morbidity associated with placenta previa can be reduced by detecting the condition in the antenatal period by ultrasound, before it becomes symptomatic. This calls for educating our patients and making them aware of the importance of antenatal care and its availability.

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CLINICAL STUDY

# Study of Orthopedic Morbidities among Postmenopausal Women in a Medical College Hospital in Rural Area of Western Maharashtra, India

SHUBHADA SUNIL AVACHAT*, SHRIKANT BALKRISHNA DESHPANDE†, MRINAL BALBHIM ZAMBARE‡, DEEPAK BABURAO PHALKE#

## ABSTRACT

**Introduction:** It is estimated that a total of 130 million Indian women are expected to live beyond menopause by 2015. Health of postmenopausal women is of growing concern because of increased longevity and various morbidities associated with old age. **Objectives:** 1) To assess various orthopedic problems among postmenopausal women in rural area. 2) To estimate magnitude of common orthopedic problems and associated sociodemographic factors. **Methodology:** A cross-sectional study was conducted at the medical college hospital in rural area of Western Maharashtra on 500 postmenopausal women availing healthcare in a medical college hospital. Data was collected with the help of predesigned questionnaire by interview technique and with the help of case records available from orthopedic department. **Results:** Backache (62%) and osteoarthritis (51.6%) were common orthopedic problems. Osteoarthritis was significantly associated with obesity.

**Keywords:** Postmenopausal women, orthopedic problems

Menopausal and postmenopausal health has emerged as an important concern owing to increased longevity and changing lifestyle of Indian women. It is estimated that a total of 130 million Indian women are expected to live beyond menopause by 2015.[1] The focus of women's health researchers and health policy planners has also shifted toward postmenopausal women since the trends suggest an increase in their numbers and life expectancy.[2]

Long-term consequences of changes in ovarian hormonal levels include morbidities associated with aging such as cardiovascular diseases, osteoporosis, problems related to memorization, urinary incontinence, skin aging and others.[3,4]

Postmenopausal women are generally affected by osteoporosis and fracture rates among them are approximately twice as high as men. The cause of osteoporosis is very complex but it is clear that hormonal changes after menopause increase the rate of bone resorption, leading to greater risk of osteoporosis. This silently progressing metabolic bone disease is widely prevalent in India and is a common cause of morbidity and mortality in women.[5] The occurrence of osteoporosis in postmenopausal women is a very common problem especially in India, as Indian women are exposed to many risk factors like low calcium diet, lack of exercise, family history and in general, lack of health awareness. The prevalence of osteoporosis increases with age and it is estimated that 70% of women over the age 80 years have osteoporosis.[6]

The problem of backache becomes more pronounced in postmenopausal women.[7] During this period of women's life, the likelihood of weight gain and manifestation of low back pain increases due to the changes of the muscles and skeleton structures as a result of aging, occupational or other factors. Osteoarthritis is also one of the common health problem among elderly women.

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Osteoarthritis strikes women more often than men and it increases in prevalence, incidence and severity after menopause.[8,9]

There is a growing recognition that various morbidities occur in postmenopausal age group, yet information on the levels and patterns of these health problems experienced by women in India is sparse. Only a few studies have been undertaken to understand the effects of menopausal transition in relation to aging process on general health profile of women in postmenopausal life. Since, a large proportion of women suffer morbidity silently and are reluctant to seek care or to visit clinics and hospitals, it is difficult to assess the true magnitude of the problem or the patterns of morbidity from which women suffer. Yet the small amount of data available suggest startlingly high levels of morbidity, for which treatment is rarely sought.

Because of inadequate medical facilities in rural areas and poor resources to obtain treatment from private medical practitioners, women in villages often become a victim of a number of health problems. Hence, studies are needed in rural areas to investigate physical, physiological and social changes experienced during the menopausal transitions along with the nature and magnitude of health problems during postmenopausal life. Orthopedic problems are very common after menopause and significantly affect the health of Indian women. Therefore, present study was conducted among postmenopausal women attending medical college hospital in a rural area to assess morbidity pattern with special reference to orthopedic morbidity.

## METHODOLOGY

### Study Design

A cross-sectional study.

### Study Setting

Study was conducted in the Dept. of Orthopedics, Rural Medical College and Hospital during January 2010 to December 2010.

### Sampling and Sample Size

All the women in postmenopausal age group attending orthopedic outpatient department (OPD) during study period and who were ready to participate were included in the study. Women who had not achieved menopause and who were not ready to participate were excluded from the study. Five hundred women of postmenopausal age who visited orthopedic department during study period were ready to participate, making the sample size 500.

### Data Collection

After explaining purpose of the study and obtaining verbal consent, data was collected from them by interview technique. A predesigned, structured questionnaire was used to collect necessary information. Questions were mainly pertaining to their complaints related to orthopedic problems. The clinical findings and X-ray findings were obtained from individual case records prepared by resident doctors and other faculty members of orthopedic department. Modified BG Prasad's classification was used for determining economic status.[10]

### Statistical Analysis

Data was tabulated and appropriate statistical analysis was done with the help of percentages and proportions. Test of significance was applied wherever required.

## RESULTS

Our study was conducted among 500 women of postmenopausal age who visited orthopedic OPD during the study period. Majority of the women were from the age group of 55-65 years. Sixty-four percent women were married, 68.6% were illiterate and most of them were from low socioeconomic status (Table 1).

Majority of women seeking healthcare from orthopedic department had either joint pain (predominantly knee) or backache. Some of the women had backache as well as knee pain. Only few women in postmenopausal age group had other orthopedic complaints like fracture, sprain and ligament problems (Table 2).

Out of 500 women, 310 (62%) were suffering from backache. Degenerative disease (osteoporosis) was the most common cause of backache observed in our study. Common X-ray findings observed among our study subjects were osteoporotic changes in spine, osteophytes in vertebrae or wedge compression (Table 3).

Joint pain with predominant involvement of knee joint was another common symptom observed in our study participants. Out of 500 women having orthopedic problems, 258 (51.6%) were suffering from osteoarthritis. Reduction of medial joint space and reduction of bone trabeculae with increase in lucency were the X-ray

**Table 1.** Sociodemographic Profile of Study Participants

| Age in years | No. of women |
|---|---|
| **Age** | |
| <50 | 9 (1.8%) |
| 50-55 | 74 (14.8%) |
| 55-60 | 111 (22.2%) |
| 60-65 | 248 (49.6%) |
| 65-70 | 47 (9.4%) |
| >70 | 11 (2.2%) |
| **Total** | **500** |
| **Marital status** | |
| Married | 324 (64.8%) |
| Widow | 159 (31.8%) |
| Unmarried | 017 (3.4%) |
| **Total** | **500** |
| **Educational status** | |
| Illiterate | 343 (68.6%) |
| Primary | 118 (23.6%) |
| Secondary and higher secondary | 37 (7%) |
| Graduate and above | 2 (0.4%) |
| **Total** | **500** |
| **Economical status** | |
| Upper (I, II, III of BG Prasad) | 186 (37.2%) |
| Lower (IV and V of BG Prasad) | 314 (62.8%) |
| **Total** | **500** |

**Table 2.** Symptom-wise Distribution of Patients (Multiple Response)

| Symptoms | No. of patients |
|---|---|
| Backache | 310 |
| Joint pain | 274 |
| Others | 053 |

findings observed in our study among patients suffering from knee joint pain. Body mass index of patients suffering from osteoarthritis was also calculated and it was observed that osteoarthritis was significantly associated with obesity in our study (Table 4).

**Table 3.** Distribution of Backache Patients According to Etiology (n = 310)

| Age group (in years) | Degenerative disc disease (osteoporosis) | Facet joint arthopathy | Spondylo-listhesis |
|---|---|---|---|
| 50-55 | 22 | 16 | 1 |
| 55-60 | 46 | 18 | 4 |
| 61-65 | 98 | 43 | 8 |
| 65-70 | 40 | 6 | 2 |
| >70 | 5 | 0 | 1 |
| **Total** | **211** | **83** | **16** |

**Table 4.** Association of Osteoarthritis and Obesity

| Osteoarthritis | No. of obese women | No. of nonobese women | Total |
|---|---|---|---|
| Present | 147 (63.6%) | 84 (36.4%) | 231 (100%) |
| Absent | 111 | 158 | 269 |
| **Total** | **258** | **242** | **500** |

$\chi^2 = 24.2$; d.f. = 1; $p < 0.001$; Highly significant.

## DISCUSSION

The abrupt endocrine changes during menopausal transition have important impacts on the physiology of female body that exacerbate risks for many diseases and disabilities during postmenopausal life. Present study was conducted among 500 postmenopausal women to assess various orthopedic problems among them; majority of women in our study population were in the age group of 60-70 years (59%), illiterate (68.6%), and belonged to low economic status. Similar finding was observed by Mandal et al in their study, 58.6% women were in the age group between 60-70 years, 61% were illiterate and majority of them belonged to low economic status.[11]

Backache and joint pain as a manifestation of osteoporosis and osteoarthritis, respectively, were the most common problems among our study subjects. Similar finding was observed by Scharla et al in their study, 85.1% postmenopausal women had back pain and 41.8% had joint pain.[12]

Many studies showed that the prevalence of osteoarthritis increases in old age and more so in women than men. Females are found to have more severe osteoarthritis and involvement of knee joint is more common.[13-15]

In our study, osteoarthritis was present among 51.6% women. Obesity is a well-known risk factor for osteoarthritis and in our study also it was significantly common among obese women. Similar to our finding, the prevalence of osteoarthritis was 49% in the study conducted by Mandal et al[11] and 57% in the study conducted by Lena et al.[16]

## CONCLUSION

Orthopedic morbidities are very common in postmenopausal women. Osteoporosis and osteoarthritis are the common orthopedic problems and large number of these health problems can be prevented and managed by simple measures like exercise, diet and proper healthcare.

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### One in Three New Students hasn't Attended Physical Classes due to Pandemic, Says Report

One in every 3 children in classes 1 and 2 has never attended physical school before because of the COVID-19 pandemic, suggests the Annual Status of Education Report (ASER) 2021.

The report said that among government school students of classes 1 and 2, about 36.8% never attended pre-primary classes. The figure is 33.6% in private schools. It further stated that around one-third of all children in classes 1 and 2 did not have access to smartphones. Additionally, only about 33.5% of children in these classes of yet to be reopened schools have received learning material from their schools, either as print or virtual worksheets, online or recorded classes or other video clips.

The survey was conducted across 25 states and 3 Union Territories, reaching 76,706 households and 75,234 children aged 5 to 16 years, besides teachers or head teachers from 7,299 government schools… (*NDTV – PTI*)

CASE REPORT

# Multisystem Inflammatory Syndrome Following COVID-19: A Rare Presentation in Adults

VIRENDRA KR GOYAL*, JITESH AGGARWAL†, BHARAT GUPTA‡

## ABSTRACT

**Background:** A growing number of reports from around the world has described a severe inflammatory syndrome in children similar to Kawasaki's disease. This syndrome has been named multisystem inflammatory syndrome in children (MIS-C). There have been anecdotal reports of MIS-C-like illness in young adults in their early twenties as well. We present the case of a healthy 33-year-old woman who developed coronavirus disease 2019 (COVID-19) with clinical characteristics resembling MIS-C, a rare form of COVID-19 described primarily in children under 21 years of age. **Case presentation:** The patient presented with abdominal pain, loose motions, difficulty in breathing since 3 days and fever since 1 day. She was otherwise healthy, with no prior medical history. Her hospital course was notable for leukocytosis, bradycardia, acute heart failure (myocarditis) and pulmonary edema. MIS-C like illness secondary to COVID-19 was suspected due to presentation of myocarditis, bradyarrhythmia and pulmonary edema. She improved after giving IV steroids, diuretics, anticoagulation and supportive care and was discharged on hospital Day 5. **Conclusion:** MIS-C like illness should be considered in adults presenting with atypical clinical findings and concern for COVID-19. Further research is needed to support the role of IVIG and aspirin in this patient population.

**Keywords:** COVID-19, multisystem inflammatory syndrome in children, myocarditis

Coronavirus disease 2019 (COVID-19) is increasingly recognized to have a protean range of clinical manifestations in adults, from respiratory illness to hyperinflammatory and coagulative complications, as well as a broad-spectrum of disease severity. When the epidemic began in China in late December 2019, case reports of pediatric illnesses were absolutely rare, and almost all children had mild clinical courses. However, a growing number of reports from the United Kingdom, Italy, the United States and elsewhere has now described a severe inflammatory syndrome in children similar to Kawasaki's disease, a vasculitic illness of unclear etiology originally described in Japan in 1967. This syndrome has been named multisystem inflammatory syndrome in children (MIS-C). Case series of MIS-C have described multisystem organ involvement including the mucocutaneous, cardiac, gastrointestinal (GI) and respiratory systems. The mortality rate of MIS-C appears to be low, though severe illness is common and a number of fatalities in children have been reported. Anecdotal reports of MIS-C-like illness have been reported in young adults in their early twenties, raising concern that this rare presentation of COVID-19 may also have some penetrance into younger adult age groups. Herein, we describe a unique case report of MIS-C-like illness in a young adult with COVID-19.

## CASE PRESENTATION

A 33-year-old previously healthy woman presented to us in emergency department at GBH General Hospital, Udaipur on 28th May, 2021 with the chief complaints of abdominal pain, loose motions, difficulty in breathing since 3 days and fever since 1 day. She was diagnosed with COVID-19 infection on 17th May, 2021. After taking treatment at home, patient was asymptomatic on 25th May, 2021. She was a nonsmoker, nonalcoholic and didn't use recreational drugs. She was not on any chronic medications and had no known allergies.

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On presentation, she was running a fever of 100.4°F, pulse rate varied from 56 to 64 beats per minute, blood pressure of 100/60 mmHg, oxygen level of 91% without oxygen therapy. She appeared ill. On auscultation, patient had bilateral fine crepitations involving lower lobes of the lungs suggestive of heart failure. Cardiac auscultation appeared to be normal. Laboratory work up was notable for profound leukocytosis and acute kidney injury. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) from nasopharyngeal swab was found to be positive. Chest X-ray and computed tomography (CT) scan were done for the patient. CT scan report of the patient, as shown in Figure 1 a and b, was suggestive of area of ground-glass haziness in bilateral lungs in perihilar location, smooth interlobular septal thickening with associated smooth thickening of bilateral oblique fissure, subpleural smooth reticular opacities seen in basal segments of bilateral lungs, and mild bilateral pleural effusion suggestive of pulmonary edema. 2D Echocardiography of the patient was also done which was suggestive of no chamber dilatation with normal left ventricular ejection fraction. Patient was admitted in hospital for hypotension with diagnosis of COVID-19 and concern for possible MIS-C-like illness due to renal, cardiac and GI involvement.

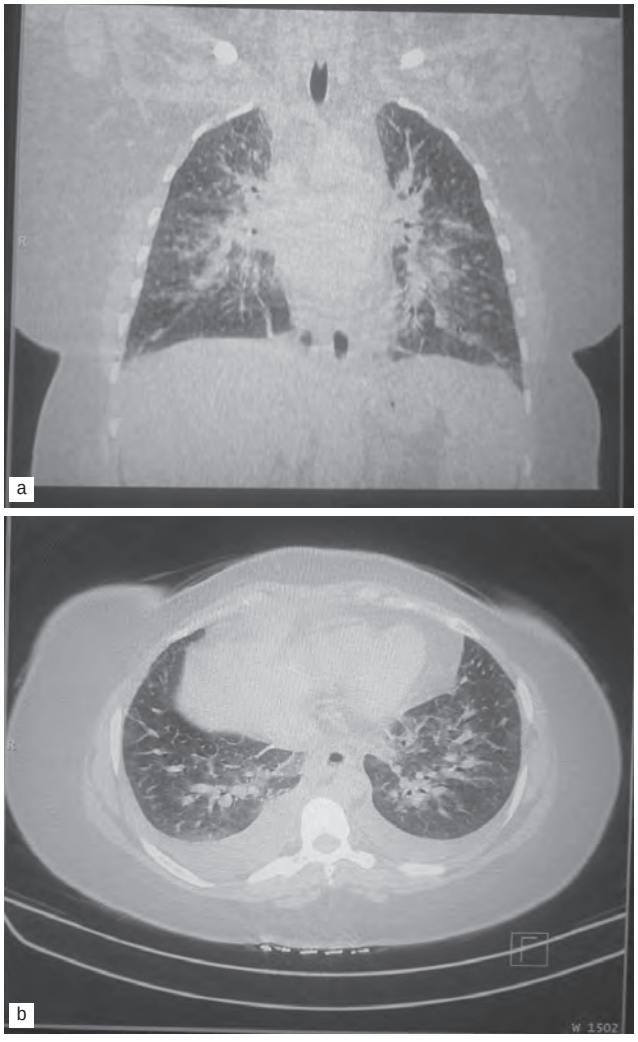


**Figure 1 a and b.** Area of ground-glass haziness in bilateral lungs in perihilar location, smooth interlobular septal thickening with associated smooth thickening of bilateral oblique fissure, subpleural smooth reticular opacities in basal segments of bilateral lungs, mild bilateral pleural effusion suggestive of pulmonary edema.

The patient's blood pressure initially normalized and her creatinine improved to 1.1 mg/dL with the help of vasopressors. During the hospital course, she developed recurrent episodes of bradycardia. Cardiac opinion was taken and creatine phosphokinase-MB (CPK-MB),

**Table 1.** Laboratory Findings on Admission and at Discharge

| Parameters | On Admission | At Discharge | Reference |
|---|---|---|---|
| WBC (*$10^3$/µL) | 13.6 | 10.2 | 4-10 |
| Hemoglobin (g/dL) | 11.2 | 10.6 | 13.5-17.5 |
| Platelets (k/uL) | 149 | 152 | 150-400 |
| Sodium (mmol/L) | 135 | 136 | 135-145 |
| Potassium (mmol/L) | 3.2 | 3.5 | 3.4-5.4 |
| Carbon dioxide (mmol/L) | 14 | 24 | 22-32 |
| Blood urea (mg/dL) | 63 | 45 | 15-45 |
| S. creatinine (mg/dL) | 1.5 | 0.7 | 0.5-1.2 |
| Alanine amino-transferase (ALT) (U/L) | 25 | 20 | 0-40 |
| Aspartate amino-transferase (AST) (U/L) | 29 | 39 | 0-40 |
| Troponin I (ng/mL) | 0.15 | 0.05 | 0-0.04 |
| B-natriuretic peptide (BNP) (pg/mL) | 293 | 80 | 0-99 |
| C-reactive protein (mg/L) | 296 | 28 | 0-10 |
| Urinalysis | 6-7 WBC/ hpf | 3-4 WBC/ hpf | 0-5 WBC/ hpf |
| D-dimer (ng/mL) | 680 | 320 | 0-574 |
| Ferritin (ng/mL) | 798 | 320 | 11-307 |

troponin I, and B-type natriuretic peptide (BNP) levels were sent for analysis. Work-up for these new symptoms revealed evidence of worsening cardiac dysfunction. Level of troponin I was detectable at 0.15 ng/mL and BNP increased to 293 pg/mL (Table 1). She was immediately shifted to contemporary cardiac intensive care unit (CICU) for further management. As the CT scan findings were suggestive of pulmonary edema, with bradyarrhythmia on electrocardiogram, with increase in cardiac markers, the possibility of myocarditis was suspected. Patient was given IV methylprednisolone, IV antibiotics, diuretics and injectable anticoagulants in the form of enoxaparin. Patient was given oxygen support to help in recovering from pulmonary edema early.

With this treatment, patient recovered successfully with mild weakness remaining. Repeat CT scan was done which suggested reduced pulmonary edema. Patient was successfully discharged on oral antibiotics, oral anticoagulation in the form of aspirin, dabigatran, short course of diuretics and mefenamic acid for fever. Patient was followed-up with stable vitals.

## DISCUSSION

The Centers for Disease Control and Prevention (CDC)'s case definition for MIS-C is - 1) An individual less than 21 years of age presenting with fever; 2) laboratory evidence of inflammation by one or more markers (such as C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], fibrinogen, etc.); 3) evidence of clinically severe illness requiring hospitalization, with greater than 2 organ systems involved (cardiac, renal, respiratory, hematologic, GI, mucocutaneous or neurological); 4) no other plausible alternative diagnosis; and 5) SARS-CoV-2 infection confirmed by reverse transcription polymerase chain reaction (RT-PCR), serology or antigen testing (or exposure to a suspected or confirmed COVID-19 case within 4 weeks before the symptom onset).

Our patient, a previously healthy young adult woman in her mid-30's, met these criteria with exception of age.

Several features of our patient's presentation raised concern for MIS-C-like illness. First, she was noted to have GI tract symptoms in the form of acute abdominal pain and loose motions upon evaluation in emergency department. Additionally, our patient had hypovolemia, bradycardia, acute kidney injury, which responded to vasopressors. While GI symptoms do occur in adults with COVID-19, they are typically less severe; by contrast, prominent GI symptoms are seen in many patients with MIS-C. Finally, our patient's stable respiratory status was itself a feature shared by patients with MIS-C, who often lack intrinsic respiratory disease.

Other features were potentially compatible with MIS-C-like illness, including low blood pressure, cardiac dysfunction, bradyarrhythmia. Like many patients with MIS-C, our patient required treatment with vasopressors in the ICU. Her low blood pressure was thought to be multifactorial including hypovolemic and cardiogenic. She had elevated troponin and BNP unlike many patients with MIS-C. She didn't have left ventricular dysfunction, coronary aneurysms or valvular dysfunction, as have been described in pediatric patients with MIS-C.

Several other features of our patient's clinical presentation were less consistent with MIS-C as it has been described in the pediatric population. Her profound kidney injury and leukocytosis were not features described in majority of MIS-C cases.

## CONCLUSION

We describe an unusual case of MIS-C-like illness in a young adult with COVID-19. MIS-C is an emerging and poorly understood clinical entity associated with COVID-19 that has been described in children with the illness and has features similar to Kawasaki's disease. Children with MIS-C are increasingly treated with IVIG, aspirin and steroids; it is not clear if any clinical feature in adults may warrant similar treatment approaches. Our patient was treated with IV antibiotics, anticoagulation and steroids. Further research into COVID-19 in the young adult population is needed to better characterize the full range of clinical manifestations, and to identify potential opportunities for targeted treatment of inflammatory processes.

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### NIH Starts Long-term Study of Children with COVID

The National Institutes of Health (NIH) has initiated a new long-term study to evaluate the impact of COVID-19 on children and young adults.

A total of 1,000 children and young adults, 3 to 21 years of age, who have tested positive for COVID-19, will be followed. The study will evaluate the effects of COVID-19 on their physical and mental health, including their development and immune responses to the virus. The NIH stated that while evaluating the long-term health effects of COVID-19, the researchers will also assess the risk factors that cause complications. They will also screen for genetic factors that could affect the response to the virus, and also determine if immunological factors have an impact on long-term outcomes… (*Source: Medscape*)

### Antibiotic Misuse During Pandemic Giving Rise to Resistant Bacteria

The Pan American Health Organization (PAHO) has cautioned that overuse of antibiotics and other antimicrobial agents during the COVID-19 pandemic is leading to the development of resistance among bacteria, which will eventually make these medicines ineffective.

Countries in the Americas, such as Argentina, Uruguay, Ecuador, Guatemala and Paraguay, are reporting increased rates of drug-resistant infections which have possibly led to the rise in mortality among hospitalized COVID-19 patients, stated the agency.

Data available from hospitals in the region indicates that 90-100% of hospitalized COVID-19 patients received an antimicrobial agent during treatment, when just 7% of them had a secondary infection, requiring the use of these medications, said PAHO director Carissa Etienne… (*Source: Reuters*)

CASE REPORT

# Mirizzi Syndrome: A Rare Cause of Obstructive Jaundice

MAHESH DAVE*, MANASVIN SAREEN†, ANUJ GOYAL†, RAM GOPAL SAINI‡, SAHIL KHARBANDA†

## ABSTRACT

Mirizzi syndrome was first described by Pablo Luis Mirrizi. The incidence of this syndrome ranges from 0.05% to 4%. This rare condition is caused by the obstruction of common hepatic duct or common bile duct due to compression caused by several impacted stones or a single large impacted gallstone in Hartmann's pouch. The clinical presentations may vary from no symptoms to severe cholangitis. It is a rare cause of obstructive jaundice and hence we are reporting a case to emphasize that while evaluating a case of obstructive jaundice, one must consider Mirizzi syndrome as a differential diagnosis.

**Keywords:** Obstructive jaundice, Mirizzi syndrome, common bile duct, cholecystoenteric fistula

Mirizzi syndrome was first described by Pablo Luis Mirizzi. The incidence of this syndrome ranges from 0.05% to 4%. It is a rare condition wherein a gallstone is impacted in the cystic duct or neck of gallbladder, which compresses the common hepatic duct. This leads to obstruction and jaundice. Obstructive jaundice can occur due to direct compression from the stone or due to fibrosis, which develops as a result of chronic cholecystitis. The clinical presentations may vary from no symptoms to severe cholangitis. There may be recurrent episodes of jaundice and cholangitis. It can be associated with cholecystitis. There can be development of a fistula between gallbladder and the common duct, with passage of stone into the common duct. It is a rare cause of obstructive jaundice and hence, we are reporting a case in order to emphasize that while evaluating a case of obstructive jaundice, one must consider Mirizzi syndrome as a differential diagnosis.

## CASE REPORT

A 49-year-old male presented to us with chief complaints of low-grade fever, yellowish discoloration of urine, itching in body and right upper abdominal pain for 5 days. The patient was a known case of type 2 diabetes mellitus for the past 8 years and was on oral hypoglycemic agents. He had history of jaundice 20 years back. On examination, the patient was conscious, cooperative and oriented to time, place and person. His vital signs were stable and temperature was 99.6°F (oral). He had no pallor, cyanosis, clubbing, lymphadenopathy or edema, but icterus was present. On systemic examination, liver was palpable but spleen and gallbladder were not palpable. We kept the diagnosis as febrile illness, possibly due to malaria, dengue fever, scrub typhus or acute cholangitis.

Patient was further evaluated and his blood biochemistry showed that renal function tests were normal (blood urea - 16 mg/dL, serum creatinine - 0.70 mg/dL). Liver function tests were deranged (total bilirubin - 5.7 mg/dL, direct bilirubin - 2.3 mg/dL, serum glutamic oxaloacetic transaminase [SGOT] - 245 U/L, serum glutamic pyruvic transaminase [SGPT] - 513 U/L, alkaline phosphatase [ALP] - 341 U/L, total protein - 7.5 g/dL, serum albumin - 3.8 g/dL). His lipid profile was also deranged (serum cholesterol - 195 mg/dL, serum triglyceride - 262 mg/dL, high-density lipoprotein cholesterol [HDL-C] - 18 mg/dL, low-density lipoprotein cholesterol [LDL-C] - 130 mg/dL). Complete hemogram showed hemoglobin - 11.5 mg/dL, mean corpuscular volume (MCV) - 60.1 fL, total leukocyte count (TLC) - 9,940/mm$^3$, platelet count - 3.51 × 10$^3$/mm$^3$. His fever profile and viral markers were negative (Malarial parasite quantitative buffy coat [MPQBC], Dengue immunoglobulin M/immunoglobulin G [IgM/IgG],

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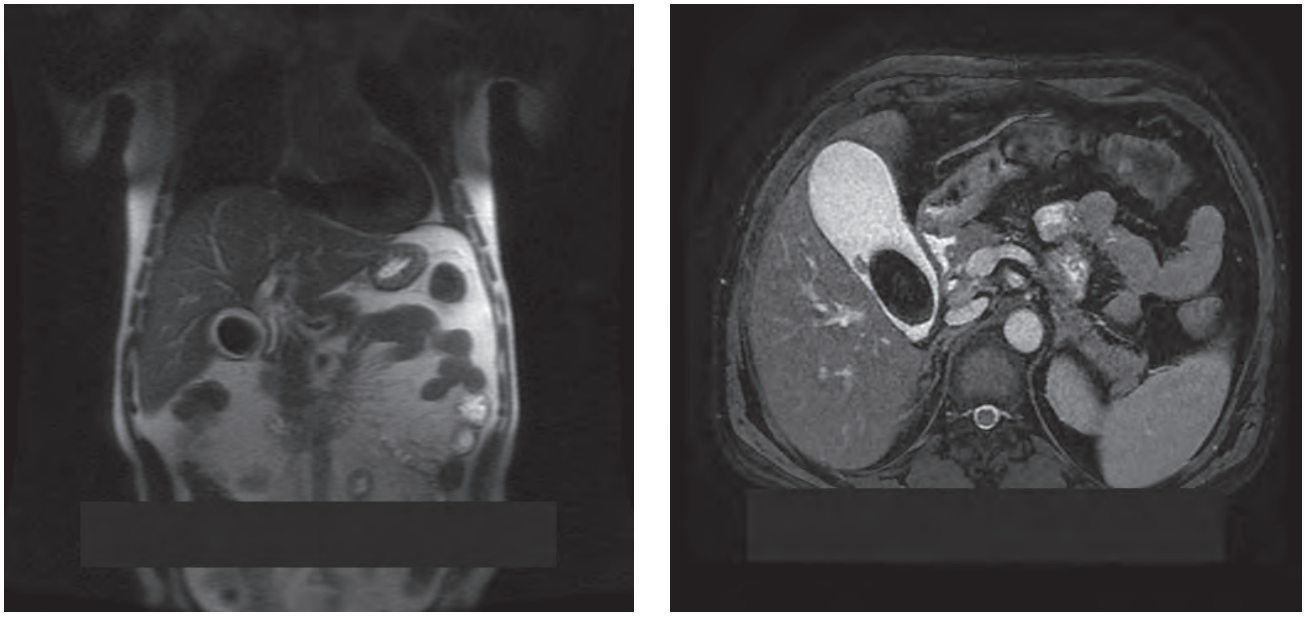

**Figure 1.** MRCP of the patient in which a 42 mm calculus is seen in gallbladder neck compressing the CBD, suggestive of Mirizzi syndrome.

scrub typhus IgM capture ELISA test, hepatitis B surface antigen [HBsAg], anti-hepatitis C virus [HCV], IgM anti-hepatitis A virus [HAV], IgM anti-hepatitis E virus [HEV], human immunodeficiency virus [HIV]). Ultrasonography (USG) showed fatty liver, cholelithiasis with ill-defined hypoechoic area in gallbladder neck region resulting in distended gallbladder with dilated intrahepatic vascular and biliary radicles, possibly indicating cholecystitis.

On further investigating, contrast-enhanced computed tomography (CECT) abdomen showed evidence of calcified calculus of size 4.4 × 2.56 cm in gallbladder lumen in body and in neck region, associated with dilatation of central (right hepatic duct [RHD] - 7 mm and left hepatic duct [LHD] - 8 mm) and peripheral intrahepatic biliary radical (IHBR). Gallbladder appeared significantly overdistended; however, wall thickness appeared normal. Dilatation of central and peripheral IHBR with overdistended gallbladder likely due to gallbladder neck calculus impact on coronary heart disease or CHD (suggestive of Mirizzi syndrome). Magnetic resonance cholangiopancreatography (MRCP) showed a 42 mm calculus noted in gallbladder neck causing compression over common bile duct (CBD). Mild IHBR dilatation was seen. These findings were suggestive of Mirizzi syndrome with cholelithiasis, as shown in the Figure 1. Hence, the diagnosis of Mirizzi syndrome was confirmed. Patient was advised surgical treatment for this, and therefore, was transferred to the surgical ward for further management.

## DISCUSSION

Mirizzi syndrome is a rare condition known to occur as a result of obstruction of the common hepatic duct or CBD due to compression from multiple impacted stones or a single large impacted gallstone in the Hartmann's pouch. The syndrome is named after Pablo Luis Mirizzi. The first published paper on this syndrome was in 1940. It is relatively uncommon and mere 0.1% of patients with gallstones have been reported to develop this condition. About 0.7% to 25% of patients who underwent cholecystectomies were found to have this condition. While it may be more common in older populations, no particular inclination has been noted for either male or female patients with gallstones. The exact pathophysiology of this syndrome is not clearly known but it appears to be associated with floppy Hartmann's pouch with multiple stones or a single large impacted stone, which causes inflammation and fistula formation. Most patients present with repeated bouts of fever, pain and jaundice.

McSherry et al proposed a classification that divides Mirizzi syndrome into 2 types based on endoscopic retrograde cholangiopancreaticography (ERCP) findings. In type 1, the hepatic duct is compressed by a large stone impacted in the cystic duct or Hartmann pouch. Associated inflammation may contribute to obstruction and formation of a stricture in the central section of the extrahepatic bile duct. In type 2, the calculus erodes the common hepatic duct to produce a cholecystocholedochal fistula.

Csendes et al modified McSherry's classification in 1989, and classified Mirizzi syndrome into 4 types:

- Type I: Extrinsic compression of the CBD by an impacted gallstone.
- Type II: Cholecystobiliary fistula present, involving one-third of the circumference of the CBD.
- Type III: Cholecystobiliary fistula present, involving two-third of the circumference of the CBD.
- Type IV: Cholecystobiliary fistula present, involving the whole circumference of the CBD.

Csendes, in 2007, added a new type (Type V) to his classification of Mirizzi syndrome, and it was validated by Beltran et al. This type corresponds to any type of Mirizzi syndrome associated with cholecystoenteric fistula with (Vb) or without (Va) gallstone ileus.

There is an increased risk of developing gallbladder cancer after Mirizzi's syndrome. USG reveals gallstones with a contracted gallbladder and intrahepatic ductal dilatation. The typical findings of MRCP and ERCP are a dilated intrahepatic biliary tract with a normal-sized bile duct, secondary to obstruction at the level of cystic duct insertion into the common hepatic duct.

A cholecystobiliary or cholecystoenteric fistula due to persistent inflammation is the most common complication of Mirizzi syndrome. Other complications include cutaneous fistula and secondary biliary cirrhosis. This syndrome may be confused with Klatskin tumor because of the appearance of obstruction and surrounding inflammation.

Management of Type I Mirizzi syndrome includes cholecystectomy with or without bile duct exploration. Types II and III can be treated with partial cholecystectomy, removal of calculus and choledochoplasty, as needed. Roux-en-Y hepaticojejunostomy is required to repair a large defect as seen in Type IV Mirizzi syndrome. In elderly patients with comorbidities and high risk of surgical complications, nonoperative methods should be considered to minimize morbidity associated with the surgery. Exploration of the CBD should be undertaken due to the occurrence of choledocholithiasis in Mirizzi syndrome. Performing a frozen section biopsy from the removed gallbladder is advisable, since there is association between Mirizzi syndrome and gallbladder cancer.

## CONCLUSION

Mirizzi syndrome can present to us in various forms, including obstructive jaundice. It is a rare cause of obstructive jaundice. So, while evaluating a case of obstructive jaundice, one must consider Mirizzi syndrome as one of the differential diagnoses.

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SHORT COMMUNICATION

# Environmental Impact of COVID-19 Epidemic and Biomedical Waste

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The recent coronavirus disease 2019 (COVID-19) pandemic has impacted the environment globally in both positive as well as negative manner. With global restrictions, there were clean beaches, decreased concentrations of many pollutants, including nitrogen dioxide ($NO_2$) and particulate matter (PM) 2.5, and reduced environmental noise level, to name a few.[1,2] However, as the pandemic progressed there was huge generation and accumulation of medical and many other types of wastes.[2,3] Medical face masks were dumped into the water bodies and now there is huge concern related to microplastic pollution and its impact on human health and environment.[4-6] Because of the increase in demand, there will be almost 20% increase in production of face masks annually between 2020 and 2025.[7] As per one estimate, every month approximately 200 billion face masks and gloves were thrown into the environment.[4] During the COVID-19 pandemic, face masks and many other types of personal protective equipments (PPEs) have been widely used. Therefore, there has been a huge mix of domestic waste with these relatively plastic rich non-biodegradable items; a cause of serious long-term concern for both aquatic and terrestrial life.[4,8] For example, a single PPE contains around 20-25% by weight of plastic and if this not recycled or managed safely, it can cause damage to the environment. If disposed in an unsafe way, it will lead to emission of dioxins and heavy metals.[9] It can lead to contamination of the environment, particularly in the form of microplastics. The best way to prevent plastic-related damage to the environment and health is rational use of PPE, strategies to minimize the need of PPE kits and safe disposal of used PPE kits, i.e., thermal destruction.[4,10] Reusing and recycling of PPE kits and the use of washable and reusable face masks can be sustainable alternatives.[7]

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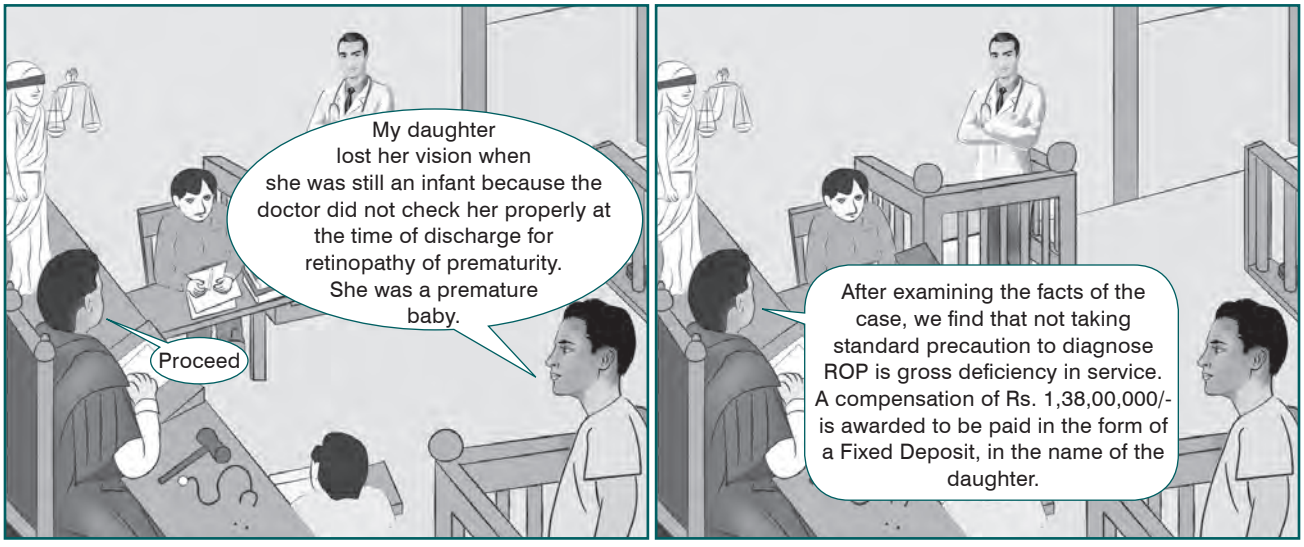
# Deficiency of Service is Gross Negligence




**Lesson:** In *V. Krishnakumar vs State of Tamil Nadu & Ors. Civil Appeal No. 5402 of 2010*, the Supreme Court of India observed: "We agree with the findings of the NCDRC that the respondents were negligent in their duty and were deficient in their services in not screening the child between 2 and 4 weeks after birth when it is mandatory to do so and especially since the child was under their care."

## COURSE OF EVENTS

- 30.8.1996: The appellant's wife was admitted in Hospital 'X' (*hereinafter referred to as Respondent No. 1*), where she delivered a premature female baby weighing 1,250 g in the 29th week of pregnancy. The infant was placed in an incubator in intensive care unit (ICU) for about 25 days. The baby was administered 90-100% oxygen at the time of birth and underwent blood exchange transfusion a week after birth.
- 23.9.1996: The mother and the baby were discharged.
- 30.10.1996: The mother and the baby visited the hospital at the chronological age of 9 weeks.
- Follow-up treatment, from 4 to 13 weeks of chronological age, was administered at the home of the appellant by Dr 'A' (*hereinafter referred to as Respondent No. 4*) of the Hospital.
- At 14-15 weeks of chronological age, the baby was checked up by Dr 'B' (*hereinafter referred to as Respondent No. 3*) of the Hospital at his private clinic.

## SOME SALIENT COURT OBSERVATIONS

- *"… the only advice given by Respondent No. 4 was to keep the baby isolated and confined to the four walls of the sterile room so that she could be protected from infection. What was completely overlooked was a well-known medical phenomenon that a premature baby who has been administered supplemental oxygen and has been given blood transfusion is prone to a higher risk of a disease known as the Retinopathy of Prematurity (hereinafter referred to as 'ROP'), which, in the usual course of advancement makes a child blind. Respondent No. 3 also did not suggest a check-up for ROP."*
- *"… the disease occurs in infants who are prematurely born and who have been administered oxygen and blood transfusion upon birth and further, that if detected early enough, it can be prevented… The disease advances in severity through five stages: 1, 2, 3, 4 and 5 (5 being terminal stage)."* Stage 5 of ROP is complete blindness.
- Some material relevant to the need for check-up for ROP for an infant is: *"All infants with a birth weight <1,500 g or gestational age <32 weeks*

*are required to be screened for ROP*." Being premature and weighing only 1,250 g at birth, the child was a high-risk candidate for ROP. The order of the National Consumer Disputes Redressal Commission (NCDRC) had stated that "*Most ROP is seen in very low-birth weight infants, and the incidence is inversely related to birth weight and gestational age. About 70-80% of infants with birth weight <1,000 g show acute changes, whereas above 1,500 g birth weight the frequency falls to <10%*." The Court regarded this as an undisputed fact.

- The Respondents, in their defence, stated that there were no deformities at the time of delivery and management and the appellant had been asked to attend postnatal OPD, which she did not comply with. They had mentioned in the discharge summary as follows: "*Mother confident; informed about alarm signs; 1) to continue breastfeeding, 2) to attend postnatal OPD, on Tuesday*."
- The Court agreed with the observations of NCDRC, "*… the said remarks are only a hastily written general warning and nothing more. After a stay of 25 days in the hospital, it was for the hospital to give a clear indication as to what was to be done regarding all possible dangers which a baby in these circumstances faces. It is obvious that it did not occur to the respondents to advise the appellant that the baby is required to be seen by a pediatric ophthalmologist, since there was a possibility of occurrence of ROP to avert permanent blindness. This discharge summary neither discloses a warning to the infant's parents that the infant might develop ROP against which certain precautions must be taken, nor any signs that the Doctors were themselves cautious of the dangers of development of ROP…*"
- The Court regarded the Respondents' contention that the appellant did not follow-up properly as "unfortunate" and termed it as "*… a desperate attempt to cover up the gross negligence in not examining the child for the onset of ROP, which is a standard precaution for a well-known condition in such a case.*"
- The Court took into account the opinion of the Medical Board dated 21.8.2007, which included four ophthalmologists of AIIMS, New Delhi, constituted in pursuance of the order of the NCDRC, which stated "*… The ROP usually starts developing 2-4 weeks after birth when it is mandatory to do the first screening of the child. The current guidelines are to examine and screen the babies with birth weight <1,500 g and <32 weeks gestational age, starting at 31 weeks post-conceptional age (PAC) or 4 weeks after birth whichever is later…*" The Court also observed that this report clearly showed that "*… in the present case, the onset of ROP was reasonably foreseeable… it is well-known that if a particular danger could not reasonably have been anticipated it cannot be said that a person has acted negligently, because a reasonable man does not take precautions against unforeseeable circumstances...*"
- The report also said that "*it may not be possible to exactly predict which premature baby will develop ROP and to what extent and why*." This in itself emphasises the need for a check-up in all such cases. "*In fact, the screening was never done. There is no evidence whatsoever to suggest to the contrary...*"
- ROP was discovered incidentally at the time of DPT vaccination when the infant was 4½ months old. The Appellant then consulted several doctors and hospitals in the country and even travelled to the US, where he "*incurred enormous expenses for surgery … but to no avail*."
- Regarding quantification of compensation, the Court said, "*Indisputably, grant of compensation involving an accident is … based on the principle of restitutio in integrum. The said principle provides that a person entitled to damages should, as nearly as possible, get that sum of money which would put him in the same position as he would have been if he had not sustained the wrong… It must necessarily result in compensating the aggrieved person for the financial loss suffered due to the event, the pain and suffering undergone and the liability that he/she would have to incur due to the disability caused by the event*."
- The Court took note of the past medical expenses incurred by the appellant in the treatment and litigation including the income lost by the mother, "*… who became her primary caregiver and was thus prevented from pursuing her own career*." The Court directed the respondents to pay this amount (Rs. 42,87,921/-) along with interest at the rate of 6% p.a. from the date of filing of the petition before the NCDRC till the date of payment.
- The Court also considered the necessary future care, education, pain and suffering, medical expenses including inflation in the future medical costs and awarded a sum of "*…Rs. 1,37,78,722.90/- rounded to Rs. 1,38,00,000/-… We direct that the said amount …. shall be paid, in the form of a Fixed Deposit, in the name of …. We are informed that the said amount would yield an approximate annual interest of Rs. 12,00,000/-.*"
- The Court did not absolve the State of Tamil Nadu under its Dept. of Health (*hereinafter referred to as*

*Respondent No. 2*) from its liability "*…It is settled law that the hospital is vicariously liable for the acts of its doctors*" vide Savita Garg vs. National Heart Institute, (2004) 8 SCC 56, Balram Prasad's case (supra) and Achutrao Haribhau Khodwa v. State of Maharashtra, (1996) 2 SCC 634.

## FINAL JUDGEMENT

The Supreme Court agreed with the findings of the NCDRC and held that there was no error of judgement as given by the Commission. The Court also held that "*the respondents were negligent in their duty and were deficient in their services in not screening the child between 2 and 4 weeks after birth when it is mandatory to do so and especially since the child was under their care…*" Since the child had become blind for life "*… It is, thus, obvious that there should be adequate compensation for the expenses already incurred, the pain and suffering, lost wages and the future care that would be necessary while accounting for inflationary trends.*"

The Court apportioned the liability of Rs. 1,38,00,000/- among the respondents to be paid within 3 months from the date of this judgement, failing which the said sum would attract a penal interest @ 18% p.a.

- "*Rs. 1,30,00,000/- shall be paid by Respondent Nos. 1 and 2 jointly and severally…*
- *Rs. 8,00,000/- shall be paid by Respondent Nos. 3 and 4 equally … and Rs. 4,00,000/- by Respondent No. 4.*"

The Court also apportioned the past medical expenses Rs. 42,87,921/- in the following manner:

- "*Respondent Nos. 1 and 2 are directed to pay Rs. 40,00,000/- jointly, along with interest @ 6% p.a. from the date of filing before the NCDRC; and*
- *Respondent Nos. 3 and 4 are directed to pay Rs. 2,87,921/- in equal proportion, along with interest @ 6% p.a. from the date of filing before the NCDRC.*"

"*If Respondent Nos. 1 and 3 have made any payment in accordance with the award of the NCDRC, the same may be adjusted…*"

Two Civil Appeals were filed before the Supreme Court; one (Civil Appeal No. 8065 of 2009) by the Appellant for enhancement of the amount of compensation awarded by the NCDRC (Rs. 5,00,000/-) and the other by Respondent No. 2 (Civil Appeal No. 5402 of 2010) against the judgement of the NCDRC dated 24th May 2009. Both the appeals were disposed off in this common judgement. "*Accordingly, Civil Appeal No. 8065 of 2009 is allowed in the above terms and Civil Appeal No. 5402 of 2010 is dismissed. No costs.*"

## REFERENCE

1. V Krishnakumar versus State of Tamil Nadu & Ors Civil Appeal No. 8065 of 2009 with Civil Appeal No. 5402 of 2010 Supreme Court of India dated July 1, 2015.

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### Preschool Children can Identify Emotions of Masked Adults

According to a study published in *JAMA Pediatrics*, a large proportion of healthy preschool kids could recognize the emotions shown in static pictures of adults with and without face masks.

In the cross-sectional study involving 276 preschool children, investigators assessed the effect of masks on their ability to identify joy, anger and sadness. The kids saw pictures of 15 actors with and without surgical face masks. Around 68.8% of the children could correctly recognize the emotion portrayed in the photograph. The correct response rate was 70.6% for unmasked faces and 66.9% for faces with masks. Correct identification of joy was found to be significantly higher for unmasked faces compared to faces with masks (94.8% vs. 87.3%). Similar was the case for correct identification of the emotion of sadness (54.1% vs. 48.9%; $p < 0.001$ for both). However, there was no significant difference in recognition of anger for unmasked and masked faces (62.2% vs. 64.6%, $p = 0.10$)… (*Source: Medscape*)

### Huge Increase in Obesity among Children in England During Pandemic

A dramatic surge has been noted in the number of obese children in England during the COVID-19 pandemic, indicate data from NHS Digital. In 2019-20, 10% of children were obese at the beginning of primary school; however, in 2020-21, it increased to over 14%. During the last year of primary school, the figure increased from 21% to more than 25%. Interestingly, the rates were nearly double in the poorest areas. According to experts, poverty, lockdowns and an increase in mental health problems could have played a role in the surge. This increase is in marked contrast to previous years, when very gradual increases were seen… (*Source: BBC*)

# HCFI Dr KK Aggarwal Research Fund

## HCFI Round Table Expert Zoom Meeting on "Breakthrough Infection after COVID Vaccination"

**6th November, 2021 (11 am-12 noon)**

### Key points

- Coronavirus disease 2019 (COVID-19) vaccines are effective at preventing infection, serious illness and death. Vaccinated persons are 8 times less likely to be infected and 25 times less likely to experience hospitalizations and death.
- Vaccines are not 100% effective; therefore, some people may still get COVID-19 even if they are fully vaccinated.
- Immunocompromised persons may not have adequate levels of protection after the 2-dose primary vaccine series. They should continue to take all precautions. The Centers for Disease Control and Prevention (CDC) has recommended an additional dose of the vaccine for moderately to severely immunocompromised persons.
- The CDC has defined breakthrough infection as when a person tests positive for COVID-19 at least 2 weeks after becoming fully vaccinated.
- Breakthrough infections are related to vaccine efficacy and immune evasion.
- A study in Washington state of more than 4 million fully vaccinated individuals showed breakthrough infection rate of about 1 in 5,000 between January 17 and August 21, 2021. But more recent studies have shown breakthrough infection rates of around 1 in 100 fully vaccinated people.
- It is not easy to track every case of breakthrough infection. Most studies give different figures and are not truly representative of a population. According to the CDC, breakthrough cases are underreported as many such infections are asymptomatic or mild and therefore not reported.
- The rate of fully vaccinated Americans who have experienced a breakthrough case resulting in hospitalization or death has remained below 0.01% (*CDC*).
- As per media reports, over 25% of healthcare workers (HCWs) were infected with the Delta variant despite full vaccination.
- As per a German study reported in the media, the suspected breakthrough infections among symptomatic COVID-19 cases in the 18 to 59 years age group were 8.2%.
- As per government data, 2.6 lakh people have tested positive for COVID-19 after being vaccinated in India till August 3 after administration of around 53 crore vaccine doses. While 1.71 lakh breakthrough infections were reported in people who had taken one dose of the vaccine, the number of breakthrough infections among the fully vaccinated population was 87,049. Kerala alone has recorded 40,000 breakthrough infections.
- Breakthrough infection is seen more in the elderly population.
- A study of HCWs has found symptomatic breakthrough infections occurring in 15 persons (13.3%), out of which one required hospitalization (*Diabetes Metab Syndr. 2021 May 3*).
- A meta-analysis of 18 studies involving 2,28,873 HCWs found the risk of COVID-19 infection to be very low in both partially and fully vaccinated HCWs; 1.3% for fully vaccinated, 3.7% for partially vaccinated and 10.1% for unvaccinated HCWs.
- The immunocompromised persons are more at risk of developing a breakthrough infection. The CDC recommends that persons with weakened immune system receive a third dose of the vaccine 28 days after the second dose.
- It has also been suggested that being vaccinated reduces the chances of long COVID.
- Breakthrough infections can be prevented by following all safety precautions. Indoor gatherings where there is overcrowding or poor adherence to masks or are ill-ventilated should be avoided.
- The course of action after a breakthrough infection is similar to that after a COVID-19 infection. Isolation is still needed.
- There are no restrictions for travelers in the US and Dubai if they are fully vaccinated and they test negative for COVID. In Dubai, 200 or less people were allowed in a hall.
- The incidence of breakthrough infections remains the same, whether they are HCWs, who get the

infection in a healthcare facility or those who get the infection outside the healthcare facility.

- There is no perfect methodology to establish how the T cells respond.
- The human leukocyte antigen (HLA) system responds differently in different individuals to infections as well as vaccine challenges. This is an area that needs to be studied; it may then be possible to identify persons who actually need a booster dose of the vaccine.
- Cellular protection is variable in comorbidities.
- Reverse transcription-polymerase chain reaction (RT-PCR) is 87% to 93% specific for COVID with different methods.
- Studies have shown that after 3 months, the antibody levels start to decline and by 6 months, they decline significantly. People who are immuno-compromised or have risk factors should be considered for a third dose. This is the right time for the Expert Committee to recommend a booster dose for HCWs, in particular those who are in direct contact with COVID patients and the immunocompromised persons as well.
- We must find out what is the half-life of immunity after vaccination.
- C-reactive protein (CRP) has excellent sensitivity for COVID but it is not specific to COVID.
- About 25% HCWs have been affected with the Delta variant.
- The currently available vaccines have been shown to be effective against the Delta variant, although work is ongoing to modify the vaccine as per the variants.
- Booster dose should be the same as the primary vaccination. The body should not be re-challenged.

**Participants:** Dr KK Kalra, Dr Ashok Gupta, Dr DP Lokwani, Dr Arun Jamkar, Dr DR Rai, Ms Balbir Verma, Ms Ira Gupta, Mr Saurabh Aggarwal, Dr S Sharma

## HCFI Round Table Expert Zoom Meeting on "Monoclonal Antibodies in COVID-19"

***Speaker: Prof Dr Arun Jamkar,*** *Ex-Vice Chancellor, Maharashtra University of Health Sciences, Nashik; Technical Consultant, Persistent Systems Ltd; Chief Medical Officer, Indx Technology, Distinguished Professor, SIU Pune*

**13th November, 2021 (11 am-12 noon)**

### Key points

- Where epitopes and receptor interactions are known and valid, monoclonal antibodies work. In COVID, the exact pathogenesis is still not well-understood.
- Kohler and Milstein provided the most outstanding proof of clonal selection theory by fusion of normal and malignant cells (Hybridoma technology) for which they were awarded the Nobel Prize in 1984.
- Transplant rejections were improved after the introduction of the first monoclonal antibody OKT3 in 1986. It was US Food and Drug Administration (FDA) approved for preventing kidney transplant rejection.
- The steps of preparation of antibodies are immunize animal, isolate spleen cells (containing antibody producing B-cell), fuse spleen cells with myeloma cells (using PEG), allow unfused B cells to die, add aminopterin to culture and kill unfused myeloma cells, clone remaining cells, screen supernatant of each clone for presence of desired antibody, grow chosen clone of cells in tissue culture indefinitely and harvest antibody from the culture.
- Nomenclature of monoclonal antibodies: If it is murine, it is called "omab"; if it is chimeric but still human, it is called "ximab" and once it is humanized (>60%), it is called "zumab". When it is fully humanized, it is called "umab".
- Monoclonal antibodies prevent viral binding and/or fusion with host cell. They bind to the spike protein, prevent the virus from attaching to human cells and tag it for destruction preventing the development of severe COVID-19.
- Tocilizumab was one of the most successful drugs in managing cytokine storm, which is a lethal event in COVID-19 and is mediated through interleukin (IL)-6 and tumor necrosis factor (TNF)-$\alpha$.
- In a meta-analysis of 16 randomized controlled trials, tocilizumab reduced mortality risk in severe to critical disease and lowered mechanical ventilation requirements. It also facilitated hospital discharge.
- If monoclonal antibodies are given within 7 days of getting the infection, they are most successful. It does not allow the virus to attach to the cell. Hence, it can be a game changer in the treatment of COVID. Only symptomatic patients – mild or moderate - can be given monoclonal antibodies.
- Casirivimab and imdevimab antibody cocktail was used in India for the first time in Medanta hospital.

- There are around 75 monoclonal antibodies available today in various stages of development. Many of them are in phase III trial.
- Bamlanivimab + etesevimab and casirivimab + imdevimab reduce viral load when given early on in the course of the infection and favorably impact clinical outcomes in patients with mild-to-moderate disease.
- Bamlanivimab + etesevimab bind to different but overlapping epitopes in the spike protein receptor-binding domain of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Their distribution was paused in the US because both the Gamma and Beta variants have reduced susceptibility to bamlanivimab + etesevimab. But distribution has been reinstated in states with low rates of these variants.
- The FDA issued emergency use authorization (EUA) for treatment of mild-to-moderate COVID-19 in adults and children ≥12 years weighing ≥40 kg and who are at high risk for progressing to severe disease and/or hospitalization. It is given as IV infusion (casirivimab 600 mg + imdevimab 600 mg). Subcutaneous injection is an alternative route. It is to be administered as soon as possible after a positive RT-PCR and within 10 days of symptom onset in high-risk patients.
- Bamlanivimab + etesevimab is not yet available in India.
- According to an observational study from Pune, combination therapy of tocilizumab and steroids is likely to be safe and effective in the management of COVID-19-associated cytokine release syndrome.
- The 2018 Nobel Prize in Physiology or Medicine was awarded to James Allison and Tasuku Honjo for their discovery of cancer therapy by inhibition of negative immune regulation. Inhibition of these molecules by immune checkpoint inhibitors can successfully activate the immune system to fight cancer.
- The immune checkpoint inhibitors act by blocking checkpoint proteins (cytotoxic T-lymphocyte-associated protein 4 [CTLA-4]) from binding with their partner proteins. This prevents the "off" signal from being sent, allowing the T cells to kill cancer cells.
- Anti-CTLA-4 opened a new field called immune checkpoint therapy.
- Ipilimumab blocks the CTLA-4 checkpoint protein. Pembrolizumab and nivolumab target the programmed cell death protein 1 (PD-1), while atezolizumab target the PD-L1 protein.
- Cancer is a disease of genome. In a survey of oncologists from the US, overall, 75% reported using next-generation sequencing (NGS) tests to guide treatment decisions.
- Monoclonal antibodies can be used not only in cancer, but also in rheumatoid arthritis.
- Challenges to the use of monoclonal antibodies are diversity of the virus, bioavailability in the lungs (most commonly affected organ).
- A larger clinical trial needs to be done with the support of the government.
- We need to find out which receptors are being used for monoclonal antibodies and which action has to be stopped. We are studying the results of the pathogenesis and not the origin and trigger of the pathogenesis.
- Monoclonal antibodies are costly and have to be administered under supervision. Infectious disease specialists at the tertiary center can supervise doctors at the periphery (community health center).

**Participants:** Dr KK Kalra, Dr Ashok Gupta, Dr Suneela Garg, Dr DP Lokwani, Dr Arun Jamkar, Dr Milind Deshpande, Ms Ira Gupta, Dr S Sharma

**Moderator:** Mr Saurabh Aggarwal

## Coronavirus Updates

### Interim results show 77.8% effectiveness of covaxin against symptomatic COVID

Interim results from a phase III trial show that Covaxin (BBV152) was highly effective against laboratory-confirmed symptomatic COVID-19 in adults. In the final per-protocol analysis, measured 14 days after the second dose, the overall vaccine efficacy was 77.8% against symptomatic COVID-19 and a higher efficacy against severe COVID-19 of 93.4%. It was well-tolerated with no safety concerns. Covaxin is an inactivated whole virus vaccine formulated with a novel adjuvant and has a two-dose regime given at a gap of 28 days… (*Source: The Lancet*)

### France recommends against Moderna vaccine for people younger than 30 years

The Haute Autorite de Sante (HAS) or the French National Authority for Health has recommended that people younger than 30 years should be given the Pfizer COVID-19 vaccine in place of the Moderna vaccine citing "very rare" risks linked to myocarditis with the

Moderna vaccine. According to HAS, this risk appears to be around five times lesser with Pfizer's jab compared to Moderna's jab... (*Source: Reuters*)

### ECG findings in COVID-19 patients

A review of the ECG findings in COVID-19 patients reported in the journal *Cardiac Electrophysiology Clinics* has described QRS axis changes, conduction abnormalities, arrhythmias (most commonly atrial fibrillation) and ST-segment and T-wave changes. The study authors write, "Clinicians should be cognizant of some of the reported ECG changes, such as abnormal QRS axis in nearly 20% of patients, conduction abnormalities in approximately 20%, atrioventricular block in about 2.5%, and premature beats in nearly 10% of patients." ST- and T-wave changes can be due to myocardial infarction or myocardial injury secondary to myocarditis, or microthrombi and so should be clinically correlated… (*Source: Cardiac Electrophysiology Clinics*).

### Unvaccinated persons have 20 times higher mortality risk

A study from Texas Department of State Health Services, US has concluded that compared to fully vaccinated people, unvaccinated persons were 13 times more likely to become infected with COVID-19. They were also 20 times more likely to die from COVID-19–related complications. The risk of death was 23 times higher in unvaccinated people in their 30s and 55 times higher for unvaccinated people in their 40s…(*Source: Texas Department of State Health Services*)

### COVID-19 generates 8 million tons of plastic waste

COVID-19 has resulted in over 8 million tons of mismanaged plastic waste globally as of August reports the *Proceedings of the National Academy of Sciences*. And, more than 25,000 tons has entered the global ocean. Nearly 90% of the excess plastic waste generated during the pandemic were the medical waste from hospitals; individual personal protective equipment (PPE) contributed to just 7.6% of the plastic waste, while 4.7% came from packaging. Almost half of all the mismanaged plastic waste was produced in Asia…(*Source: PNAS*)

### LZTFL1 gene predisposes South Asians to high risk of severe COVID-19

Researchers from Oxford University have identified a gene "leucine zipper transcription factor-like 1 (LZTFL1)" leads to a twofold increase in the risk of respiratory failure and death from COVID-19. The high-risk form of this gene is present in 60% of South Asians, 15% of Europeans and just 2% of persons with African-Caribbean ancestry and 1.8% of people of East Asian descent. This gene does not affect the immune system, but affects the lungs. The study published in the journal *Nature Genetics* attempts to explain why some ethnic groups are at higher risk from COVID… (*Source: Medscape*)

### More than 28 million excess years of life lost in 2020 during pandemic

A *BMJ* study has reported that more than 28 million excess years of life were lost in 2020 in 31 countries, with a higher rate in men than women (except New Zealand, Taiwan and Norway, where there was a gain in life expectancy in 2020). Excess years of life lost linked with the COVID-19 pandemic in 2020 were over fivefold higher compared to those linked to the seasonal influenza epidemic in 2015. The study evaluated the changes in life expectancy and years of life lost in 2020 associated with the COVID-19 pandemic in 37 upper-middle and high-income countries. The highest reduction in life expectancy was observed in Russia, the United States, Bulgaria, Lithuania, Chile and Spain… (*Source: BMJ*)

### Single dose J&J COVID-19 vaccine is 74% effective in preventing COVID-19

A retrospective analysis of electronic health records of nearly 9,000 adults from the multistate Mayo Clinic Health System who received the single dose J&J shot during the first 5 months of its authorization reported in *JAMA Network Open* showed an actual effectiveness of 74%, which is in accordance with the 66.9% effectiveness reported in the phase III clinical trial of the vaccine. COVID-19 cases declined by 3.73-fold after the vaccination. The vaccinated group had 60 cases of COVID-19 compared to 2,236 cases in the unvaccinated group … (*Source: Medscape*)

### "When to test": A free online tool from NIH to decide if you need a COVID test

The National Institutes of Health (NIH)'s Rapid Acceleration of Diagnostics (RADx) initiative has launched the "When to Test Calculator for Individuals", a companion to the version for organizations introduced last winter. It is available at https://whentotest.org/. The new individual impact calculator helps to decide when should a person get tested for COVID-19—now or soon. It was developed and tested by computer modelers to help people determine if they are at risk of getting or transmitting COVID-19 based on a few variables, including vaccination status, transmission rates in the geographic area, and mitigation behaviors… (*Source: NIH*)

### Eye manifestations of COVID-19

Several eye manifestations have been linked to COVID-19, according to findings presented at the annual meeting of the American Academy of Ophthalmology (AAO). These include conjunctivitis, photophobia, retinal hemorrhage, optic neuritis. Rhino-orbital-cerebral mucormycosis (ROCM) is more likely in patients with diabetes and those on steroids. Some eye manifestations are related to sequelae of COVID-19 such as meningitis, ptosis, eye muscle movements, eye fatigue. Corneal verticillata may develop in COVID patients who develop arrhythmia and are put on amiodarone… (*Source: Medpage Today*)

### Low mortality risk in COVID patients on SSRIs

According to a retrospective multicenter study reported in *JAMA Network Open*, COVID-19 patients prescribed a selective serotonin reuptake inhibitor (SSRI) had a modest but significant 8% reduced risk of death. Overall, 14.6% of patients on an SSRI died from COVID-19 compared to 16.6% of patients who had never taken an SSRI. Specifically, the risk was lower in COVID-19 patients on fluoxetine; 9.8% vs. 13.3%, respectively… (*Source: JAMA Network Open*)

### Effectiveness of public health measures in reducing COVID-19

Reiterating the effectiveness of public health measures, a new systematic review and meta-analysis from Monash University in Australia has shown 53% reduction in the incidence of COVID-19 with mask wearing and a 25% reduction with physical distancing, and recommends that COVID-19 protocols such as handwashing, mask wearing and physical distancing should be continued together with vaccination… (*Source: BMJ*)

### WHO updates its guidelines on management of children with COVID-19-associated MIS-C

The WHO has updated its guidelines on the management of multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19. The two new recommendations include:

- Conditional recommendation to use corticosteroids + supportive care (rather than either IVIG and supportive care or supportive care alone), for hospitalized children aged 0 to 18 years who meet a standard case definition for MIS-C.
- Conditional recommendation to use corticosteroids + standard of care for hospitalized children aged 0 to 18 years who meet a standard case definition for MIS-C and fulfill the diagnostic criteria for Kawasaki disease.

*(Source: WHO)*

### Antibodies from mild COVID-19 may not protect against new emerging variants

A preprint study from Australia involving 43 patients with mild COVID-19 has concluded that while 90% still had antibodies 1 year after recovery, neutralizing antibodies against the original virus were detected in only 51.2%; the levels declined to 44.2% against the Alpha variant, 11.6% against Gamma and 4.6% against Beta. Only 16.2% showed neutralizing antibodies against the Delta variant. These findings suggest that the antibodies may not be protective against the new emerging variants… (*Source: medRxiv*)

### A vendor in Wuhan market is probably the first case of COVID

A vendor at an animal market in Wuhan, China, was probably the first person to contract COVID-19, with onset of illness on December 11, 2019, suggests a study reported in the journal *Science,* discounting the earlier notion that the first person thought to have contracted COVID-19 was a male accountant in Wuhan who lived miles from the market, did not visit the market, and reported COVID symptoms around December 16, 2019. "Hospital records and a scientific paper that reports his COVID-19 onset date as 16th December and date of hospitalization as 22nd December indicate that he was infected through community transmission after the virus had begun spreading from Huanan Market." … (*Source: Medscape*)

### Study shows direct effect of SARS-CoV-2 on blood clotting

COVID-19 is characterized by a hypercoagulable state, which has been attributed to the hyperinflammatory response induced by the virus. A new study reported in the *International Journal of Biological Macromolecules* has now shown that the virus itself also has a direct effect on blood clotting and coagulation. The SARS-CoV-2 spike protein competitively binds to heparan resulting in an abnormal increase in activity of thrombin thereby causing blood clotting and coagulation… (*Source: International Journal of Biological Macromolecules*)

*With inputs from Dr Monica Vasudev*

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# 79th AIOC 2021: All India Ophthalmological Society

## CONQUERING THE BLACK ROCK HARD CATARACTS

**Dr Arup Chakraborty, Kolkata**

Dr Arup discussed about the management of black cataracts in his presentation and put forward the challenges encountered, which include absence of protective epinuclear layer, paucity of cortex, absence of red reflex, potential laxity of zonules, chances of PCR, increased risk of corneal endothelial damage and wound burn. He discussed the required accessories to tackle these rock hard cataracts, including dispersive viscoelastics, CTR, iris hooks, capsular hooks and Cionni. He discussed the strategies to manage rock hard cataracts.

## ELECTROOCULOGRAM AND VISUAL EVOKED POTENTIALS

**Dr Nidhi Gadkar, Ranchi**

Discussing about electrooculogram (EOG), Dr Nidhi said that it tests retinal pigment epithelium (RPE) layer and outer retina. It measures changes in the standing potential in light and dark conditions. She discussed about the requirements of the test and gave an exhaustive explanation of the procedure of the test. She also discussed about Arden's ratio. She stated that the indications for EOG include best dystrophy, butterfly (pattern) dystrophy, chloroquine dystrophy, Stargardt's dystrophy. She mentioned that EOG correlates with electroretinogram (ERG). She also discussed about pattern visual evoked potential (VEP), onset and offset VEP, flash VEP, sweep VEP and multifocal VEP.

## 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.

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# News and Views

## Treating Young Adults with Raised LDL may be Cost-effective

Treating raised low-density lipoprotein cholesterol (LDL-C) levels in adults below 40 years of age with statins appears to be highly cost-effective in men, and intermediately cost-effective among women, suggested a new study published online in the *Journal of the American College of Cardiology*.

A simulated model based on data from the US National Health and Nutrition Examination Survey (NHANES) revealed that decreasing lipid levels with statins or lifestyle interventions in this age group would result in prevention or reduction of the risk of atherosclerotic cardiovascular disease (ASCVD) and help improve quality of life in later years.

Incremental cost-effectiveness ratios (ICERs) were found to be $31,000/QALY for statin treatment in young adult men having LDL-C ≥130 mg/dL, and $106,000/QALY for statin treatment in young women having LDL-C level of ≥130 mg/dL… (*Source: Medscape*)

## Early Biologic Therapy Yields Better Results in Juvenile Idiopathic Arthritis

For patients with polyarticular juvenile idiopathic arthritis (JIA), use of early combination therapy resulted in better outcomes compared to the conventional step-up approach or initial biologic monotherapy, noted a prospective observational study presented at the American College of Rheumatology (ACR) virtual meeting.

At 24 months, 59.4% of the patients who had received early combination therapy with a conventional disease-modifying antirheumatic drug (DMARD) and a biologic had attained clinically inactive disease (CID) and were not on glucocorticoids. On the other hand, 48% of the patients who had started treatment with biologic monotherapy achieved CID and were off glucocorticoids at 24 months, but only 40.1% of the patients who initially received step-up therapy starting with a conventional DMARD followed by addition of a biologic after 3 or more months if required… (*Source: Medpage Today*)

## Breakthrough COVID-19 Increases Risk of Health Problems and Death

While coronavirus disease 2019 (COVID-19) has been reported to be less severe in vaccinated patients, breakthrough infections are not benign, suggests a large study.

Investigators assessed data aggregated by the US Veterans Affairs Administration from 16,035 survivors of breakthrough infections, 48,536 unvaccinated COVID survivors and around 3.6 million uninfected individuals. At 6 months following the infection, after accounting for the risk factors, individuals who had breakthrough infections were found to have lower rates of death and long-term health problems compared to unvaccinated COVID-19 patients. However, in comparison with people who never had COVID-19, those with breakthrough infections were shown to have a 53% increased risk of death and a 59% higher risk of having at least one new health problem, especially those affecting the lungs and other organs.

Despite the fact that breakthrough infections did not need hospital admission, the increased risks of death and long-term effects were not insignificant, noted the investigators. They concluded that breakthrough COVID-19 will lead to a considerable overall burden of death and disease… (*Source: Reuters*)

## Coronavirus Persists Longer in Public Areas, Washrooms with Dead Zones: Study

Researchers from IIT-Bombay have noted that infectious aerosols can persist in the air up to 10 times longer in the so-called dead zones in enclosed spaces.

The dead zones include areas above washbasins in washrooms, behind the doors, in the corners and around the furniture. Slow air circulation in these zones can result in COVID infection transmission, stated the report titled "Effects of Recirculation Zones on the Ventilation of a Public Washroom".

The researchers noted that the odds of infection are increased significantly in these dead zones as infectious aerosols linger up to 10 times longer in these spaces, in comparison with other well-ventilated areas in a room. They recommended the use of additional fans or ducts facing the dead zones in order to check the spread of infection. They also noted that keeping a washroom door partially open facing the basin could also help… (*Source: ET Healthworld*)

## Severe Glucose Swings Common in Dialysis Patients

According to a new retrospective study, severe hypoglycemic and hyperglycemic crises requiring immediate care are highly common in patients with diabetes and end-stage kidney disease (ESKD) who are on dialysis, and are far higher than those reported in nondialysis patients with chronic kidney disease (CKD).

Investigators made use of data from the United States Renal Data System (USRDS) registry and identified 5,21,789 patients with diabetes and ESKD who had at least 3 months of dialysis before the index date and established diabetes as of the index date. Patients were enrolled in the registry from 2013 to 2017. The median duration of dialysis at cohort entry was 3 months and patients were observed for a median of about 2 years. Around 7.9% patients experienced at least one hypoglycemic crisis with an overall incidence rate of 53.64 per 1,000 person-years.

A lesser number of patients experienced at least one hyperglycemic crisis from 2013 through 2017 at a rate of 1.8% overall, with an adjusted incidence rate of 18.2 events per 1,000 person-years… (*Source: Medscape*)

## Screen Patients with Long COVID GI Symptoms for Mental Health Problems

A survey has shown that long COVID gastrointestinal (GI) symptoms are associated with mental health symptoms and a more severe illness doubled the risk of post-COVID GI symptoms.

The survey covered 749 patients who had tested positive for COVID-19 at the Columbia University Irving Medical Center from April to November 2020 and had recovered from the infection. The minimum follow-up period was for 6 months for the eligible participants. Women comprised 67% of the surveyed population. Fifteen percent of the participants were admitted to hospital and 1.7% required mechanical ventilation.

Out of the 749 patients evaluated, 220 (29%) reported COVID-related GI symptoms. The most commonly reported symptom was heartburn (16%), followed by constipation (11%), diarrhea (9.6%) and abdominal pain (9.4%); 7% reported nausea or vomiting.

Pre-COVID mental health symptoms were reported by 39 patients (5%), while post-COVID mental health symptoms, most commonly anxiety and sadness, were reported by as many as 280 patients (37%).

Analysis of data further showed that the probability of having GI symptoms was higher in those patients who had pre-COVID mental health symptoms; 49% vs. 28%, respectively. And, those patients who developed mental health symptoms after COVID were more likely to also have GI symptoms post-COVID; 55% with sadness or anxiety vs. 14% of those who had no mental health symptoms. Patients who had severe COVID-19 and required hospitalization were more prone to have post-COVID GI symptoms compared to those who were not hospitalized; 51% vs. 26%, respectively.

Thirteen out of the 33 patients with abdominal pain met the Rome IV criteria for irritable bowel syndrome (IBS) after reporting weekly pain and change in stool form or frequency for a minimum of 6 months.

Patients with mental health symptoms either before or after COVID-19 were more likely to report post-COVID GI symptoms. Increasing severity of GI symptoms was associated with higher risk for new anxiety or sadness.

These survey findings, published in the journal *Gastroenterology*, highlight the strong association between mental health symptoms and post-COVID GI symptoms; 11% patients surveyed described their GI symptom as the *"most bothersome current symptom"*.

Feeling anxious or sad may aggravate functional GI disorders such as IBS, the symptoms of which in turn may add to the anxiety or sadness creating a vicious cycle. Hence, physicians treating GI symptoms in patients with long COVID should also screen them for anxiety and other mental health symptoms. (*Source: Gastroenterology. 2021 Oct 30:S0016-5085(21)03712-4.*)

## Pandemic Led to 16% Increase in Deaths in OECD Countries: Report

The COVID-19 pandemic led to an increase of 16% in expected deaths among the 38 members of the Organization for Economic Cooperation and Development (OECD), and hit the overall life expectancy in 24 of the 30 members, stated the organization.

Life expectancy was found to decrease the most in Spain and the United States, with the United States losing 1.6 years of life per capita on average during the year and a half of the pandemic. Spain lost 1.5 years, noted the organization. The report stated that Japan, Switzerland and Spain lead a group of 27 OECD countries where life expectancy at birth exceeded 80 years in 2019. Another group, which includes the United States and several central and eastern European countries, had a life expectancy of 77 to 80 years… (*Source: CNN*)

## Sleep Apnea Associated with Severe COVID-19

The risk of severe COVID-19 is greater in individuals with obstructive sleep apnea and other breathing problems that are known to result in a fall in oxygen levels during sleep, noted researchers.

In a study published in *JAMA Network Open*, investigators tracked 5,402 adult patients with these problems and noted that around one-third of them tested positive for COVID-19. Although the likelihood of being infected did not increase with the severity of their problems, but those who had higher scores on the apnea-hypopnia index appeared to have higher odds of requiring hospitalization or dying from COVID-19, noted researchers.

It is not known whether treatments that improve sleep apnea, such as CPAP machines, would reduce the risk of severe COVID-19, stated Cinthya Pena Orbea and Reena Mehra of the Cleveland Clinic… (*Source: Reuters*)

## Measles an Renewed Global Threat, Millions of Babies Missed Vaccines During Pandemic: CDC

The world faces a renewed threat of measles as 22 million babies missed their vaccinations due to disruptions caused by the COVID-19 pandemic, cautioned the US Centers for Disease Control and Prevention (CDC).

The CDC stated that the reported measles cases declined in 2020 after a resurgence from 2017 to 2019. However, the agency mentioned that large and disruptive measles outbreaks in 2020 indicate that measles transmission was underreported. The agency said that more than 22 million infants missed their first vaccine dose, which is 3 million higher than in 2019 and the highest annual increase in more than 2 decades.

Dr Kate O'Brien, Director of the Dept. of Immunization, Vaccines and Biologicals at the World Health Organization (WHO), said that though the reported cases of measles declined in 2020, this could possibly be the calm before the storm, adding that the risk of outbreaks continues to grow… (*Source: CNN*)

## Novel Urine Biomarker for Prostate Cancer Indicates Amount of Aggressive Tumor

A novel urine biomarker for prostate cancer can detect the presence of aggressive tumors and can also signal the amount of these tumors, suggests new research published online in *Life*.

In a study of biopsy and prostatectomy samples, the multigene Prostate Urine Risk-4 (PUR-4) signature was found to have a strong correlation with the presence and amount of Gleason pattern 4 tumors, but not with tumors of less aggressive histology.

Considering that more cases of Gleason pattern 4 tumors are linked with disease progression in patients at intermediate risk, the study indicated that PUR can identify men at intermediate risk who may need treatment and those who may be managed conservatively with surveillance.

Based on biopsy samples from 215 men with prostate cancer, it was noted that PUR-4 signature values had a significant correlation with increasing Gleason grade… (*Source: Medscape*)

## Add Dairy Foods in Diet to Reduce Risk of Falls and Fractures

Increasing intake of dietary calcium and protein in older adults who have adequate vitamin D levels reduces the risk of falls and fragility fractures, according to a new *BMJ* study from Australia.

The randomized controlled trial involved 7,195 institutionalized, but ambulatory older adults, with mean age 86 years. Women participants were 4,920 (68%) in number. They had sufficient vitamin D levels, but their intake of calcium and protein was lower than 1,300 mg/day and 1 g protein/kg body weight, respectively. Residents of 30 facilities were given diets with extra milk, yogurt, cheese and calcium supplements amounting to 1,142 mg of calcium/day and 1.1 g/kg body weight of protein (69 g/day). Residents of the other 30 facilities, which acted as the control group, continued with their regular diets 700 mg/day calcium and 0.9 g of protein/kg body weight (58 g/day).

After 2 years, there were 324 fractures in total (121 in the study group vs. 203 in the control group) and 4,302 falls; 1,974 deaths occurred during the study. Addition of calcium and protein in the diet reduced the risk of all fractures by 33% (121 vs. 203), and falls by 11% (1879 vs. 2423). The risk of hip fractures reduced by 46% with fewer hip fractures occurring in the intervention group compared to the control group; 42 vs. 93, respectively. The risk reduction in hip fractures became evident after 3 months of the dietary intervention. However, there was no difference in all-cause mortality between the two groups (900 vs. 1,074).

This study highlights the importance of educating older adults about adequate nutrition, particularly calcium and proteins by using readily available dairy foods, to reduce their risk of falls and fractures as complementary to anti-osteoporotic drugs. (*Source: BMJ. 2021;375:n2364.*)

### Problem of Diabetes Making Africa More Vulnerable to COVID Deaths: WHO

The WHO has stated that death rates from COVID-19 are much higher in diabetes patients in Africa, where the number of people with diabetes is increasing fast.

An analysis of data from 13 countries in Africa noted that there was a case fatality rate of 10.2% in COVID-19 patients with diabetes, in comparison with 2.5% for COVID-19 patients overall. WHO Regional Director for Africa, Matshidiso Moeti, said that COVID is giving a clear message - fighting the diabetes epidemic in Africa is as significant as the fight against COVID-19. As per the health agency, about 70% of people with diabetes in Africa were not aware that they had the disease.

The International Diabetes Federation estimates that the number of people with diabetes in Africa may reach 55 million by 2045, up from 24 million this year… (*Source: Reuters*)

### Multivitamins Associated with Slowed Brain Aging

According to new research presented at the 14th Clinical Trials on Alzheimer's Disease (CTAD) conference, a daily multivitamin taken for 3 years is tied to a 60% slowing of cognitive aging. Additionally, the effects were particularly marked in patients with cardiovascular disease (CVD). The COSMOS-Mind study also looked at the effect of cocoa flavanols but found no beneficial effect. This is a substudy of a large parent trial that compared the effects of cocoa extract (500 mg/day cocoa flavanols) and a multivitamin-mineral (MVM) with placebo on cardiovascular and cancer outcomes in over 21,000 older participants.

The COSMOS-Mind study included 2,262 adults, 65 years of age and above, without dementia. The participants underwent cognitive testing at baseline and every year for 3 years. While there was no effect of cocoa on global cognitive function, there was a positive effect of multivitamins for the active group compared to placebo, peaking at 2 years… (*Source: Medscape*)

### Fortified Baby Formulas Provide No Long-term Cognitive Benefit

Infants raised on fortified formula milk were found to have no added advantage in academic performance as adolescents, noted researchers in England.

There were no significant differences in the UK math exam scores in students at age 16 who had participated in clinical trials comparing formulas fortified with long-chain polyunsaturated fatty acids (LC-PUFAs), iron or nutrients, with standard formulas, as infants. Instead, there was a slight reduction in academic performance in children at 11 years of age who were randomized to receive LC-PUFA-supplemented formula, noted the study.

The study pooled data from seven randomized clinical trials conducted between 1993 and 2001. The findings are published in the *BMJ*… (*Source: Medpage Today*)

### Specific BP-lowering Medications Prevent Onset of New Diabetes

Lowering blood pressure (BP) can prevent the onset of diabetes; however, the effects may vary according to the antihypertensive drug class, suggests a meta-analysis.

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB) have the strongest association with prevention of diabetes onset, while β-blockers and thiazide diuretics appear to be tied to an increased risk of new-onset diabetes, noted the analysis published in *The Lancet*. It suggests that besides the well-known beneficial effects of reducing cardiovascular events, BP-lowering can also help prevent diabetes, noted Milad Nazarzadeh and colleagues with the Blood Pressure Lowering Treatment Trialists' Collaboration. The varying effects of the drug classes help decision-making for antihypertensive drug choice based on an individual's risk profile, noted investigators… (*Medscape*)

### Sarcoma Patients have High COVID-19 Complication Rates

Patients with sarcoma, especially those with high-risk factors, had a higher likelihood of developing complications from COVID-19, noted a registry-based retrospective study.

About 49% of the patients included in the study were hospitalized with COVID-19, and 9% died within 30 days of diagnosis, reported Michael Wagner of the University of Washington and Seattle Cancer Care Alliance, at the virtual Connective Tissue Oncology Society annual meeting. One-third of these patients were given supplemental oxygen, 12% were admitted to the ICU and 6% needed mechanical ventilation. Additional follow-up revealed that 16% had died due to any cause. The factors that were most associated with poor outcomes included Eastern Cooperative Oncology Group (ECOG) performance status (≥2 vs. 0) with an adjusted odds ratio (aOR) of 17.28, metastatic cancer to the lung vs. no metastatic cancer with aOR 7.65, other metastatic cancer vs. no metastatic cancer with aOR 4.28, pre-existing renal disease with aOR 3.33 and male sex with an OR of 2.13… (*Source: Medpage Today*)

# What are Satvik Offerings in Vedic Literature?

- **Food offerings:** Panchashasha (grains of five types – brown rice, mung or whole green gram, til or sesame, mashkalai (white urad dal) or any variety of whole black leguminous seed, jowar or millet).
- **Panchagobbo:** Five items obtained from cow (milk, ghee or clarified butter, curd, cow dung and gomutra), curd, honey, brown sugar, three big noibiddos, one small noibiddo, three bowls of madhupakka (a mixture of honey, curd, ghee and brown sugar for oblation), bhoger drobbadi (items for the feast), aaratir drobbadi mahasnan oil, dantokashtho, sugar cane juice, an earthen bowl of atop (a type of rice), til oil (sesame oil).
- **Water offerings:** Ushnodok (lukewarm water), coconut water, sarboushodhi, mahaoushodhi, water from oceans, rain water, spring water, water containing lotus pollen.
- **Three aashonanguriuk** (finger ring made of kusha).
- **Puja Items:** Sindur (vermillion), panchabarner guri (powders of five different colors – turmeric, rice, kusum flowers or red abir, rice chaff or coconut fiber burnt for the dark color, bel patra or powdered wood apple leaves), panchapallab (leaves of five trees – mango, pakur or a species of fig, banyan, betel and Joggodumur or fig), pancharatna (five types of gems – gold, diamond, sapphire, ruby and pearl), panchakoshay (bark of five trees – jaam, shimul, berela, kool, bokul powdered in equal portions and mixed with water), green coconut with stalk, three aashonanguriuk (finger ring made of kusha).
- **Panchamrit:** A mixture of honey, milk, curd, ghee and brown sugar.

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## BP Control Rates Declined During Pandemic

The proportion of hypertensive patients with BP control declined considerably in the United States during the COVID-19 pandemic, provided the data from 24 health systems in the country is representative of national trends. The fall in BP control corresponded with a decline in follow-up visits for uncontrolled hypertension from the same data source, stated investigators. The BP Track study collected electronic medical data of around 1.8 million patients with hypertension between 2017 and 2020. Till the end of 2019 and before the pandemic started, a little less than 60% of the patients had BP control (BP <140/90 mmHg). When assessed from the start of the pandemic until the end of last year, the proportion of patients with BP under control declined by 7.2%, to just above 50%. For the target BP of <130/80 mmHg, the proportion dropped 4.6% over the same period, with only about 25% at that level of control. The findings were presented at the American Heart Association scientific sessions… (*Source: Medscape*)

## Hypertension is a Risk Factor for Epilepsy

Hypertension increases the risk of developing epilepsy, suggests a new study reported in the journal *Epilepsia.*

The study examined the role of modifiable vascular risk factors in predicting subsequent epilepsy among participants aged 45 years or older in the Framingham Heart Study (FHS). The number of participants enrolled in the study was 2,986 with a mean age of 58 years. The vascular risk factors included diabetes mellitus, hypertension, hyperlipidemia and smoking.

At the end of the follow-up period of 19 years, 55 patients developed epilepsy. Among the risk factors evaluated, hypertension was found to almost double the risk of developing epilepsy (hazard ratio [HR] 1.93). Secondary analysis of data after exclusion of participants with normal BP on antihypertensive drugs showed a 2.44-times higher association of hypertension with epilepsy (50 new epilepsy cases). Hypertension is a modifiable risk factor for CVDs and diabetes. It is now also a risk factor for epilepsy in older age, as is evident from this study. Hypertension is a very widely prevalent condition. Aggressive management can not only reduce the chances of heart diseases and diabetes, but also epilepsy. (*Source: Epilepsia. 16 November 2021. https://doi.org/10.1111/epi.17108*)

**INSPIRATIONAL STORY**

# Life is a Gift

Before you think of saying an unkind word – think of someone who is not even able to speak. Before you complain about the taste of food today – think of someone who has nothing to eat.

Before thinking of complaining about your spouse – think of someone who does not have a companion. Before complaining about life – think of someone who left this world too early.

Before complaining about your children – think of someone who cannot have children of their own. Before complaining about your dirty house because someone didn't clean or sweep – think of those living in the streets.

Before complaining about the distance you have to drive – think of someone who walks that distance with their feet. Before you complain about your job – think of the unemployed and those who wished they had your job.

Before pointing a finger at someone – remember no one is are without sin. Before depressing thoughts overpower you and get you down – smile and thank God you're alive.

*Life is a gift. Live it to the fullest, enjoy it, celebrate it.*

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### Coffee and Tea could be Linked to a Lower Risk of Stroke, Dementia

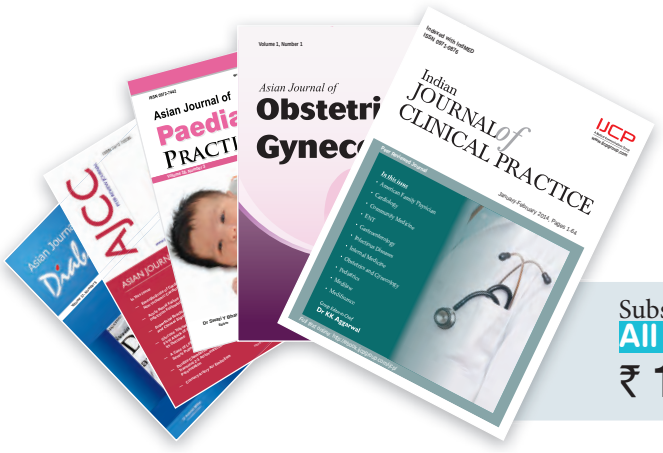
In a new study of over 3,60,000 participants evaluated for 10 to 14 years, people who drank 2 to 3 cups of coffee, 3 to 5 cups of tea, or 4 to 6 cups of coffee or tea combined in a day, were noted to have the lowest risk of stroke and dementia. The authors stated that moderate consumption of coffee and tea, individually or in combination, could reduce the risk of stroke and dementia. Individuals who drank 2 to 3 cups of coffee and 2 to 3 cups of tea a day, which amounts to a total of 4 to 6 cups, had the best outcomes. They had a 28% lower risk of dementia and 32% lower risk of suffering a stroke, compared to people who didn't consume either of the two beverages, reported the authors… (*Source: CNN*)

### Screening School Children for Depression

School-based screening can successfully identify students with symptoms of major depressive disorder (MDD) and help them begin treatment, according to a randomized clinical trial published in *JAMA Network Open*.

Researchers from the Penn State College of Medicine and Penn State PRO Wellness conducted a study to examine the impact of school-based screening on diagnosis of depression. The 3-year study enrolled 12,909 students from 9th to 12th grades attending 14 public high schools in Pennsylvania. Many of the students in the study were from lower socioeconomic status. A questionnaire was used to screen students for symptoms of depression. Either 9th and 11th grades or 10th and 12th graders underwent universal screening, while the other grades were assigned to targeted screening. Compared to usual targeted student referral based on observed behaviors of concern, students who were assigned to universal screening were nearly six times more likely to have symptoms of MDD and twice more likely to start treatment for MDD. The prevalence of symptoms of depression was higher in girl students and minority students, although not many of them started treatment for their symptoms.

This study has public health implications. Mental health problems often begin from a very early age. There is now evidence to show that even children suffer from depression, which affects their academic progress. Quite often, only targeted screening of children, mostly at the doctor's clinic, is done. However, this randomized controlled trial has shown that universal screening of school children for symptoms of depression was able to successfully pick up cases of adolescent depression, who would otherwise fall through the cracks and increased the chances of initiating treatment of MDD. Screening for vision and hearing is routinely done for school children. Similarly, they should also be screened for symptoms of depression. Instead of relying only on physician diagnosis, a school-based screening program can be a more effective approach. (*Source: JAMA Netw Open. 2021;4(11):e2131836.*)



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# Lighter Side of Medicine

HUMOR

## A NICE BOY?

One night a teenage girl brought her boyfriend home to meet her parents, and they were appalled by his appearance: leather jacket, motorcycle boots, tattoos and pierced nose.

Later, the parents pulled their daughter aside and confessed their concern. "Dear," said the mother diplomatically, "he doesn't seem very nice."

"Oh please, Mom," replied the daughter, "if he wasn't nice, why would he be doing 500 hours of community service?"

## TELL HIM I CAN'T SEE HIM

The nurse came in and said, "Doctor, there is a man here who thinks he's invisible."

The doctor said, "Tell him I can't see him."

## COMPUTER POWER

A man dragged himself home and dropped his chair.

His wife was standing there with a cool drink and a comforting word.

"You look tired," she said. "It must have been a hard day. What happened to make you so exhausted?"

"It was terrible," the man said, "The computer broke down and all of us had to do our own thinking."

## HOW DO YOU START A FLOOD?

A doctor had bought a villa on the French Riviera. He met an old lawyer friend whom he hadn't seen in years.

The lawyer had also bought a nearby villa. They discussed how they came to live at the Riviera. The lawyer said that the office complex he had bought caught fire, and he retired there with the fire insurance proceeds.

The doctor said that he had bought real estate in Mississippi. But the river overflowed, and he came to the Riviera with the flood insurance proceeds. He said that it was amazing how both of them ended up there in similar ways.

The lawyer looked puzzled and asked, "How do you start a flood?"

## IDENTITY

A little girl, when asked her name, would reply, "I'm Mr Sugarbrown's daughter."

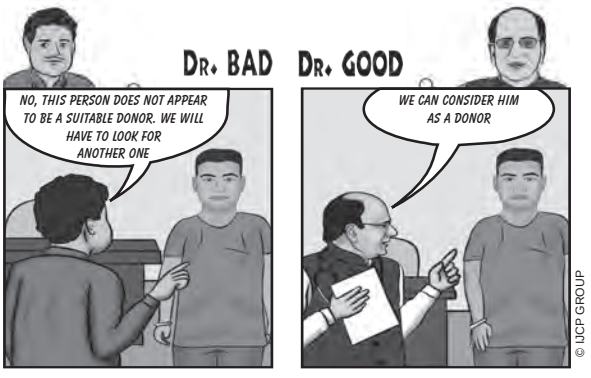
Her mother told her that must say, "I'm Jane Sugarbrown."

The Vicar spoke to her in Sunday School and said, "Aren't you Mr Sugarbrown's daughter?"

She replied, "I thought I was, but her mother says she's not."

## Dr. Good and Dr. Bad

**SITUATION:** A patient who had to get corneal transplantation done told the doctor that he was getting a donor who had insulin-dependent diabetes mellitus and medical complications resulting from the disease.




**LESSON:** Although corneas from donors with insulin-dependent diabetes mellitus and medical complications resulting from the disease have lower mean values of endothelial cell density in contrast to other donors, a retrospective review has suggested that corneas of these people are equally likely to be included in the donor pool for corneal transplantation.

*Cornea. 2017;36(5):561-6.*

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

### Books

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

### Articles in Books

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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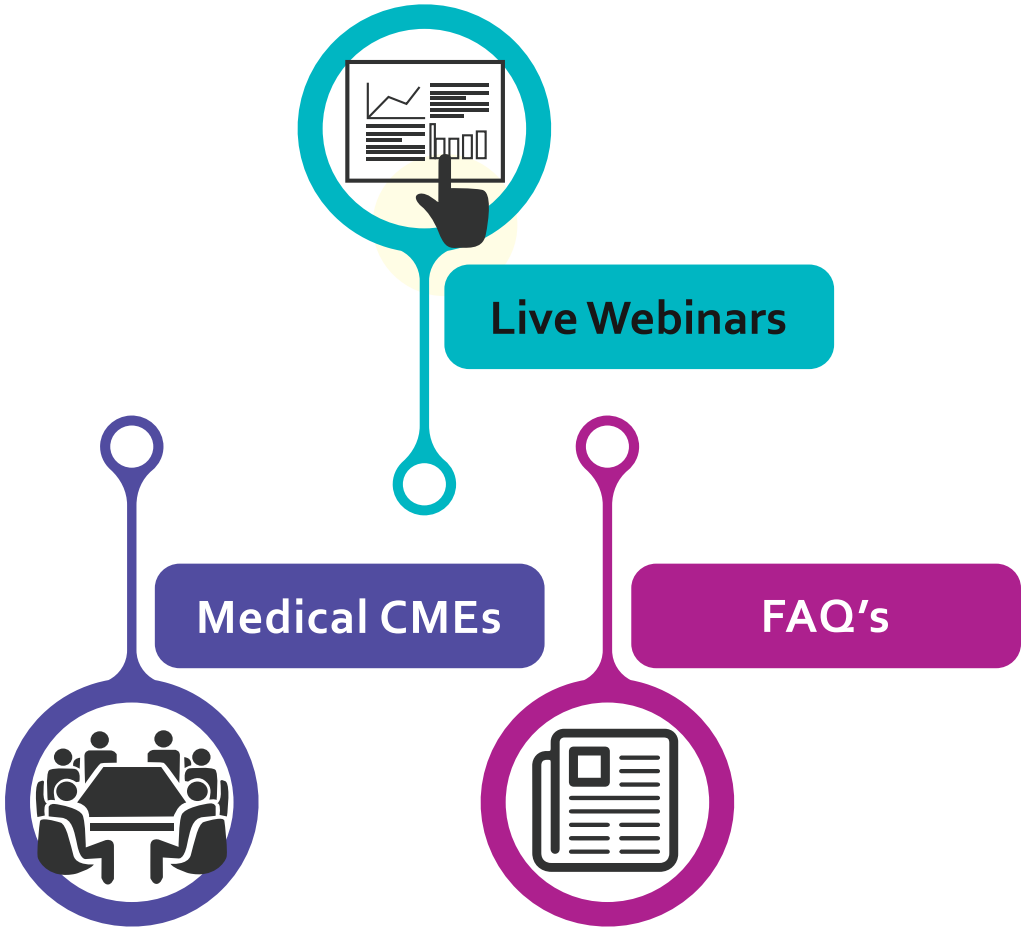


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