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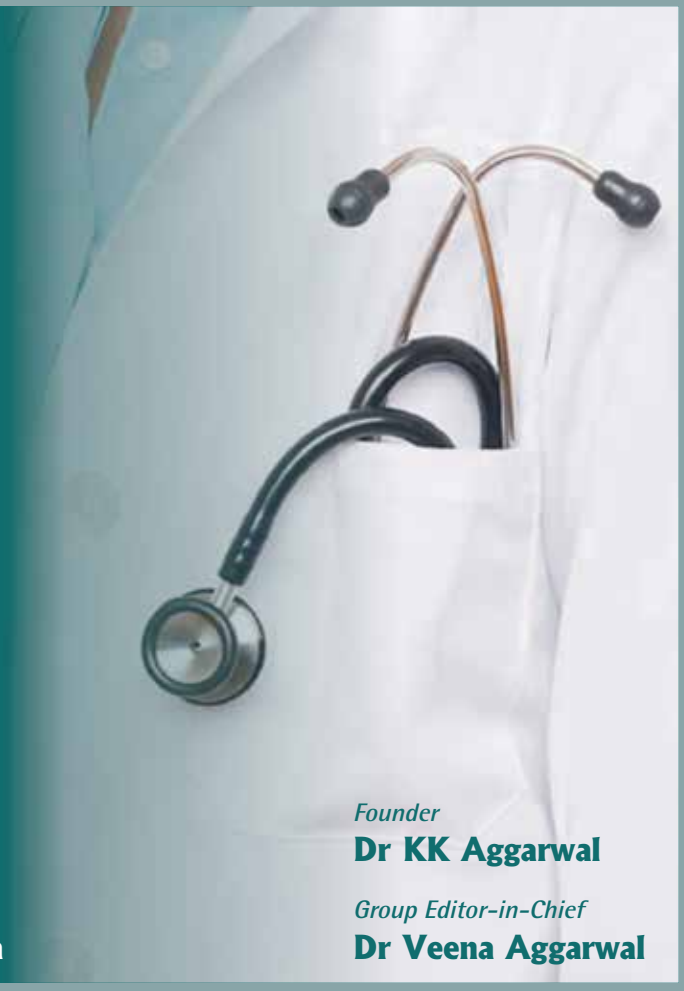

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EDITORIAL

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Hyperemesis Gravidarum: A Novel Risk Factor for Heart Disease?

Women with hyperemesis gravidarum or extreme morning sickness during pregnancy are at higher risk of developing cardiovascular disease (CVD) necessitating hospital admission in the long-term compared to women without hyperemesis, suggests a study of over 1.4 million women from Canada published in the *Journal of the American Heart Association.*[1] Women who had both hyperemesis and pre-eclampsia had the highest risk.

To investigate the risk of future CVD in women with hyperemesis gravidarum with or without pre-eclampsia, data of 1,413,166 pregnant women in Quebec between 1989 and 2021 was analyzed in this retrospective study. Out of these, 16,288 (1.2%) had hyperemesis gravidarum, 69,645 (4.9%) had pre-eclampsia, while 1,103 (0.08%) had both the conditions during pregnancy.

All women were followed from their first pregnancy up to 3 decades later. The authors found that the incidence of CVD was 17.7 per 100 women among those who had hyperemesis gravidarum only when they were pregnant with adjusted hazard ratio (aHR) of 1.46, 28.2 per 100 women among those with pre-eclampsia only (aHR 2.58) and 30.9 per 100 women in those with both the conditions (aHR 3.54). Among women who had neither hyperemesis gravidarum or pre-eclampsia, the incidence of CVD was 14.0 per 100 women.

Women who had both the conditions during pregnancy were 3.5 times more likely to be hospitalized because of cardiac causes with HR of 3.54. The risk of hospitalization was more than doubled among women with pre-eclampsia with HR of 2.58, whereas in those with hyperemesis only, the HR was 1.46. A strong association with valvular heart disease (HR, 3.38), heart failure (HR 3.43) and cardiomyopathy (HR 4.17) was noted in the group with both hyperemesis gravidarum and preeclampsia.

The study concluded that hyperemesis gravidarum is linked to long-term CVD regardless of presence or absence of pre-eclampsia. While hyperemesis gravidarum was associated with an increased risk of nonischemic disorders such as heart failure and valve disease, no association was noted for ischemic heart disease such as myocardial infarction, stroke.

Hence, hyperemesis gravidarum may be considered as a novel pregnancy-related risk cardiovascular factor in cardiovascular guidelines especially for CVD of nonischemic origin, according to the authors. These women, in particular women with coexisting hyperemesis gravidarum and pre-eclampsia, merit close monitoring over the years to prevent cardiovascular events. They should also be encouraged to lead a heart-friendly lifestyle after childbirth.

REFERENCE

1. Cécile B, Potter BJ, Lewin A, Healy-Profitós J, Brousseau É, Auger N. Risk of cardiovascular disease in women with a history of hyperemesis gravidarum, with and without preeclampsia. J Am Heart Assoc. 2023;12(11):e029298.

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Biosimilars and Generics: A New Class Needed for Hormonal and Herbal Preparations

ABSTRACT

Strict regulations are in place for the manufacture and approval of pharmaceutical products. Specific drugs such as biological products are governed by specific rules, which take cognizance of the extra diligence required for their production. This communication describes two classes of drugs: hormones and herbal products, which should be subject to stringent regulations. It explains the rationale behind this, and calls for added vigilance in regulatory oversight.

Keywords: Estrogen, good manufacturing practice, herbal products, hormones, pharmacovigilance, phytopharmaceutical, thyroxine

A vast multitude of pharmaceutical preparations exists today. With advances in technology, and with expanding industrial capacity, this number is increasing day by day. Regulatory authorities across the world try to keep pace with evolving needs and requirements by updating their guidance.

One such trend has been noted in the approval mechanism for biosimilars and generics. Classification of drugs as generics and biosimilars serves to differentiate chemical entities from biological products.[1,2] This ensures that entities such as insulin, erythropoietin and monoclonal antibodies undergo a relatively stringent process of approval. While this is welcome, there is a need for a more comprehensive rubric to classify various drugs.

HORMONES

Various hormones and hormone mimetics used in the management of disease are classified as generic drugs; however, their production (manufacture), preparation (formulation) and presentation (storage) require specific and stringent conditions. These safeguards are necessary to ensure efficacy as well as safety. The production of some hormones may lead to an endocrine disruptor effect, as metabolites of androgens and estrogens may act as endocrine disruptor chemicals if released into the environment.[3] All tablets need excipients for stability, and some of these may be associated with adverse events. Thyroxine should be stored at a temperature not exceeding 25°C, and should be protected from light and moisture. Similar advice is suggested for desmopressin acetate.[4]

It makes sense, therefore, to reclassify hormones as non-generic drugs. Suggested terminologies, such as **steroid similars** (for dydrogesterone), **peptide products** or **peptide pills** (for desmopressin, semaglutide) **endocrine elixirs** (liquid thyroxine), **endocrine extracts** (desiccated thyroid extract) or **hormonal generics**, may help differentiate these medicinal products from simpler chemical entities (like paracetamol, for example), and allow tighter regulatory control.

This is important for both public health as well as individual clinical care. Stricter regulation will ensure avoidance of possible endocrine disruption at the manufacturing and distribution level, as well as ensure

Table 1. Precision and Perfection in Hormonal Products

- Pedigree: quality of manufacturing unit
- Procurement (of raw materials): from quality controlled sources
- Preparation: in uniform manner, following good manufacturing practices (GMP)
- Presentation: in environment-proof packaging

optimal cold chain networks. Most hormones have a narrow therapeutic index, (and are therefore known as Goldilocks hormones).[5] Separate rules for regulatory approval will ensure that no substandard medications reach the public.

Particular attention should be paid to steroid hormones (dydrogesterone, micronized progesterone) and to peptides (desmopressin) while crafting new processes. Newer guidance should also keep in mind novel methods of formulation such as nanotechnology,[6] which may influence the quality of hormonal medicinal products (Table 1).

HERBAL PRODUCTS

Another class of drugs, which needs regulatory advice is herbal products. Traditionally phytopharmaceuticals are regarded as safe, and are not subject to rigorous oversight. However, these too, are biological products, just as insulin and erythropoietin. This means that the concepts of biosimilarity and interchangeability, which apply to such medicines, should be applicable to herbal products or phytopharmaceuticals as well.

While multiple formulations of botanical extracts are available in the Indian market, it is doubtful that they will demonstrate equivalence in terms of pharmacodynamic or pharmacokinetic profiles.[7] In fact, the inter-batch variability in phytopharmaceuticals is difficult to control even within the same manufacturing unit. This calls for a specific terminology for these medicinal products, too. 'Botanical biosimilars' or 'mineral-based medicinal' mimetics may be used to differentiate these from simpler chemical entities, which can continue to be called generics.

SUMMARY

Our regulatory authorities exhibit a proactive and dynamic approach towards keeping their policies updated in tune with advances in the pharmaceutical and clinical arena. Attention needs to be paid, however, to various hormonal and phytopharmaceutical preparations, which have been currently re-clubbed in the 'generic' class of generic drugs. Understanding the heterogeneity of hormones, the nuances involved in their manufacture and the necessity for precise delivery of accurate dosage, will facilitate perfection in the process of endocrine drug development and marketing. This will be a valuable contribution towards achieving optimal endocrine health for all.

REFERENCES

1. Kalra S, Azad Khan AK, Raza SA, Somasundaram N, Shrestha D, Latif ZA, et al. Biosimilar insulins: informed choice for South Asia. Indian J Endocrinol Metab. 2016;20(1):5-8.
2. Dhamija P, Sharma PK, Kalra S. Only generics (drugs/names): Is India ready? Indian J Endocrinol Metab. 2015;19(5):541-5.
3. Sharma A, Mollier J, Brocklesby RWK, Caves C, Jayasena CN, Minhas S. Endocrine-disrupting chemicals and male reproductive health. Reprod Med Biol. 2020;19(3):243-53.
4. Kalra S, Zargar AH, Jain SM, Sethi B, Chowdhury S, Singh AK, et al. Diabetes insipidus: the other diabetes. Indian J Endocrinol Metab. 2016;20(1):9-21.
5. Santoro N. Follicle stimulating hormone: the Goldilocks hormone, too little, too much, just right. Fertil Steril. 2023;119(2):165.
6. Sertova MN. Contribution of nanotechnology in animal and human health care. Advanced Materials Letters. 2020;11(9):1-7.
7. Gouws C, Hamman JH. What are the dangers of drug interactions with herbal medicines? Expert Opin Drug Metab Toxicol. 2020;16(3):165-7.

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CLINICAL STUDY

Assessing the Prevalence of Age-related Enzyme Deficiency in Indian Population and the Efficacy of Supplementing with a Combination of Alpha-Amylase and Papain Enzyme in this Population

KRISHNA DEEPAK SATHIRAJU

ABSTRACT

Background: Enzymes are crucial for proper bodily functions, but as individuals age or experience medical conditions, their levels decrease, leading to several health issues most common being the gastrointestinal (GI) problems like dyspepsia, constipation and irritable bowel syndrome (IBS). The study assessed age-related enzyme deficiency in the Indian population and investigated the effectiveness of a combined supplementation of alpha-amylase and papain enzymes. **Methods:** The study was a retrospective study in July 2023 used a questionnaire-based survey to assess the prevalence of age-related enzyme deficiency in Indian population and the efficacy of supplementing with a combination of alpha-amylase and papain enzyme in this population. The study used a validated questionnaire with 18 questions, and data was entered into a software database. Complete cases were analyzed, and missing data was excluded due to low occurrence. The final report was prepared after cleaning the data. **Result:** The study included 134 doctors from various medical specializations. Results showed that the majority of doctors were GI specialists, with the highest frequency of patients with age-related enzyme deficits in the 40 to 60 years age groups (55.2%). The combination of alpha-amylase and papain was found to relieve proton pump inhibitor (PPI) overuse adverse effects. The safety profile was neutral (64.9%), with 30.6% stating it as safe and 2.2% as very safe. The combination was found to be neutral (48.5%), effective (45.5%) and very effective (3.7%), with age-related considerations being the main factor. Most doctors rated the combination as neutral (64.9%), with 29.1% giving a good rating and 5.2% giving a very good rating. **Conclusion:** In conclusion, this study sheds light on the prevalence of age-related enzyme deficiency in the Indian population and provides evidence for the potential efficacy of a combined alpha-amylase and papain enzyme supplement in addressing these deficiencies.

Keywords: Age-related enzyme deficiency, Indian population, efficacy, alpha-amylase, papain enzyme

Human aging occurs gradually over the years, and understanding age-related health concerns is crucial. Enzymes are essential for various physiological functions, such as digestion and food absorption. With age, enzyme aiding in these important physiological processes also decline. In India, people retire from work at age 60, marking the beginning of lesser physical activities and a more sedentary lifestyle, which in turn triggers age-related health issues.[1]

Aging is inversely correlated with increased physiological and organ-specific health issues, particularly noncommunicable ones. About 25% of patients have cardiovascular disease, while 20% have general colds, coughs, fever and gastrointestinal (GI) disturbances.[2]

Enzymes are crucial for the efficient functioning of the digestive, neurological and muscular systems.[3,4] However, some individuals low levels of digestive enzymes or experience improper enzyme release, leading to functional GI disorders such as constipation, dyspepsia and irritable bowel syndrome (IBS).[5-7] This has led to the overuse of proton pump inhibitors (PPIs), which increase the risk of infections, bone fractures and renal damage.[8,9]

Enzyme supplements therapy may be beneficial for these malabsorption of nutrients and GI infections, providing relief from acid reflux, gas, bloating and diarrhea while also assisting the body's digestion and nutrient absorption.[9]

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Amylase, protease, lactase, lipase, diastase and papain are important digestive enzymes. Several instances have been reported in which the administration of enzymes has proved effective.

Amylase, a crucial enzyme for metabolizing starch produced in the pancreas and saliva, speeds up the digestion process and helps relieve from constipation and other GI diseases.[10] Amylases break down starch into smaller molecules, producing maltose, which is then broken down by maltase into two molecules of glucose. To continue breaking down the incoming starch, a lot of pancreatic amylase is delivered into the duodenum via the pancreatic duct.[11]

It can be elevated in pancreatic illness, salivary disease, reduced metabolic clearance, intestinal disease, macroamylasemia and lowered in disorders such as pancreatic damage, injury, nephropathy, pregnant toxemia and pancreatic cancer.[12,13]

Papain is one of the best and most potent digestive enzymes, helping to break down even the most resistant protein fibers and relieve IBS symptoms, reducing inflammation and expediting healing following surgery. The declining levels of the digestive systems reduce digestive efficiency, leading to various health problems.[14]

Functional dyspepsia (indigestion) is typically treated with medications that reduce the production of acid, such as PPIs and H2-receptor antagonists. Long-term use of PPIs increases the risk of dementia, enteroendocrine tumors of the digestive tract, kidney, liver and cardiovascular disease, as well as the susceptibility to respiratory and GI infections and decreased nutrient absorption.[15,16]

Postprandial digestive symptoms such as diarrhea, abdominal distension, flatulence, bloating and fullness sensation are frequent complaints with unidentified etiology and pathophysiology. Numerous studies have documented the beneficial effects of products containing various combinations of digestive enzymes.[17]

Ayurvedic medicine favors the use of papaya fruit containing papain as digestives and stomachics and its latex to relieve from dyspepsia. Papain preparation significantly reduced constipation, painful, difficult stool motions and flatulence in 139 volunteers with functional GI complaints compared to placebo.[18]

This study aims to determine the prevalence of age-related enzyme deficiency in the Indian population and evaluate the efficacy of alpha-amylase and papain enzyme supplementation in treating GI disorders. It also explores physicians' opinions and experiences regarding the combination of alpha-amylase and papain enzyme in treating these disorders.

METHODS

Study Design and Setting

The study was a retrospective study conducted via a questionnaire-based survey among all doctors in July 2023. It is a mixed-method study to assess the prevalence of age-related enzyme deficiency in Indian population and the efficacy of supplementing with a combination of alpha-amylase and papain enzyme in this population.

Study Population

All qualified doctors (General Physicians, Consulting Physicians, Dietician, Gastroenterologists, Endocrinologists, etc.) practicing modern medicine were eligible for the survey and were approached to participate. The survey intended to include doctors across all clinical departments, work experience and professional hierarchy. In this study, 134 Indian doctors participated in the questionnaire survey on use of the prevalence of age-related enzyme deficiency in Indian population and the efficacy of supplementing with a combination of alpha-amylase and papain enzyme in this population.

Data Collection

The survey tool was a validated questionnaire containing 18 questions. It was in the form of a closed-ended questionnaire, was developed by an expert panel comprising a physician, and a pharmacologist. The questionnaire was specifically focused on the study aims and tailored contextually to fit local situations.

All filled forms were entered into the software database. For discrepancies related to data entry alternate forms were physically cross-checked. Complete cases were analyzed and missing data were not included because of low occurrence. The data were analyzed after cleaning the data and final report was prepared.

RESULTS

A total of 134 doctors from different medical specialization participated in the study with an aim to assess age-related enzyme deficiency in the Indian population and investigate the effectiveness of a combined supplementation of alpha-amylase and papain enzymes. Approximately 54.5% of them were Gastroenterologists, followed by General Physician (38.1%) and the rest together made up 7.4% (Fig. 1).

The doctors reported that the percentage of frequency of patients who came with age-related enzyme deficits sometimes was the highest (55.2%) (Fig. 2) and was most prominent (69.4%) in the age group 40 to 60 years, followed by people who were 60 years and above (29.9%) as seen in Figure 3.

As the Figure 4 depicts, 48.5% doctors were moderately familiar with the combination of alpha-amylase and papain as a treatment option for dyspepsia, functional GI disorders or age-related disorders, followed by 23.9% doctors who were somewhat familiar and 23.1% doctors who were very well familiar with the benefits of the combination.

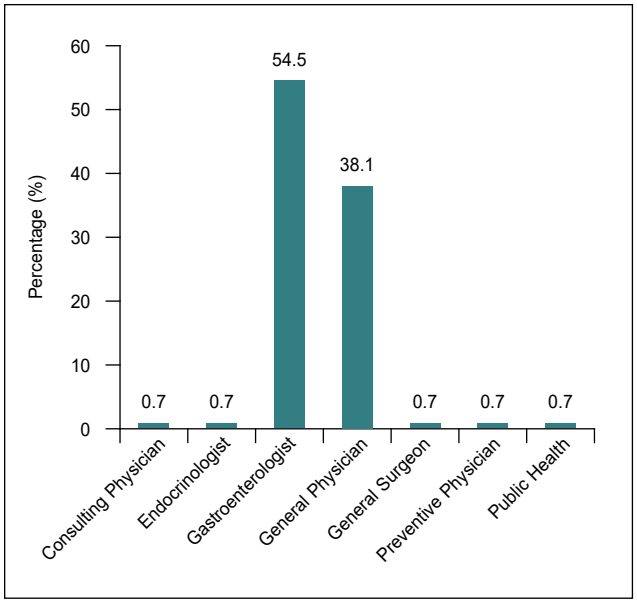

Figure 1. Percentage of doctors from different medical specialization participating in the study.

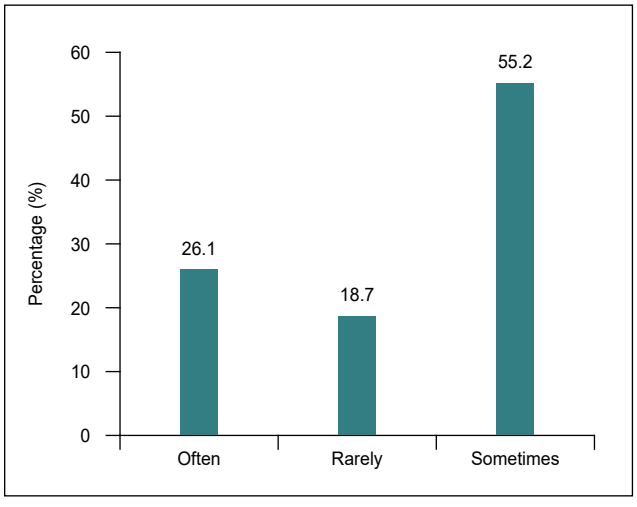

Figure 2. Frequency of patients with age-related enzyme deficits reporting to doctors.

Nearly 83.6% of doctors agreed with the fact that combination of alpha-amylase and papain can be helpful in relieving PPI overuse adverse effects such as GI disorders and malabsorption of several nutrients compared to 16.4% doctors who did not as visible from the graph in Figure 5.

Figure 6 shows that majority of doctors prescribing the combination of alpha-amylase and papain was moderately often (57.5%), followed by prescribing frequently (17.9%), then occasionally (14.2%).

As observed in Figure 7, patient preferences is the most important factor (53.7%), followed by efficacy (24.65%), cost-effectiveness (12.75) and safety profile (8.2%) being the other factors influencing the doctors decision to prescribe the combination of alpha-amylase and papain.

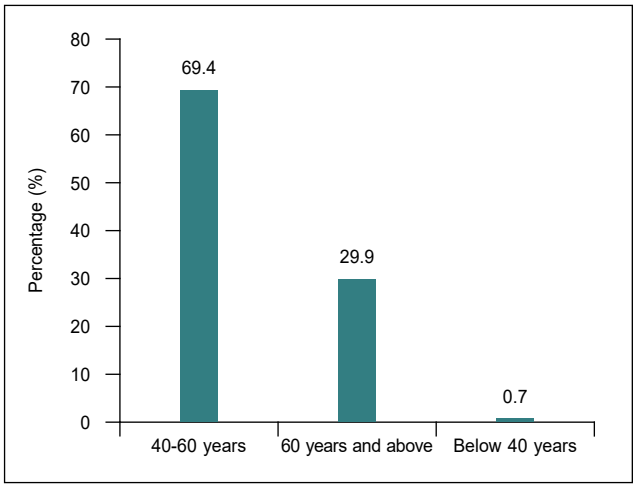

Figure 3. Age group of patients having prevalent digestive problems.

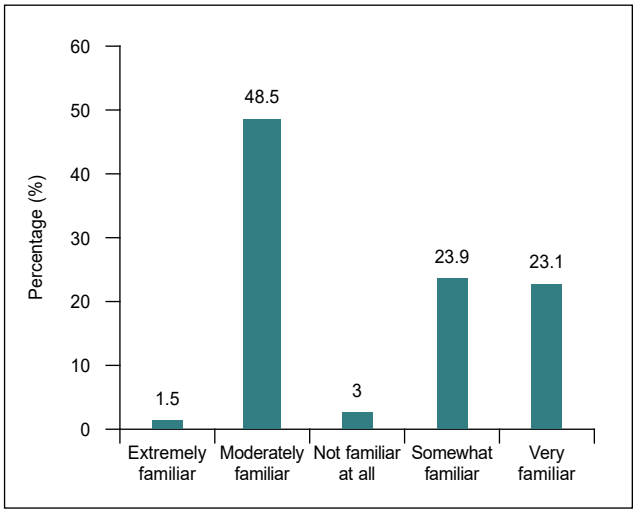

Figure 4. Familiarity with the combination of alpha-amylase and papain as a treatment option for dyspepsia, functional GI disorders or age-related disorders.

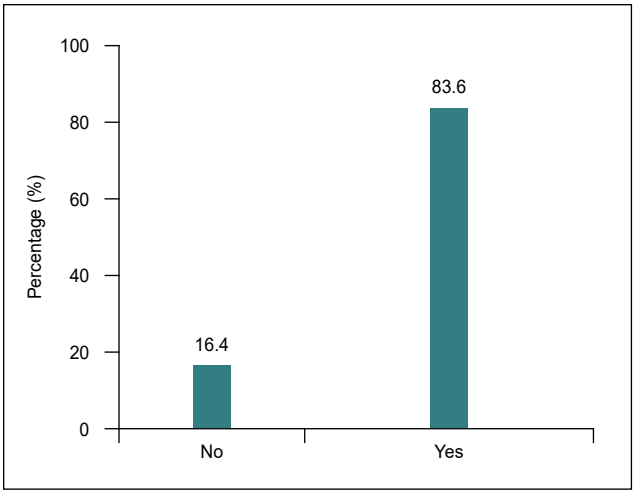

Figure 5. Usefulness of alpha-amylase and papain combination in relieving PPI overuse adverse effects.

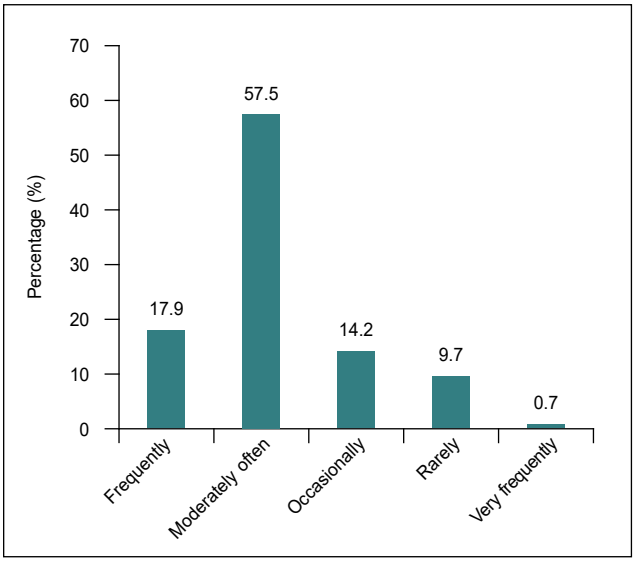

Figure 6. Frequency of prescribing the combination of alpha-amylase and papain.

Safety profile was found to be neutral (64.9%) as agreed by majority of doctors, followed by 30.6% stating it as safe and 2.2% agreeing that the combination was very safe. Only 1.5% doctors had the view that it was unsafe as shown in Figure 8.

Majority of the doctors (98.5%) said that they did not encounter any adverse events or side effects in patients who were prescribed the combination of alpha-amylase and papain, as is evident in Figure 9. Only 1.5% stated that they had observed some minor side effects such as spasmodic pain as reported by some doctors.

The effectiveness of the combination of alpha-amylase and papain was shown in Figure 10. Mostly it was found to be neutral (48.5%), followed by effective (45.5%), then

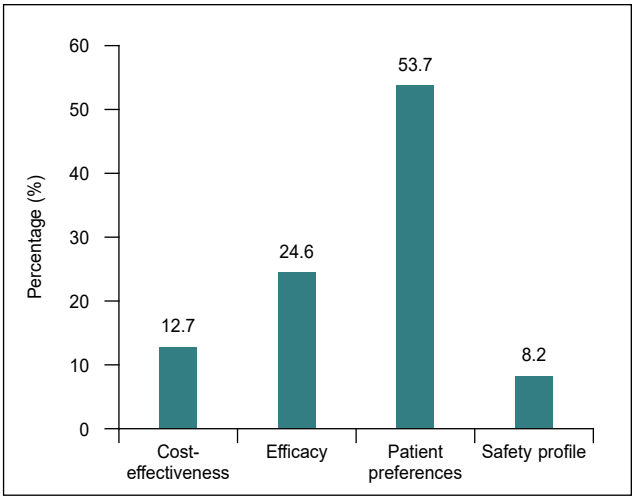

Figure 7. Factors influencing prescribing the combination of alpha-amylase and papain over other treatment options.

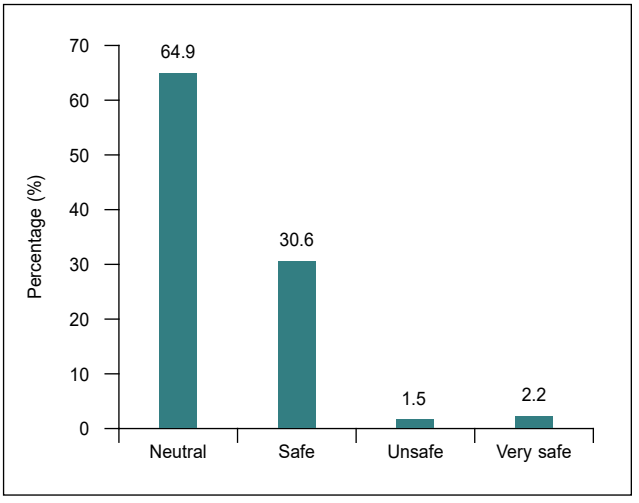

Figure 8. Safety profile of the combination of alpha-amylase and papain.

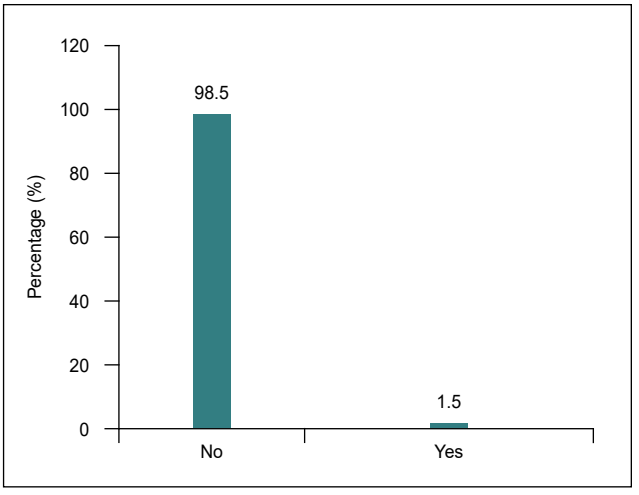

Figure 9. Response-related to encountering any adverse side effects.

very effective (3.7%), while only 1.5% agreed that the combination had no effect.

The study in Figure 11 also showed that majority of doctors (46.3%) agreed that the effectiveness of the combination of alpha-amylase and papain compared to other combinations was equally effective, while 44.8% were not sure of the effectiveness compared to other combinations.

Figure 12 shows the suitability of the alpha-amylase and papain in elderly. It was seen that though 68.7% were not sure about the suitability in elderly 24.6% doctors agreed that the combination was helpful in elderly.

The study also highlighted the fact that age-related considerations were the main factor (59.7%), which the doctors considered when determining the chronic usage of the combination of alpha-amylase and papain in elderly patients, followed by patient compliance (28.4%) as shown in Figure 13.

The majority of doctors rated the combination as neutral (64.9%), while 29.1% gave a good rating with 5.2% giving a very good rating for the combination of alpha-amylase and papain as a treatment option for dyspepsia, functional GI disorders or age-related disorders as is evident in Figure 14.

Figure 15 showed the satisfaction level with the combination. Nearly 67.9% were moderately satisfied, while 30.6% were extremely satisfied.

Ninety-four percent of doctors agreed that they would suggest combination of alpha-amylase and papain to their co-workers or other medical professionals as a supplement for age-related enzyme deficiencies as is seen in Figure 16.

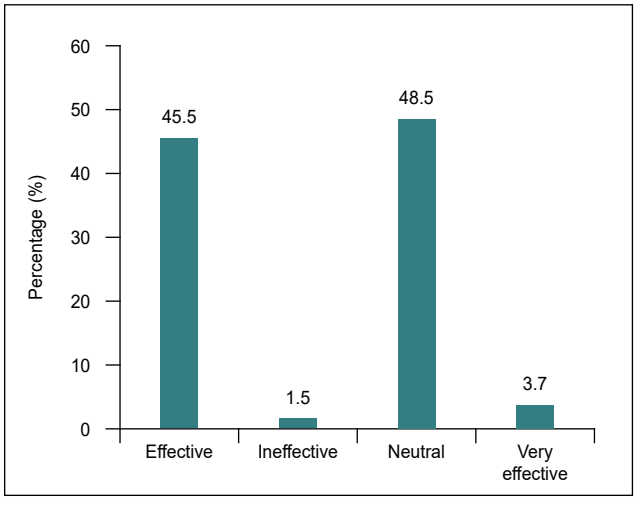

Figure 10. Efficacy of the combination of alpha-amylase and papain.

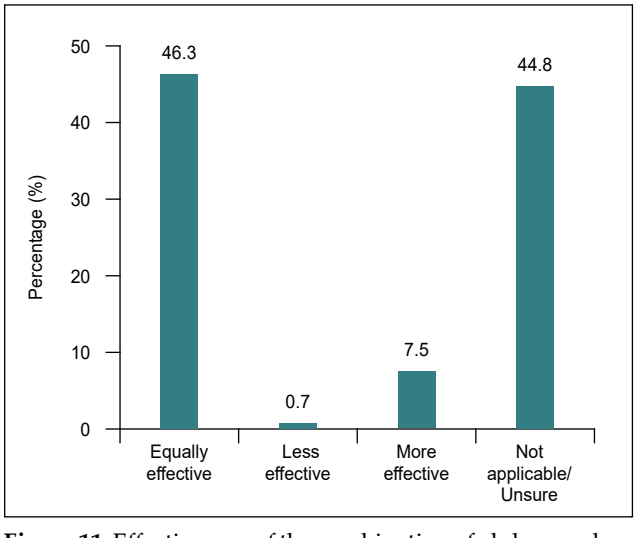

Figure 11. Effectiveness of the combination of alpha-amylase and papain compared to other combinations.

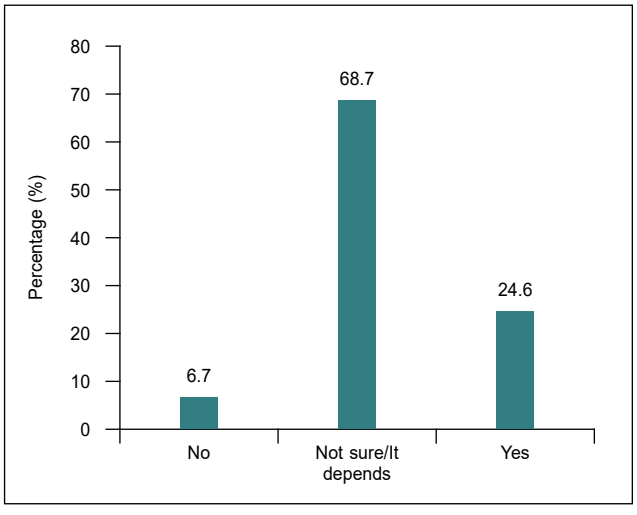

Figure 12. Suitability in the elderly population.

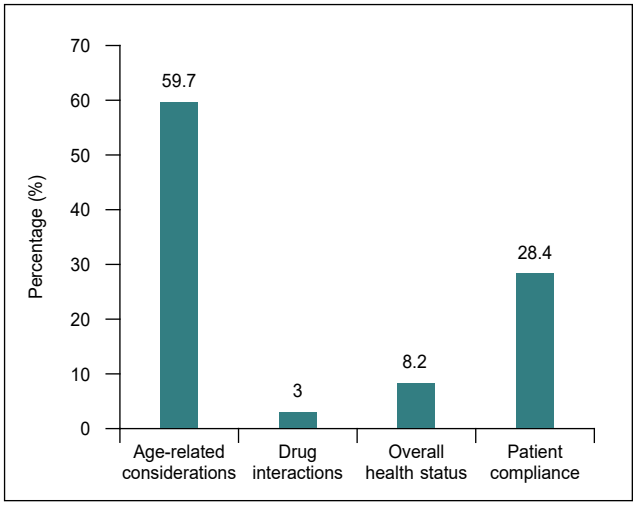

Figure 13. Factors determining the chronic usage.

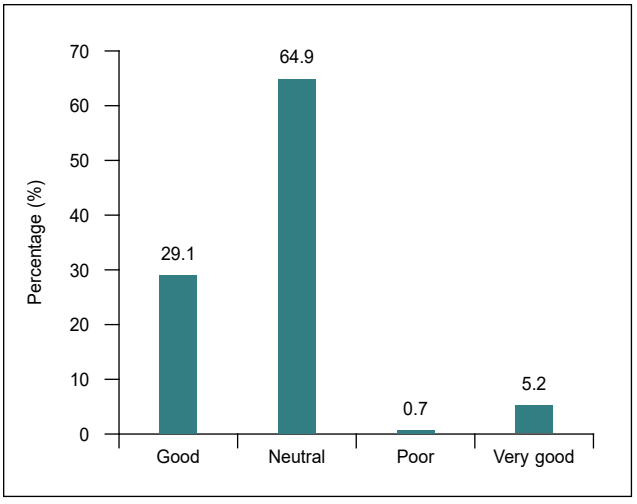

Figure 14. Rating the combination of alpha-amylase and papain.

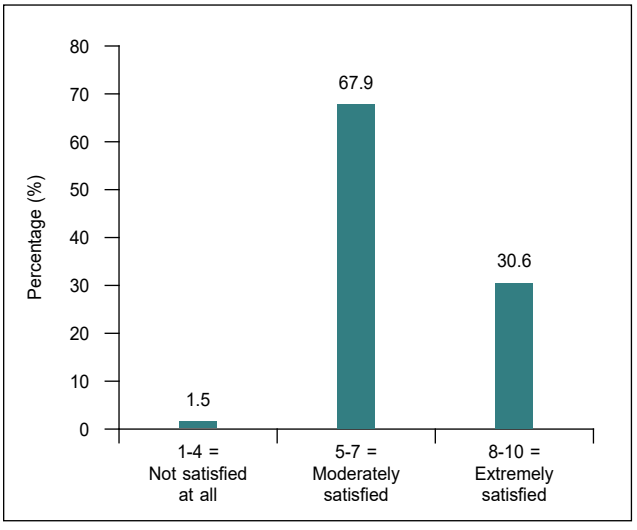

Figure 15. Satisfaction levels of doctor with the combination.

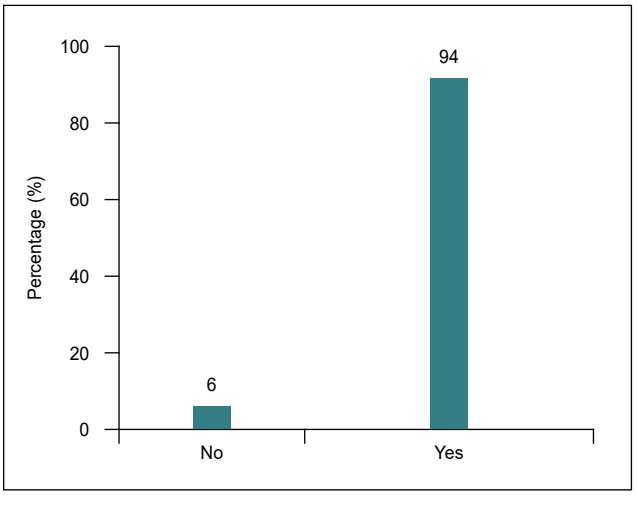

Figure 16. Percentage of doctors agreed to prescribe the alpha-amylase and papain combination to co-workers.

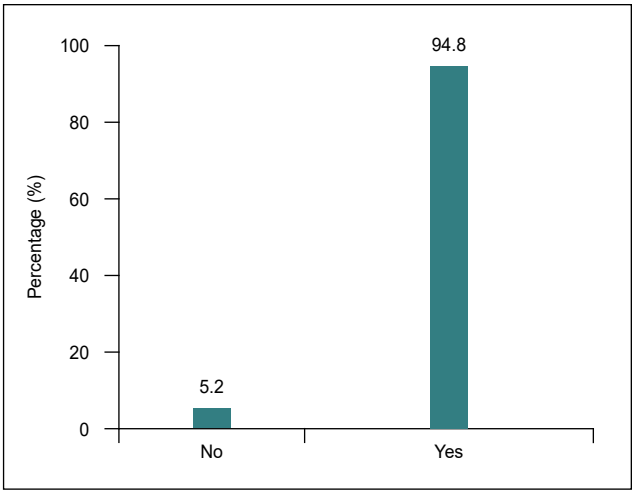

Figure 17. Percentage of doctor agreeing with the fact that the combination of alpha-amylase and papain aids faster recovery and overall well-being.

Finally, 94.8% doctors agreed that the combination of alpha-amylase and papain aids faster recovery and overall well-being as is observed in Figure 17.

DISCUSSION

The effectiveness of the digestive systems is reduced as we age, which causes a number of health issues. By the age of 40, the enzyme level in the digestive system may be around 25% lower, and by the ages of 60 or 70, it might be significantly lower. Basic functional GI illnesses like IBS, functional dyspepsia or functional constipation, among others, rise as a result of these declining enzyme levels.[19]

Mostly, it has been observed that patients visit Gastroenterologists due to unexplained abdominal pain.[20] The current study shows that 54.5% of the medical professionals participating in the study were Gastroenterologists showing that in the real-world scenario also patients mostly visit the Gastroenterologists, followed by General Physician (38.1%) and the rest together made up 7.4% (Fig. 1).

The prevalence of digestive problems (gastroesophageal reflux disease [GERD]) in large population-based studies in India is approximately 10% and is probably increasing due to lifestyle changes and altered eating habits and aging. Hence, the burden on Gastroenterologists and proper medication to treat these digestive problems is also increasing.[20]

Figure 2 demonstrates that the percentage of frequency of patients who came to doctors with age-related enzyme deficits. It was the highest (55.2%) in the sometimes or occasionally visits with the predominance (69.4%) in the

age group 40 to 60 years, followed by people who were 60 years and above (29.9%) as seen in Figure 3.

Literature shows that aging has an impact on all gastro-intestinal system (GIS) processes, including motility, enzyme and hormone production, digesting and absorption. The GIS is frequently impacted by side effects and is also crucial for the metabolism and absorption of medications.[21]

Digestion enzymes are heavily taxed by the traditional Indian diet, which is frequently abundant in complex carbohydrates and protein-rich meals. In India, the prevalence of GERD varies from 7.6% to 30%; it is often less than 10% in population studies and higher in cohort studies.[22]

Common complaints of sometimes unidentified etiology and pathophysiology include postprandial GI symptoms such diarrhea, abdominal distension, flatulence, bloating and a sense of fullness.[17,23]

In the present study, Figure 4 shows that the 48.5% doctors were moderately familiar, 23.9% doctors were somewhat familiar and 23.1% doctors who were very well familiar with the benefits of the combination of alpha-amylase and papain as a treatment option for dyspepsia, functional GI disorders or age-related disorders.

The calcium metalloenzyme alpha-amylase facilitates digestion by dissolving larger polysaccharide molecules into smaller ones like glucose and maltose.[24] The enzyme breaks down or digests proteins, lipids and carbohydrates and aid in treating indigestion and stomach discomfort.

A study by Majeed et al (2018) supported the clinical evidence related to the safety and efficacy of multienzyme complex as a dietary supplement in the management of dyspeptic symptoms in patients with functional dyspepsia characterized by bloating, early satiety, postprandial fullness, nausea, anorexia and heartburn, regurgitation and burping.[19]

One of the strongest digestive enzymes, papain helps to break down even the most resistant protein fibers and can aid with IBS symptoms, inflammation reduction and postoperative recovery.

Newer studies have shown that enzyme supplementation therapy may play an important role in several digestive and malabsorption disorders. Combination of different enzymes might constitute an intriguing therapeutic option in the future.[9]

Nearly 83.6% of doctors agreed with the fact that combination of alpha-amylase and papain can be helpful in relieving PPI overuse adverse effects such as GI disorders and malabsorption of several nutrients compared to 16.4% doctors who did not as visible from the graph in Figure 5.

PPI are now being used excessively and inappropriately. The likelihood of abuse and misuse has grown enormously in India where there are over 500 branded formulations of PPI accessible. Many a times, PPIs don't work well for many people. In such a situation, both the patients and the medical professionals' looks for some effective alternative with better effectiveness and safety profile.[25]

As observed in Figure 7, patient preferences is the most important factor (53.7%), followed by efficacy (24.65%), cost-effectiveness (12.75%) and safety profile (8.2%) being the other factors influencing the doctors decision to prescribe the combination of alpha-amylase and papain. Safety profile was found to be neutral (64.9%) as agreed by majority of doctors, followed by 30.6% stating it as safe and 2.2% agreeing that the combination was very safe. Only 1.5% doctors had the view that it was unsafe as shown in Figure 8.

Majority of the doctors (98.5%) said that they did not encounter any adverse events or side effects in patients who were prescribed the combination of alpha-amylase and papain, as is evident in Figure 9.

The effectiveness of the combination of alpha-amylase and papain was shown in Figure 10. Mostly, it was found to be neutral (48.5%), followed by effective (45.5%), then very effective (3.7%), while only 1.5% agreed that the combination had no effect. Figure 11 also showed that majority of doctors (46.3%) agreed that the effectiveness of the combination of alpha-amylase and papain compared to other combinations was equally effective.

A recent Indian post-marketing survey that included 2,125 individuals with functional dyspepsia showed that approximately 87% of patients who were treated for functional dyspepsia reported better symptoms after taking a multienzyme cocktail including amylase. At day 14, the average percentage of dyspepsia sufferers decreased from 66% at baseline to 8%, the condition's severity decreased from 0.95 to 0.09, and the feeling of fullness decreased from 63% to 7%.[26]

According to the present study, only 1.5% stated that they had observed some minor side effects such as spasmodic pain. Similarly, very insignificant or no side effects were seen in a multicenter, randomized, placebo-controlled crossover study by Ran et al (2009). The study involving 151 dyspeptic patients showed significant reductions in symptoms such as an

epithymia, abdominal distension, belching, diarrhea, abdominal pain and epigastric burning after being treated with a combination of pancreatin and *Aspergillus oryzae* enzyme extract (amylase).[27]

Study by Muss et al showed significant reduction in constipation, painful, difficult stool motions and flatulence in 139 volunteers with functional GI complaints after being treated with papain preparation compared to placebo.[18]

Another study showed that papain decreased stomach inflammation in a clinical investigation involving 200 participants who had dyspepsia. It reduced symptoms including heartburn, nausea, vomiting, burping and bloating as compared to the placebo.[28]

A recent study by Annaházi et al (2021) examined the effects of papain on guinea pig corpus and antrum strips. Papain increased the antrum's ongoing phasic contractions, but the muscle tone and frequency stayed the same. It caused the corpus to constrict for a brief period of time while before relaxing for a considerable period of time. Hence, it is hypothesized that papain-like cysteine proteases may also have a direct impact on the GI muscles, potentially alleviating IBS symptoms.[29]

Postprandial digestive symptoms as diarrhea, abdominal distension, flatulence, bloating and a fullness sensation are frequent complaints with frequently unidentified etiology and pathophysiology. Numerous studies, including a number of randomized placebo-controlled trials, have documented the beneficial effects of products containing various combinations of digestive enzymes.[17]

Figure 12 shows the suitability of the alpha-amylase and papain in elderly. It was seen that though 68.7% were not sure about the suitability in elderly, 24.6% doctors agreed that the combination was helpful in elderly. The study also highlighted the fact that age-related considerations were the main factor (59.7%) which the doctors considered when determining the chronic usage of the combination of alpha-amylase and papain in elderly patients, followed by patient compliance (28.4%) as shown in Figure 13.

Functional dyspepsia is found to be one of the most common conditions in elderly worldwide. According to a Korean study, functional dyspepsia is more common in those under 60 years old (11% vs. 10% of people up to that age) in Asia.[30] Digestive enzymes including amylase, protease and lipase are produced and secreted by the GI system. These enzymes aid in digestion by facilitating the break down of larger molecules contained in food such as carbohydrates, proteins and lipids. It is also believed that a lack of digestive enzymes is one of the contributing reasons of functional dyspepsia, even if the potential relevance of enzyme deficit in the etiopathogenesis of functional dyspepsia is yet unclear. However, studies have shown that providing functional dyspepsia patients with multienzyme formulations may help to minimize their postprandial discomfort and symptoms of gas, bloating, belching and fullness.[19]

The findings revealed a notable prevalence of age-related enzyme deficiency, particularly among older individuals. Preliminary results from this study are promising, suggesting that enzyme supplementation could lead to improved digestive function and nutrient absorption among the target population.

IMPLICATIONS AND LIMITATIONS

The questionnaire-based survey offers valuable insights for health care professionals in India to better understand age-related enzyme deficiencies. While the study results could lead to personalized dietary recommendations for the Indian population, especially older individuals. Incorporating alpha-amylase and papain enzyme supplements could potentially enhance digestion and mitigate related health issues but still, it is essential to acknowledge its limitations.

The survey's reliability may be affected by sampling bias, as only physicians who agreed to participate share their views on age-related enzyme deficiency in the Indian population. The study's duration may challenge evaluating long-term effects or adverse consequences. Response bias may arise from subjective responses, and low response rates raise concerns about nonresponse bias. Mitigating these limitations and implementing mitigation strategies can maximize the survey's reliability and credibility.

CONCLUSION

To conclude, the study shows a significant prevalence of age-related enzyme deficiency in the Indian population, particularly among older individuals. The retrospective study conducted via a questionnaire-based survey suggests supplementation with alpha-amylase and papain enzymes could enhance digestive function, nutrient absorption and are effective and safe to maintain the overall health outcomes, especially among elderly.

REFERENCES

1. Kaczor JJ, Ziolkowski W, Antosiewicz J, Hac S, Tarnopolsky MA, Popinigis J. The effect of aging on anaerobic and aerobic enzyme activities in human skeletal muscle. J Gerontol A Biol Sci Med Sci. 2006;61(4):339-44.

2. Ganguly BB, Kadam NN. Age-related disease burden in Indian population. J Natl Med Assoc. 2020;112(1):57-73.
3. Rodin J. Aging and health: effects of the sense of control. Science. 1986;233(4770):1271-6.
4. Enzymes: How they work and what they do? Updated July 8, 2022. Available from: https: //www.medicalnewstoday.com/articles/319704#examples. Accessed May 24, 2023.
5. Hall DA. Enzymes and survival. Mechanisms of Ageing and Development. 1984;28(2-3):219-28.
6. Lam R, Muniraj T. Hyperamylasemia. [Updated 2022 Dec 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559273/
7. Black CJ, Drossman DA, Talley NJ, Ruddy J, Ford AC. Functional gastrointestinal disorders: advances in understanding and management. Lancet. 2020;396 (10263):1664-74.
8. Castellana C, Pecere S, Furnari M, Telese A, Matteo MV, Haidry R, et al. Side effects of long-term use of proton pump inhibitors: practical considerations. Pol Arch Intern Med. 2021;131(6):541-9.
9. Ianiro G, Pecere S, Giorgio V, Gasbarrini A, Cammarota G. Digestive enzyme supplementation in gastrointestinal diseases. Curr Drug Metab. 2016;17(2):187-93.
10. Akinfemiwa O, Zubair M, Muniraj T. Amylase. [Updated 2022 Nov 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557738/
11. Peyrot des Gachons C, Breslin PA. Salivary amylase: digestion and metabolic syndrome. Curr Diab Rep. 2016;16(10):102.
12. High and low amylase: what it is and why it increases or decreases? Available from: https://en.nature-via.com/high-and-low-amylase-what-it-is-and-why-it-increases-or-decreases. Accessed May 23, 2023.
13. Yamane N, Ikeda A, Tomooka K, Saito I, Maruyama K, Eguchi E, et al. Salivary alpha-amylase activity and mild cognitive impairment among Japanese older adults: the Toon Health Study. J Prev Alzheimers Dis. 2022;9(4):752-7.
14. The connection between aging and digestive enzymes. Available from: https://www.genf20plus.info/the-connection-between-aging-and-digestive-enzymes.php#:~:text=Among%20the%20numerous%20health%20issues%20that%20may%20arise,insufficiency%20could%20actually%20speed%20up%20the%20aging%20process. Accessed June 6, 2023.
15. Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse effects associated with proton pump inhibitor use. Cureus. 2021;13(1):e12759.
16. Pinto-Sanchez MI, Yuan Y, Hassan A, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. Cochrane Database Syst Rev. 2017;11(11):CD011194.
17. Graham DY, Ketwaroo GA, Money ME, Opekun AR. Enzyme therapy for functional bowel disease-like postprandial distress. J Dig Dis. 2018;19(11):650-6.
18. Muss C, Mosgoeller W, Endler T. Papaya preparation (Caricol®) in digestive disorders. Neuro Endocrinol Lett. 2013;34(1):38-46.
19. Majeed M, Majeed S, Nagabhushanam K, Arumugam S, Pande A, Paschapur M, et al. Evaluation of the safety and efficacy of a multienzyme complex in patients with functional dyspepsia: a randomized, double-blind, placebo-controlled study. J Med Food. 2018;21(11):1120-8.
20. API-ISG Consensus Guidelines for Management of Gastrooesophageal Reflux Disease. Available from: http://www.isg.org.in/img/ISG_API_GERD.pdf#:~:text=The%20prevalence%20of%20GERD%20in%20large%20population-based%20studies,due%20to%20lifestyle%20changes%20and%20increase%20in%20obesity. Accessed Aug 15, 2023.
21. Dumic I, Nordin T, Jecmenica M, Stojkovic Lalosevic M, Milosavljevic T, et al. Gastrointestinal tract disorders in older age. Can J Gastroenterol Hepatol. 2019;2019:6757524.
22. Bhatia SJ, Makharia GK, Abraham P, Bhat N, Kumar A, Reddy DN, et al. Indian consensus on gastroesophageal reflux disease in adults: a position statement of the Indian Society of Gastroenterology. Indian J Gastroenterol. 2019;38(5):411-40.
23. Sharma M, Kishore A, Roy D, Joshi K. A comparison of the Indian diet with the EAT-Lancet reference diet. BMC Public Health. 2020;20(1):812.
24. Kaur N, Kumar V, Nayak SK, Wadhwa P, Kaur P, Sahu SK. Alpha-amylase as molecular target for treatment of diabetes mellitus: a comprehensive review. Chem Biol Drug Des. 2021;98(4):539-60.
25. Gupta Y, Bhandari S, Govil A, Gupta R, Goyal J, Goyal B, et al. Use and inappropriate use of proton pump inhibitors in hospitalized patients. Int J Basic Clin Pharmacol. 2019;8(11):2490-7.
26. Post-Marketing Surveillance Study to assess the efficacy and tolerability of Al5zyme - A multienzyme preparation in patients with functional dyspepsia. 2013. Available from: https://docplayer.net/101353008-Post-marketing-surveillance-study-to-assess-the-efficacy-and-tolerability-of-al5zyme-a-multienzyme-preparation-in-patients-with-functional-dyspepsia.html. Accessed June 6, 2023.
27. Ran ZH, Yuan YZ, Li ZS, Wang JY, Zong CH, Xie WF, et al. The efficacy of Combizym in the treatment of Chinese patients with dyspepsia: a multicenter, randomized, placebo-controlled and cross-over study: Shanghai Combizym Clinical Cooperative Group. J Dig Dis. 2009;10(1):41-8.
28. Ahmad M, Ahmad M, Munir T. Prevention of functional dyspepsia with *Carica papaya* extract. Ann King Edward Med Univers. 2018;24(1):610-7.
29. Annaházi A, Schröder A, Schemann M. Region-specific effects of the cysteine protease papain on gastric motility. Neurogastroenterol Motil. 2021;33(7):e14105.
30. Walker MM, Talley NJ. Functional dyspepsia in the elderly. Curr Gastroenterol Rep. 2019;21(10):54.

CLINICAL STUDY

Risk Factors Linked to Development of Cardiomyopathy in Adults with Beta-Thalassemia Major in a Tertiary Care Hospital

RAJESH K MEENA*, RAMESH CHAND MEENA*, SOURABH SHARMA†

ABSTRACT

Beta-thalassemia major is a genetic disorder adversely affecting the life of the patient and the whole family. Repeated blood transfusions are required to maintain the hemoglobin level, which create a state of iron overload in the body leading to ectopic iron deposition in the heart, liver, pancreas and other organs. Thalassemia cardiomyopathy is the most dreaded complication of this resultant iron overload. The present study was a cross-sectional study involving 77 patients with thalassemia major, whose age, body mass index (BMI), blood pressure (BP), hemoglobin, serum ferritin levels were correlated with their two-dimensional echocardiographic findings. Out of the total 77 patients, 63 had diastolic dysfunction, 6 had systolic dysfunction and remaining 8 had normal left ventricular function. The mean age of the patients was 22.42 years and their mean BMI was 16.82. Patients with systolic dysfunction had lower hemoglobin and higher serum ferritin levels as compared to other patients. The study concluded that cardiac dysfunction is seen more in younger age, higher BMI, lower BP, low hemoglobin levels and raised serum ferritin levels. Thus, early intensive iron chelation therapy should be provided to all the patients to curb this dreaded complication.

Keywords: Iron overload, thalassemia, cardiomyopathy, iron chelation

Beta-thalassemia major is an inherited disorder of hemoglobin synthesis leading to ineffective erythropoiesis. There is absence of beta-globin chain synthesis but the production of alpha chains proceeds at a normal rate. These alpha chains accumulate to form toxic inclusion bodies and kill the developing erythroblasts in the marrow. The life of erythrocytes is shortened leading to severe hemolysis. The resultant profound hemolytic anemia stimulates erythropoietin release and compensatory erythroid hyperplasia in extramedullary tissues like liver and spleen. This erythroid hyperplasia leads to maxillary and frontal bone marrow expansion, thereby producing the characteristic 'chipmunk' facies appearance. Thalassemia patients require repeated blood transfusions to maintain their hemoglobin level. Repeated blood transfusions act as a necessary evil and create a state of iron overload in the body, affecting the heart, liver, pancreas, etc. Heart injuries in iron overload cause dilatation of atria and ventricles, arrhythmia, valvular dysfunction, pericarditis and finally heart failure in a few decades. Major risk factors causing cardiomyopathy are chronic anemia, reactive free oxygen radicals and iron overload. This devastating complication can be postponed by early intensive iron chelation therapy by deferoxamine, deferasirox and deferiprone.

However, despite therapeutic advancements, thalassemia cardiomyopathy still remains the leading cause of mortality in such patients. The aim of the present study was to determine the clinical and laboratory parameters associated with higher risk of cardiomyopathy.

METHODS

A cross-sectional study was done on 77 patients of beta-thalassemia major attending the Adult Thalassemia Day Care Centre at Lady Hardinge Medical College and Associated Hospitals in New Delhi during the period from January to March 2019. All the patients were confirmed for beta-thalassemia major by liquid

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chromatography. The patients underwent a detailed history and physical examination, with emphasis on cardiovascular features.

Further, their age, body mass index (BMI), blood pressure (BP), hemoglobin, serum ferritin level and two-dimensional echocardiography findings were analyzed for any statistical significance. All the patients were older than 18 years of age. Echocardiography was performed on the same machine and by a single person to eliminate intraobserver differences. Complete M-mode, two-dimensional, color flow mapping and Doppler studies were conducted on all the patients.

STATISTICAL ANALYSIS

Descriptive statistics was calculated for various parameters including demographic, hematological and echocardiographic features and are reported as, mean ± standard deviation (SD). Comparison of means of different parameters was done for normal versus systolic patients and normal versus diastolic patients to establish the significantly different parameters. $P < 0.05$ was considered statistically significant. All statistical analysis was done using GraphPad Prism software.

RESULTS

A total of 77 patients were screened, out of which 32 were female and remaining 45 were male. Sixty-three patients had diastolic dysfunction, 6 had systolic dysfunction and remaining 8 had normal left ventricular (LV) function. Out of the 6 patients with systolic dysfunction, 4 were male and remaining 2 were female.

The mean age of patients with systolic dysfunction was 18.33 years, while those with diastolic dysfunction were 21.97 years. The mean weight of all the patients was 46.4 kg, while those with systolic dysfunction were 41.5 kg.

The mean BMI was higher in patients with systolic dysfunction (19.03) as compared to those with diastolic dysfunction (16.6). The mean systolic and diastolic BPs of the patients was 106.98 and 71.58 mmHg, respectively. Both systolic and diastolic BPs were greater in patients with diastolic dysfunction as against patients with systolic dysfunction.

Almost all patients had hemoglobin of less than 10 gm%, with a mean of 9 gm%. Again, mean hemoglobin was more in patients with diastolic dysfunction (8.85) as compared to those with systolic dysfunction (8.5). Serum ferritin levels were raised with a mean of 2,914.67 ng/mL. The mean ferritin levels were 2,819.27 ng/mL in patients with diastolic dysfunction and 5,340.83 ng/mL in patients with systolic dysfunction. Echocardiography revealed the grade of diastolic dysfunction to be grade 1, 2 and 3 in 41, 17 and 5 patients, respectively. Pulmonary artery hypertension was found in patients with both systolic and diastolic dysfunction, with pressures higher in systolic dysfunction group (58.71 mmHg) as compared to diastolic dysfunction group (42.83 mmHg).

The mean left atrial volumes were more in patients with systolic dysfunction (76.07 mL) than in patients with diastolic dysfunction (69.52 mL). Mean E/A ratio was also more in systolic dysfunction group (1.11) as compared to diastolic dysfunction group (1.09). Further, mean E/E′ in patients with systolic dysfunction was 8.83 and those with diastolic dysfunction were 9.37. The comparison of mean values of demographic and hematological data of thalassemia patients and association with systolic and diastolic LV dysfunction has been depicted in Table 1 and Table 2, respectively. Comparison of mean values of echocardiography data of thalassemia patients and association with systolic and diastolic LV dysfunction has been depicted in Table 3 and Table 4, respectively.

Table 1. Comparison of Mean Values of Demographic and Hematological Data of Thalassemia Patients and Association with Systolic LV Dysfunction

Parameters	Normal LV function (n = 8)	Systolic LV dysfunction (n = 6)	P value at 95% significance level
Age (years)	29.13 ± 3.63	18.33 ± 0.44	0.000039
Male	2	4	-
Female	6	2	-
Height (cm)	1.76	1.47	0.000449
Weight (kg)	52	41.5	0.018458
BMI	16.724	19.03	0.013587
Systolic BP (mmHg)	117.5 ± 3.89	96.67 ± 3.65	<0.00001
Diastolic BP mmHg)	79.38 ± 4.13	63.33 ± 6.65	0.000448
Hemoglobin (gm%)	9.66	8.5 ± 0.5	0.004989
Serum ferritin (ng/mL)	2,914.67	5,340.83	0.049358

LV = Left ventricular; BMI = Body mass index; BP = Blood pressure.

Table 2. Comparison of Mean Values of Demographic and Hematological Data of Thalassemia Patients and Association with Diastolic LV Dysfunction

Parameters	Normal LV function (n = 8)	Diastolic LV dysfunction (n = 63)	P value at 95% significance level
Age (years)	29.13 ± 3.63	21.97 ± 3.78	<0.00001
Male	2	39	-
Female	6	24	-
Height (cm)	1.76	1.66	0.023417
Weight (kg)	52	46.298	0.01072
BMI	16.724	16.630	0.00325
Systolic BP (mmHg)	117.5 ± 3.89	106.63 ± 7.45	0.000179
Diastolic BP mmHg)	79.38 ± 4.13	71.38 ± 7.81	0.007044
Hemoglobin (gm%)	9.66	8.8	0.05107
Serum ferritin (ng/mL)	2,914.67	2,819.27	0.051291

Table 3. Comparison of Mean Values of Echocardiography Data of Thalassemia Patients and Association with Systolic LV Dysfunction

Parameters	Normal LV function (n = 8)	Systolic LV dysfunction (n = 6)	P value at 95% significance level
LVEF (%)	61 ± 1.7	36.67 ± 2.25	<0.00001
LA volume (mL)	48.39 ± 5.28	76.07 ± 7.66	<0.00001
E/A	1.39 ± 0.11	1.11 ± 0.31	0.0342
E/E'	6.26 ± 0.73	8.83 ± 0.91	<0.00001
IVRT (msec)	71.81 ± 3.88	79.92 ± 4.17	0.0028
LVDD (mm)	45.88 ± 4.53	79.79 ± 6.31	<0.00001
LVSD (mm)	28.57 ± 2.43	35.86 ± 4.55	0.0022
PASP (mmHg)	19.92 ± 2.56	58.71 ± 6.01	<0.00001

LVEF = Left ventricular ejection fraction; LA = Left atrial; E = Early diastolic transmitral flow velocity; A = Late (atrial) transmitral flow velocity; E' = Early diastolic mitral annular velocity; IVRT = Isovolumic relaxation time; LVDD = Left ventricular diastolic dysfunction; LVSD = Left ventricular systolic dysfunction; PASP = Pulmonary arterial systolic pressure.

Table 4. Comparison of Mean Values of Echocardiography Data of Thalassemia Patients Association with Diastolic LV Dysfunction

Parameters	Normal LV function (n = 8)	Diastolic LV dysfunction (n = 63)	P value at 95% significance level
LVEF (%)	61 ± 1.7	55.40 ± 2.83	<0.00001
LA volume (mL)	48.39 ± 5.28	69.52 ± 4.98	<0.00001
E/A	1.39 ± 0.11	1.09 ± 0.28	0.0039
E/E'	6.26 ± 0.73	9.37 ± 1.29	<0.00001
IVRT (msec)	71.81 ± 3.88	80.52 ± 3.86	<0.00001
LVDD (mm)	45.88 ± 4.53	69.82 ± 3.46	<0.00001
LVSD (mm)	28.57 ± 2.43	33.85 ± 3.03	<0.00001
PASP (mmHg)	19.92 ± 2.56	42.83 ± 4.96	<0.00001

DISCUSSION

Our study of 77 adult beta-thalassemia major patients has shown that cardiac dysfunction is seen more in younger age, higher BMI, lower BP, low hemoglobin levels and raised serum ferritin levels. Pulmonary artery pressure was more in patients with systolic dysfunction as compared to diastolic dysfunction.

One unit of packed red blood cells contains approximately 200-250 mg of iron.[1] After transfusion of approximately 20 units of red cells, ectopic iron deposition starts in tissues such as liver, pancreas, heart, etc. As iron overload progresses, transferrin is saturated and generation of free hydroxyl radicals is promoted, which causes iron deposition in tissues, leading to their cell death and fibrosis.[2] The heart is affected more than other tissues as it takes up labile iron in the plasma directly, which is toxic for the cardiac myocytes. Several guidelines support that early iron chelation therapy is beneficial in delaying cardiac dysfunction.[2]

Serum ferritin is a simple, noninvasive, easily available and reproducible test to assess iron overload in the body. It is also an acute phase reactant and so, it may be falsely elevated in infections and inflammation. Still, it remains the most widely used tool in evaluating iron overload. Moreover, ferritin levels <2,500 correlated with greater survival without heart disease and ferritin levels >2,500 correlated with increased death due to cardiomyopathy in patients of thalassemia.[3]

Two-dimensional echocardiography is another simple, noninvasive, reproducible test, which can be done

to detect cardiac dysfunction at an early stage and also, it can monitor the disease process. It has gained importance over the past few decades due to its ability to detect cardiomyopathy before clinical signs appear. Once the patient becomes symptomatic, the prognosis usually gets worse. Several studies in the past also indicate that echocardiography plays a significant role in early detection of cardiac dysfunction.[4]

Cardiac magnetic resonance imaging (MRI) can be done to measure iron deposition. However, it is expensive and not easily available, so cannot be used for serial monitoring. MRI T2 relaxation time of <20 msec indicates increased iron deposition and consequent lower ejection fraction.[5] However, there is no linear correlation between iron deposition and reduced ejection fraction.[6]

The currently available iron chelators include deferoxamine, deferasirox and deferiprone.[1] Deferoxamine is the oldest chelator, given parenterally and occasionally causes cataracts, deafness and local skin reactions like urticaria. It is given by slow infusion and the constant presence of the drug improves the efficacy of chelation and protects the tissues from occasional release of free iron radicals. Deferiprone is given orally, but causes agranulocytosis. Deferasirox is the latest iron chelator, which is given orally in a dose of 20-30 mg/kg, but may lead to renal impairment and gastric disturbances.

CONCLUSIONS

Thalassemia requires a special mention as it affects the life of the individual and the whole family. Cardiomyopathy occurs as a consequence of chronic anemia, damage by reactive free oxygen radicals and iron overload. Early detection, screening and monitoring of cardiac dysfunction should be done in each patient. Iron chelation therapy is of paramount importance and should be started at 5 to 8 years of age to delay the disease process. Bone marrow transplantation in beta-thalassemia has been found to be curative in 80% to 90% of patients, but the decision to transplant is best made in consultation with specialized centers as majority of patients survive into adult life.[7] Gene therapy in thalassemia is still inexperimental stages.

REFERENCES

1. Cazzola M, Malcovati L. Myelodysplastic syndromes - coping with ineffective hematopoiesis. N Engl J Med. 2005;352(6):536-8.
2. Bennett JM; MDS Foundation's Working Group on Transfusional Iron Overload. Consensus statement on iron overload in myelodysplastic syndromes. Am J Hematol. 2008;83(11):858-61.
3. Olivieri NF, Nathan DG, MacMillan JH, Wayne AS, Liu PP, McGee A, et al. Survival in medically treated patients with homozygous beta-thalassemia. N Engl J Med. 1994;331(9):574-8.
4. Eghbali A, Taherahmadi H, Bagheri B, Nikanjam S, Ebrahimi L. Association between serum ferritin level and diastolic cardiac function in patients with major β-thalassemia. Iran J Ped Hematol Oncol. 2015;5(2):83-8.
5. Anderson LJ, Holden S, Davis B, Prescott E, Charrier CC, Bunce NH, et al. Cardiovascular T2-star (T2*) magnetic resonance for the early diagnosis of myocardial iron overload. Eur Heart J. 2001;22(23):2171-9.
6. Davis BA, O'Sullivan C, Jarritt PH, Porter JB. Value of sequential monitoring of left ventricular ejection fraction in the management of thalassemia major. Blood. 2004;104(1):263-9.
7. Prakash A, Aggarwal R. Thalassemia major in adults: short stature, hyperpigmentation, inadequate chelation, and transfusion-transmitted infections are key features. N Am J Med Sci. 2012;4(3):141-4.

CASE REPORT

Nonclassical Celiac Disease in an Adolescent Male with Vague Abdominal Pain: A Case Report and Literature Review

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ABSTRACT

The abdomen, often referred to as the "Pandora's Box", presents diagnostic challenges, especially in cases of chronic pain. This report details a perplexing case of chronic, vague abdominal pain accompanied by nonspecific laboratory findings, ultimately leading to the diagnosis of atypical celiac disease through duodenal biopsy and serological investigations. The presented case highlights the significance of a thorough and methodical work-up in managing chronic conditions, emphasizing the importance of considering celiac disease in cases of ambiguous abdominal pain.

Keywords: Gluten sensitivity, celiac disease, malabsorption, abdominal pain, biopsy

Celiac disease (CD) is an immune-mediated intestinal condition triggered by the consumption of gluten, which is found in wheat, rye and barley. It is recognized as one of the most prevalent lifelong food-related disorders worldwide. Formerly referred to as celiac sprue, the term "sprue" derived from Dutch and was used to describe a condition resembling tropical sprue, characterized by symptoms like diarrhea, emaciation, aphthous stomatitis and malabsorption.[1,2] While the symptoms and indications of CD have been acknowledged for over a century, it was during the 1940s that Dicke, a Dutch pediatrician, established a connection between the exposure to gluten, a protein component found in wheat and CD.[3] It is triggered in genetically predisposed individuals upon consuming gluten, the primary storage protein found in wheat and similar grains. Initially considered a rare malabsorption syndrome affecting children, it is now understood to be a common condition that can be diagnosed at any age and affects multiple organ systems. Diagnosis involves a combination of CD serology and histological examination of small intestinal tissue obtained during a gluten-containing diet. Currently, the only effective treatment for CD is a lifelong strict gluten-free diet.[2]

CASE DETAILS

A 17-year-old male of North-East Indian ethnicity presented to our outpatient clinic with a 1-month history of decreased appetite. The onset of decreased appetite coincided with the initiation of medication for a skin rash, which he had been taking for a month. The patient also reported experiencing generalized abdominal pain for the past 2 years. He denied any significant medical history, including previous abdominal surgeries or gastrointestinal disorders. There was no family history of similar symptoms or significant medical conditions.

On examination, the patient's height was 177 cm, weight was 71 kg and body mass index (BMI) was 22.66 kg/m^2, indicating a healthy weight range. He appeared well-nourished and showed no signs of pallor or edema. His cardiovascular examination revealed a regular rhythm with a heart rate of 56 beats per minute. Blood pressure in the supine position was measured at 110/70 mmHg. Respiratory examination demonstrated normal vesicular breath sounds. Abdominal examination did not reveal any organomegaly or tenderness. His skin examination did not reveal any itchy, bilaterally symmetrical rash, suggestive of dermatitis herpetiformis.

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Table 1. Investigation Details of the Patient

Test parameters	Patient's data	Normal range
Complete blood count		
Hemoglobin	14.3 (g/dL)	13.0-16.5 (g/dL)
Total WBC count	7.42 × 10^3/mm^3	4-11 × 10^3/mm^3
Neutrophils	56%	40-80%
Lymphocytes	36%	20-40%
Monocytes	7%	02-10%
Platelet count	150 × 10^3/mm^3	150-450 × 10^3/mm^3
ESR	8	0-20 mm/hour
Liver function tests		
Total bilirubin	0.7 mg/dL	0.0-1.3 mg/dL
Direct bilirubin	0.4 mg/dL	0.0-0.5 mg/dL
Indirect bilirubin	0.3 mg/dL	0.0-1.2 mg/dL
SGOT/ AST	61 U/L	<31 U/L
SGPT/ALT	85 U/L	<34 U/L
ALP	146 U/L	<98
GGTP	63 U/L	<140 U/L
Serum albumin	4.4 g/dL	3.2-4.6 g/dL
Serum globulin	3.6 g/dL	2.0-3.5 g/dL
Renal function tests		
Urea	9 mg/dL	13-43 mg/dL
Creatinine	0.9 mg/dL	0.6-1.1 mg/dL
Special tests		
Anti-tTG antibody (IgG and Ig A)	IgG: 3.07 IgA: 61.19	Negative: <20 Weak positive: 20-30 Moderate to strong positive: >30 U/mL
Random blood sugar	96 mg/dL	<99 mg/dL
ANA screening	Negative	Negative

WBC = White blood cell; ESR = Erythrocyte sedimentation rate; SGOT = Serum glutamic-oxaloacetic transaminase; AST = Aspartate aminotransferase; SGPT = Serum glutamic-pyruvic transaminase; ALT = Alanine aminotransferase; ALP = Alkaline phosphatase; GGTP = Gamma-glutamyl transpeptidase; tTG = Tissue transglutaminase; ANA = Antinuclear antibody.

Initial laboratory investigations revealed elevated transaminases and serum globulin levels. However, there was no evidence of anemia. Further details of the investigations have been listed in Table 1. Considering the patient's symptoms and laboratory findings, further investigations were pursued. The ultrasound scan of the abdomen was normal. An esophagogastroduodenoscopy was performed to further evaluate the nonspecific abdominal symptoms. It revealed scalloping of the duodenal mucosa in the D2 segment, and a biopsy was taken for histopathological examination.

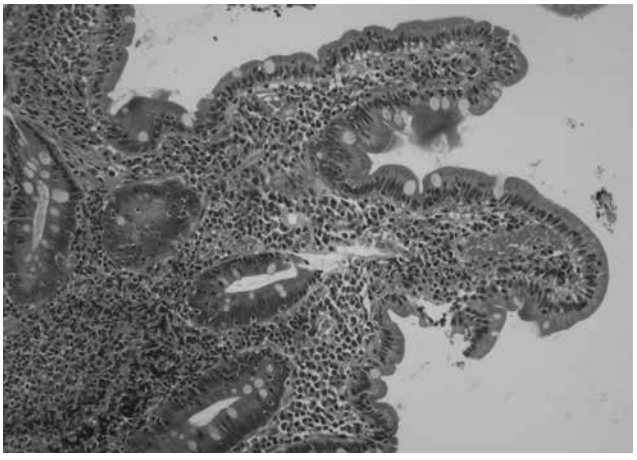

Figure 1. Photomicrograph of 100x magnification showing chronic duodenitis with mild villous blunting and focal increase in intraepithelial lymphocytes.

Microscopic examination of the duodenal biopsy demonstrated fragments of duodenal mucosa exhibiting focal villous blunting. Focal activity was noted, along with a mild increase in intraepithelial lymphocytes. The lamina propria showed expansion with a lymphoplasmacytic infiltrate, occasionally forming aggregates. Evidence of cryptitis was present, but no crypt abscess was observed. These findings were consistent with chronic duodenitis with mild villous blunting and focal increase in intraepithelial lymphocytes, with a modified Marsh Classification type 3a,[4] suggestive of CD (Fig. 1). Tissue transglutaminase (tTG) antibodies were positive, indicating the presence of CD.

The patient was started on gluten-free diet (GFD) and showed marked improvement in his clinical features on first follow-up.

DISCUSSION

Abdominal pain is a frequently encountered issue in primary care, with various possible causes that can present challenges for diagnosis and treatment. The nonspecific nature of the symptoms and the lack of clear correlation to specific organ pathology often make it difficult to reach accurate diagnoses. While many cases of abdominal pain are harmless, a considerable portion of patients may have severe conditions that necessitate a careful and thorough management approach to avoid complications and potential fatalities. [5]

Celiac disease is a known contributor to persistent abdominal pain, with a worldwide pooled prevalence of biopsy-confirmed cases at 0.7%.[1] The age-adjusted

prevalence of celiac autoantibodies in different regions of India was found to be 1.23% in the northern region, 0.87% in the northeastern region and 0.10% in the southern region.[6]

The specific elements associated with CD are human leukocyte antigen (HLA)-DQ2 and HLA-DQ8, an autoantigen called tTG and an environmental trigger known as gluten. The pathogenesis involves several steps: partially digested gliadin fragments interact with chemokine receptor 3 on the epithelium's apical side, leading to the release of zonulin, which then interacts with the intestinal epithelium, causing increased intestinal permeability. The compromised gut barrier allows gliadin peptides to move from the lumen to the lamina propria. Gliadin peptides stimulate the release of interleukin-15, which results in the upregulation of maturation markers and the release of proinflammatory cytokines. Innate immune-mediated apoptosis of intestinal cells leads to the release of intracellular tTG, resulting in the partial deamidation of gliadin peptides. DQ2/8+ antigen presenting cells recognize deamidated gliadin and present it to T helper cells. T helper cells then activate and mature B cells, which produce antibodies (IgM, IgG and IgA) against tTG. These mechanisms collectively initiate enteropathy. Damaged enterocytes enhance the trafficking of gluten from the gut lumen to the lamina propria, ultimately causing crypt hyperplasia and villous blunting due to intestinal epithelial cell death induced by intraepithelial lymphocytes.[2,7]

In 2011, the Oslo classification of CD established the following clinical presentations: classic, nonclassic, subclinical potential and refractory.[8] Additionally, a more practical classification was proposed by Caio et al, categorizing it as intestinal or extraintestinal.[7]

In classical CD, which accounts for 27% of cases, individuals experience symptoms such as diarrhea, weight loss and malabsorption. Nonclassical disease, making up 52% of cases, is characterized by symptoms like constipation, anemia, hypertransaminasemia, neurologic disorders and dermatitis herpetiformis. Asymptomatic celiac disease, observed in 21% of cases, does not present any noticeable symptoms.[7] This case clearly fulfilled the classification of nonclassical CD.

Diagnosing CD can pose difficulties, particularly in nonclassical and subclinical presentations. However, the presence of anemia, unexplained elevation of transaminases and steatorrhea observed in stool examination should raise suspicion and prompt the clinician to consider CD as a potential diagnosis. Individuals suspected of having CD need to follow a gluten-containing diet before undergoing serological and histological testing. For serological testing, the initial step is to perform IgA tTG testing, which has a high sensitivity and specificity (average of 94% and 97%, respectively) for diagnosing CD. If the IgA-tTG test is weakly positive, IgA endomysial antibody (EMA) testing can also be used. If an individual has positive celiac serology, the diagnosis of CD is confirmed through histological examination of duodenal biopsies taken from the duodenal bulb and distal duodenum. Taking at least four biopsies improves the diagnostic rate. Histological features of CD include an increase in intraepithelial lymphocytes, crypt hyperplasia and villous atrophy.[9] Additional genetic studies to look for HLA-DQ2/HLA-DQ8 positivity increase the probability of diagnosing the celiac disease.[7]

After confirming a diagnosis of CD, physicians should strongly advise individuals to follow a strict GFD and ensure they understand the reasons behind it. The GFD involves the complete exclusion of wheat, rye and barley from the diet, preferably with the guidance of a specialized dietitian.[9,10] In preliminary studies, ZED1227, an inhibitor of transglutaminase 2, showed promising results in reducing gluten-induced damage to the duodenal mucosa in patients with CD. This suggests that it could potentially be a promising treatment option for CD in the future.[11] According to the current guidelines from the National Institute for Health and Care Excellence (NICE), individuals with CD should have annual follow-up appointments.[9]

Approximately 30% of patients may not respond well to therapy, and persistent or recurring symptoms are often attributed to noncompliance with the dietary regimen. If an individual has been managing the GFD for more than 12 months, and other possible diagnoses have been ruled out, a diagnosis of refractory CD may be considered. In cases where concerning symptoms such as abdominal pain, diarrhea and weight loss continue despite strict adherence to a GFD, it is crucial to investigate and exclude complications associated with CD, such as small intestinal adenocarcinoma, refractory sprue and enteropathy-associated T-cell lymphoma.[2,9]

CONCLUSION

This case report highlights the challenges involved in diagnosing nonclassical CD, particularly in adolescents presenting with vague abdominal pain. Early recognition and appropriate management of CD are crucial to prevent complications and improve the patient's quality of life. This case underscores the

importance of maintaining a high index of suspicion for CD in patients with atypical presentations, emphasizing the need for further research and awareness to facilitate early diagnosis and intervention.

Declaration by Authors

Ethical Approval: Not applicable.

Consent: Telephonic consent has been obtained from the patient, on the condition of anonymity.

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REFERENCES

1. Lindfors K, Ciacci C, Kurppa K, Lundin KEA, Makharia GK, Mearin ML, et al. Coeliac disease. Nat Rev Dis Primers. 2019;5(1):3.
2. Green PH, Cellier C. Celiac disease. N Engl J Med. 2007;357(17):1731-43.
3. van Berge-Henegouwen GP, Mulder CJ. Pioneer in the gluten free diet: Willem-Karel Dicke 1905-1962, over 50 years of gluten free diet. Gut. 1993;34(11):1473-5.
4. Yantiss R, Johncilla M. Malabsorption disorders. In: Wang HL, Chen ZE (Eds.). Practical Gastrointestinal Pathology. Springer, Cham; 202. pp. 89-108. Available from: https://link.springer.com/chapter/10.1007/978-3-030-51268-2_5. Accessed July 5, 2023.
5. Govender I, Rangiah S, Bongongo T, Mahuma P. A primary care approach to abdominal pain in adults. S Afr Fam Pract (2004). 2021;63(1):e1-e5.
6. Ramakrishna BS, Makharia GK, Chetri K, Dutta S, Mathur P, Ahuja V, et al. Prevalence of adult celiac disease in India: regional variations and associations. Am J Gastroenterol. 2016;111(1):115-23.
7. Caio G, Volta U, Sapone A, Leffler DA, De Giorgio R, Catassi C, et al. Celiac disease: a comprehensive current review. BMC Med. 2019;17(1):142.
8. Ludvigsson JF, Leffler DA, Bai JC, Biagi F, Fasano A, Green PH, et al. The Oslo definitions for coeliac disease and related terms. Gut. 2013;62(1):43-52.
9. Rej A, Sanders DS. An update on coeliac disease from the NHS England National Centre for Refractory Coeliac Disease. Clin Med (Lond). 2021;21(2):127-30.
10. Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, et al; ESPGHAN Working Group on Coeliac Disease Diagnosis; ESPGHAN Gastroenterology Committee; European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr. 2012;54(1):136-60.
11. Schuppan D, Mäki M, Lundin KEA, Isola J, Friesing-Sosnik T, Taavela J, et al; CEC-3 Trial Group. A randomized trial of a transglutaminase 2 inhibitor for celiac disease. N Engl J Med. 2021;385(1):35-45.

■■■■

Targeting Lymphatic Filariasis: India's Pledge to Achieve Elimination by 2027, Says Health Minister

New Delhi: India is resolutely dedicated to eradicating Lymphatic filariasis by 2027, a target set 3 years ahead of the global objective. This endeavor is being pursued through a collaborative effort involving multiple partners and sectors, as Union Health Minister Dr Mansukh Mandaviya stated recently.

He inaugurated the second phase of the Annual Nationwide Mass Drug Administration (MDA) initiative in the capital. He emphasized that with collective participation from the public and a comprehensive approach encompassing various government departments and society as a whole, the ministry is poised to eliminate this ailment.

The initiative's second phase, which commenced on August 10, aims to cover 81 districts across nine states where the disease is endemic. These states include Assam, Bihar, Chhattisgarh, Jharkhand, Karnataka, Maharashtra, Odisha, Telangana and Uttar Pradesh. Furthermore, he emphasized the necessity of fostering strong collaboration between state and central governments to ensure the health and well-being of the nation.

Reflecting on the successes of health-related 'Jan Andolan' movements, such as the Ni-kshay Mitra initiative, he stressed the importance of community engagement. Highlighting the potential of mass actions, he underscored the need for awareness campaigns at the village and panchayat levels to amplify the mission's reach.

To further reinforce these efforts, Dr Mandaviya advocated for administering medicines in the presence of health care workers or professionals to combat this disease effectively. The event also marked the release of national guidelines for diagnosing dengue and chikungunya fever.

(*Source: https://health.economictimes.indiatimes.com/news/policy/india-committed-to-eliminating-lymphatic-filariasis-by-2027-health-minister-mandaviya/102634999*)

BRIEF COMMUNICATION

Patient Counseling for Finerenone

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ABSTRACT

Finerenone is a nonsteroidal mineralocorticoid receptor antagonist, which is used to retard the progression of chronic kidney disease in persons with type 2 diabetes. This communication describes the various aspects of patient counseling needed to ensure safe and effective usage of the molecule. It utilizes the 5C checklist: Confirmation of clinical indication; Caveats and contraindications; Concerns and checkpoints; Caution and use with concomitant medication; and Constraints and cost, to create a simple, yet comprehensive tool for clinical use.

Keywords: Aldosterone antagonist, chronic kidney disease, diabetic kidney disease, mineralocorticoid receptor antagonist, patient-centered care, person-centered care, type 2 diabetes

Finerenone is a novel nonsteroidal mineralocorticoid receptor antagonist, which has been approved for use in persons with chronic kidney disease (CKD) and type 2 diabetes (diabetic kidney disease or DKD), to retard the progression of DKD.[1]

Finerenone offers an alternative pathway to treat CKD associated with type 2 diabetes by blocking mineralocorticoid receptor overactivation, which contributes to CKD progression and cardiovascular damage. The development of finerenone represents a major breakthrough in the prevention and management of DKD, as it has proven cardiovascular and renal benefits in two long-term renal and cardiovascular outcome trials (CVOTs). Two large CVOTs, FIDELIO and FIGARO, along with their pre-specified analysis, FIDELITY, have demonstrated a statistically significant improvement in various cardiocentric and renocentric composite outcomes.[2-4]

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SHARING INFORMATION AND DECISION-MAKING

Shared and informed decision-making is ingrained in modern medical practice, and persons living with diabetes should be active partners in their management.[5] Therapeutic patient education, per se, has been shown to improve long-term results in persons with diabetes.[6]

It would be good clinical sense, therefore, to discuss the education counseling, and support that is required while prescribing finerenone to a person living with diabetes.

THE 5C CHECKLIST

We have used the 5C rubric (Box 1) to list the **C**linical indications; **C**aveats and contraindications; **C**oncerns and check points; **C**autionary advice, including usage with concomitant medication; and **C**onstraints and cost-associated with finerenone usage.

This simple framework assists health care professionals in discussing and explaining finerenone usage in persons with DKD. The format also works as a useful checklist, not only for finerenone, but for all other interventions in medical practice.

THE WAY FORWARD

Finerenone usage is endorsed by the American Diabetes Association (ADA) and American Association of Clinical Endocrinology (AACE) clinical practice guidelines, which suggest its use in patients with CKD who are at increased risk for cardiovascular events or CKD progression or in those who do not tolerate sodium-

glucose co-transporter-2 (SGLT2) inhibitors. The ADA recommends targeting a ≥30% reduction in urinary albumin-creatinine ratio (UACR), though it does not specify a time frame for this.[7,8]

As finerenone usage increases, the need for patient counseling will increase. We hope that the 5C counseling checklist will assist physicians in offering the best possible care to all persons living with diabetes and DKD.

Box 1. Counseling for Finerenone

Confirmation of Clinical indications

- Statistically significant improvement in cardiovascular and renal outcomes, in persons with type 2 diabetes and DKD, as reported by the FIDELIO, FIGARO and FIDELITY results.
- Finerenone is indicated to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, cardiovascular death, nonfatal myocardial infarction and hospitalization for heart failure in adult patients with CKD associated with type 2 diabetes.
- Initiation of finerenone treatment is recommended in CKD and type 2 diabetes persons with an eGFR >25 mL/min/1.73 m^2, or with UACR >30 mg/g, and with normokalemia.

Caveats and Contraindications

Caveats

- No approved so far on persons with type 1 diabetes.
- No approved so far on persons with non-DKD.
- Not indicated for use in heart failure or refractory hypertension.

Contraindications

- End-stage renal disease.
- Initiation is not recommended if serum potassium >5.0 mmol/L (5 mEq/L).
- Severe hepatic impairment (Child-Pugh C).
- Addison's disease.
- Preconception, pregnancy and lactation.

Concerns and Checkpoints

Concerns

- The risk of side effects is less with finerenone than with earlier mineralocorticoid receptor antagonists such as spironolactone and eplerenone.
- Hyperkalemia leading to permanent discontinuation may occur in ≈2% of patients and the risk of sexual and other side effects is minimal.

Checkpoints

- Serum potassium must be monitored 1 month after onset of therapy, at regular (≈4 monthly) intervals thereafter, and whenever a change in electrolyte levels is anticipated or suspected, e.g., vomiting, diarrhea, addition of diuretics, renotoxic drugs, other concomitant medication, which may interfere with finerenone metabolism.
- While there is no specific recommendation for the frequency and regularity of monitoring UACR, it would be prudent to assess this 4 months after onset of therapy. More frequent assessment may be justified if it can help allay patient anxiety and/or inform changes in choice and/or dosage of finerenone/concomitant therapy.

Caution and Concomitant usage

Caution during use

- Finerenone is a once-daily oral tablet that can be taken at any time of the day.
- Begin with 10 mg/day finerenone in persons with eGFR <60mL/min/1.73 m^2, and 20 mg/day in those with eGFR >60 mL/min/1.73 m^2.
- If potassium levels are normal (<4.8 mEq/L) after 1 month, up-titrate to 20 mg/day.
- If potassium levels are >5.5 mEq/L, withhold finerenone; check potassium after a few days (as it has a short half-life), and restart 10 mg/day if serum potassium ≤5.0 mEq/L.
- If potassium levels are between 4.8 and 5.0 mEq/L, maintain the dose and take an individualized, case-based decision, keeping in mind the risk benefit ratio of continuing finerenone and assessing the ability to screen for hyperkalemia, and manage it if needed.

Concomitant medication

- No extra diuresis occurs with finerenone, and it can be used with thiazide, thiazide-like, and loop diuretics.
- Finerenone is not indicated with other mineralocorticoid receptor antagonists, spironolactone and eplerenone.
- In a patient who has been on spironolactone or eplerenone for an indication such as hypertension or heart failure, and now needs finerenone for management of DKD, an individualized needs and priority assessment should be done.
- Finerenone is not contraindicated in patients taking concomitant medications that are strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, ritonavir, nelfinavir, cobicistat, clarithromycin, telithromycin and nefazodone).
- Concomitant intake of strong CYP3A enzyme inducers like rifampicin, carbamazepine, phenytoin, phenobarbital and St John's Wort may lead to decrease in plasma concentration of finerenone and results in reduced therapeutic effect and should be avoided.
- Finerenone can be used with all glucose-lowering drugs, including SGLT2 inhibitors.

Constraints and Cost

- Share details about the cost of therapy with the patient, especially in a pay-from-pocket scenario, and assist in performing an informal cost-benefit analysis.
- Explain that the cost of 10 mg and 20 mg tablets is same, to preclude suboptimal dosing.

REFERENCES

1. Bayer Zydus Pharma Private Limited, India. Kerendia Prescribing Information, 2022.
2. Bakris GL, Agarwal R, Anker SD, Pitt B, Ruilope LM, Rossing P, et al; FIDELIO-DKD Investigators. Effect of finerenone on chronic kidney disease outcomes in type 2 diabetes. N Engl J Med. 2020;383(23):2219-29.
3. Pitt B, Filippatos G, Agarwal R, Anker SD, Bakris GL, Rossing P, et al; FIGARO-DKD Investigators. Cardiovascular events with finerenone in kidney disease and type 2 diabetes. N Engl J Med. 2021;385(24):2252-63.
4. Agarwal R, Filippatos G, Pitt B, Anker SD, Rossing P, Joseph A, et al; FIDELIO-DKD and FIGARO-DKD investigators. Cardiovascular and kidney outcomes with finerenone in patients with type 2 diabetes and chronic kidney disease: the FIDELITY pooled analysis. Eur Heart J. 2022;43(6):474-84.
5. Kalra S, Baruah MP, Kalra B. Diabetes care: evolution of philosophy. Indian J Endocrinol Metab. 2017;21(4):495-7.
6. Golay A, Lagger G, Chambouleyron M, Carrard I, Lasserre-Moutet A. Therapeutic education of diabetic patients. Diabetes Metab Res Rev. 2008;24(3):192-6.
7. American Diabetes Association Professional Practice Committee. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes—2022. Diabetes Care. 2022;45(Suppl 1):S175-S184.
8. Blonde L, Umpierrez GE, Reddy SS, McGill JB, Berga SL, Bush M, et al. American Association of Clinical Endocrinology Clinical Practice Guideline: Developing a Diabetes Mellitus Comprehensive Care Plan-2022 Update. Endocr Pract. 2022;28(10):923-1049.

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Early Diagnosis of Type 1 Diabetes in Young Children is Important to Preempt DKA-associated Cognitive Decline

Mild cognitive decline may occur expeditiously in children aged 3 to 5 years with type 1 diabetes following an episode of diabetic ketoacidosis (DKA), irrespective of the severity of the event, suggests a multicenter clinical trial published in the journal *Endocrinology, Diabetes & Metabolism*.[1]

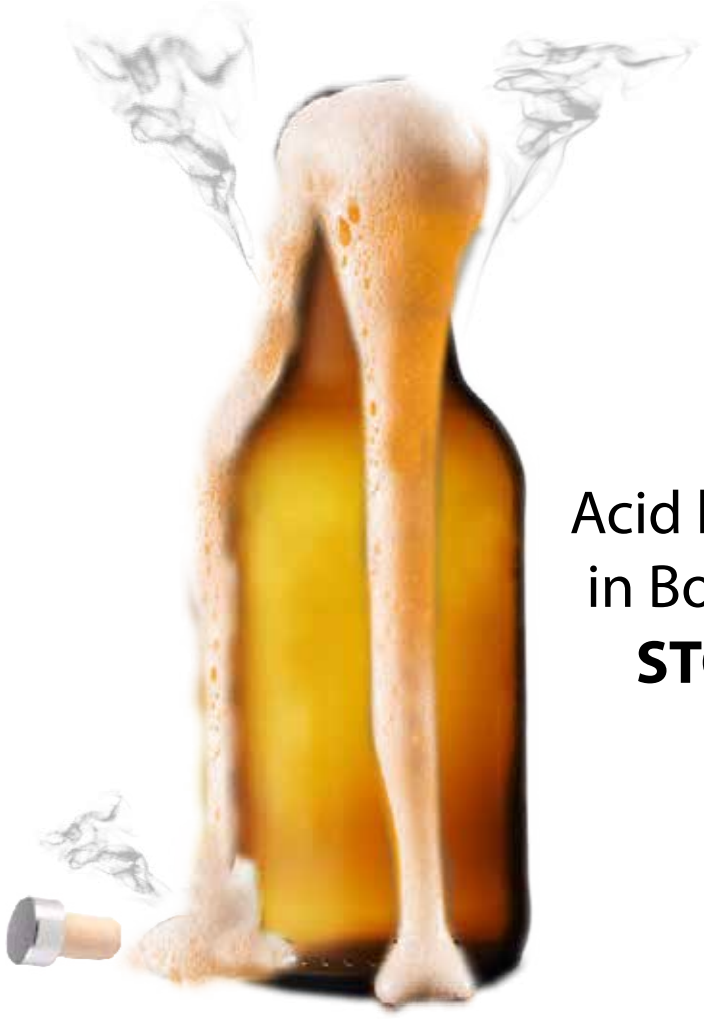
A randomized clinical trial was conducted at 12 hospitals to evaluate the impact of a single episode of DKA on cognitive function in young children. These centers were a part of the Pediatric Emergency Care Applied Research Network (PECARN) Fluid Therapies Under Investigation in DKA (FLUID) trial. For this, researchers selected 22 children with moderate to severe DKA and 24 children with mild DKA with a recent diagnosis of type 1 diabetes, in <2 years of their enrollment. The control group included 27 age- and duration matched children with type 1 diabetes but without DKA. Children with DKA underwent one-time neurocognitive evaluation 2 to 6 months after occurrence of DKA. Children in the control group were evaluated immediately after their enrollment. Children with hypoglycemia (<70 mg/dL) or hyperglycemia (>350 mg/dL) were evaluated at a later date. A pH value from 7.20 to 7.25, or serum biocarbonate between 10 and 15 mmol/L were considered as mild DKA. The features of moderate/severe DKA were pH ≤7.19 or serum bicarbonate ≤9 mmol/L.

Children who developed DKA showed significantly lower IQ scores on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) (English version) compared to children who did not have DKA. Severity of the DKA had no impact on this. This effect was seen even after adjusting for ethnicity and socioeconomic status. "Patient demographic variables had no statistical difference as a function of DKA status" observed the authors.

These findings demonstrate the strong association of DKA on cognitive function in young children with type 1 diabetes as those who had had a single episode of DKA were found to exhibit lower IQ scores compared to age-matched patients without DKA just within 6 months of the episode. Hence, "early detection of diabetes and prevention of DKA in young children" assumes great significance.

Reference

1. Ghetti S, et al; Pediatric Emergency Care Applied Research Network (PECARN) DKA FLUID Study Group. Cognitive function following diabetic ketoacidosis in young children with type 1 diabetes. Endocrinol Diabetes Metab. 2023;6(3):e412.



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BRIEF COMMINICATION

Adolescent Obesity and Type 2 Diabetes Mellitus: Synaptics and Heuristics

MEENAKSHI VERMA*, DAVINDER SINGH BATTH†, MOHAN T SHENOY‡, SUNEET K VERMA#

ABSTRACT

The adolescent population is the foundation for a Nation's progress. Their shoulders therefore must be emboldened with health and dignity to ensure a developed Nation. However, the multitude of prevailing epidemics have left nostone unturned to enfeeble their strength. Type 2 diabetes mellitus (T2DM) and obesity stand amongst the top shotguns. There is a dire need to execute preventive as well as therapeutic actions to contain the epidemic, for which one must be well versed with the attributable risk factors. In this article, we will understand the synaptics of adolescent obesity and T2DM and what strategies are recommended by the health authorities to prevent and overcome this rising epidemic.

Keywords: Adolescent obesity, diabetes mellitus, adolescent health, healthy lifestyle, motivation, obesity

Until recently, young children and adolescents almost never got type 2 diabetes (T2DM), which is why it used to be called as 'adult-onset diabetes'. The majority of cases of diabetes mellitus among this population were immune-mediated type 1a diabetes. However, over the past two decades, the incidence of T2DM among the adolescents has shown a dramatic rise. In a systematic review of literature on the incidence of T2DM among children and adolescents from 25 countries/territories, Wu et al estimated ~41,600 new cases of youth-onset T2DM globally in 2021.[1]

Most of these cases were irrefutably preventable. Youth with T2DM have more rapid disease progression resulting in earlier and more severe micro- and macrovascular complications compared to both adult-onset T2DM and youth-onset type 1 diabetes (T1DM).[2] Such complications include but are not limited to atherosclerotic cardiovascular disease, stroke, myocardial infarction and sudden death, renal insufficiency and chronic renal failure, limb-threatening neuropathy and vasculopathy, and retinopathy leading to blindness.[3] Moreover, the available treatment options for children and adolescents with T2DM are more limited than for adult patients.

SYNAPTICS OF ADOLESCENT OBESITY AND TYPE 2 DIABETES MELLITUS

Insulin resistance is the major risk factor for T2DM at all ages. In adolescent population, the exogenous factor responsible for most cases of insulin resistance is obesity which, when coupled with relative insulin deficiency particularly the physiologic insulin resistance of puberty, leads to the development of overt T2DM. A systematic review and meta-analysis of 53 studies including 8,942 participants found that 75.27% of children with T2DM had obesity, and 77.24% had obesity at diagnosis.[4]

The increasing frequency, earlier onset and greater severity of childhood obesity in the past 50 years together with increasingly sedentary lifestyles and an increasing frequency of intrauterine exposure to diabetes are important drivers of the epidemic of youth-onset T2DM.[5]

STRATEGIES TO CONTROL ADOLESCENT OBESITY AND PREVENT TYPE 2 DIABETES MELLITUS

The following strategies should be implemented to help an adolescent child with obesity lead a healthy lifestyle and prevent the onset and progression of T2DM as per Table 1.

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Table 1. Strategies to Control Adolescent Obesity and Prevent Type 2 Diabetes Mellitus

Physical activity	• How much • How often • Parents' role
Family-based approach	• Food choices • Lifestyle
Screening	• Whom to screen • When to screen • How often to screen • Role of genetic testing • Diagnostic criteria • Confirming diabetes type

PHYSICAL ACTIVITY

There is no denying the fact that adolescent population is overburdened with today's education trends. But a good education is of no worth if the body is not in synchronization with the mind. One of the constants in approach towards a healthy body is physical activity. One must make conscious efforts to inculcate the habits of involving themselves into one or the other physical activities.

- A daily moderate to vigorous physical activity of 30 to 60 minutes, either at once or in 2 to 3 sessions, at least 5 days per week (and strength training on at least 3 days per week), aiming to achieve 7% to 10% decrease in excess weight, is recommended.[6]
- Parents should appreciate even a small amount of progress shown by their child.
- Engage the child into a fitness or sport activity.
- Active family outings must be planned every fortnight to keep the children away from screens, especially during the weekends.
- Involving the children in household chores in the form of fun activities helps to keep them moving on daily basis.

FAMILY-BASED APPROACH

Family is a child's first school. The journey towards a healthy body would not be difficult for a child with obesity if the whole family commits to a healthy lifestyle. Bringing the following lifestyle changes in the family is as mandatory as sending the child to school for good education. Table 2 illustrates the suggestions that could be included in family-based approach.

Table 2. Suggestions that can be Included in the Family-based Approach in Adolescent Obesity and Type 2 Diabetes Mellitus

- Eliminate or gradually reduce sugar intake for everyone in the family
- Include more of fruits and vegetables in the plate
- Adopt healthier alternatives of favorite foods
- Involve kids in food shopping and preparation
- Teach the children to read food labels
- Demonstrate and encourage them to eat slowly
- Discourage TV or gadgets while eating
- Have family meals more often
- Reward them with praises instead of food
- Serve smaller portions and let them to ask for seconds

SCREENING

Risk-based screening for prediabetes and/or T2DM is recommended in the adolescents having one or more of the following risk factors.[5]

- **Risk Factors**
  - Body mass index (BMI) >85th percentile for age and sex, weight for height >85th percentile or weight >120% of ideal for height.
  - Genetics/epigenetics manifested as a strong family history of T2DM in first- or second-degree relatives.
  - Offspring of a pregnancy complicated by gestational diabetes mellitus (GDM)
  - Minority race/ethnicity (Native American, African American, Latino, Asian American, Pacific Islander).
  - Small-for-gestational-age birth weight.
  - Physiologic insulin resistance of puberty.
  - Having signs of insulin resistance or conditions associated with insulin resistance like acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome.
- **Time of screening:** After the onset of puberty or after 10 years of age, whichever occurs earlier.
- **Frequency of screening:** Every 3 years, until the diagnosis is established or refuted.
- **Role of genetic testing:** Testing for monogenic forms of diabetes (Maturity-onset diabetes of the young [MODY], Donohue syndrome and Rabson-Mendenhall syndrome) should be considered as

well, especially if impaired insulin sensitivity and reduced insulin secretion are present in otherwise healthy youth with a family history of T2DM.[7]

- **Diagnostic criteria for overweight and obesity:** The Indian cut-off levels as per Indian Academy of Pediatrics (IAP) are as below:[8]
  - Overweight: BMI ≥23 kg/m^2
  - Obesity: BMI ≥27 kg/m^2
  - Extreme obesity: BMI ≥120% of the 95th percentile or ≥35 kg/m^2.
- **Diagnostic criteria for diabetes in adolescents:**[9]
  - Prediabetes: HbA1c level of 5.7 to <6.5 or fasting glucose ≥100 but <126 mg/dL or 2-hour plasma glucose ≥140 but <200 mg/dL.
  - Diabetes: HbA1c level of >6.5 or fasting glucose ≥126 mg/dL or 2-hour plasma glucose ≥200 mg/dL or random plasma glucose >200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis.
  - Confirming diabetes type:
    - Clinical signs helpful in distinguishing T2DM from T1DM are obesity and signs of insulin resistance.
    - Children and adolescents with overweight/obesity in whom the diagnosis of T2DM is being considered should have a panel of pancreatic autoantibodies tested to exclude the possibility of autoimmune T1DM.
    - Genetic evaluation to exclude monogenic diabetes should also be based on clinical characteristics and presentation.
    - The distinction between these forms of diabetes in youth with obesity has important implications for treatment, since Ab$^+$ youth (with phenotype of T2DM) present more like individuals with T1DM, progressing to insulin requirement more rapidly, and are at risk for other autoimmune disorders. Therefore, measurement of pancreatic autoantibodies (GAD-65 and insulinoma-associated protein 2) is recommended in all youth with clinical characteristics of T2DM.[10]

TAKE HOME MESSAGE

- One should suspect and screen and be aware of Indian cut-offs for obesity.
- Support family-based, school-based and community-based interventions for prevention of this menace.
- Seek and stick to medical advice, as appropriate.

REFERENCES

1. Wu H, Patterson CC, Zhang X, Ghani RBA, Magliano DJ, Boyko EJ, et al. Worldwide estimates of incidence of type 2 diabetes in children and adolescents in 2021. Diabetes Res Clin Pract. 2022;185:109785.
2. Bjornstad P, Chao LC, Cree-Green M, Dart AB, King M, Looker HC, et al. Youth-onset type 2 diabetes mellitus: an urgent challenge. Nat Rev Nephrol. 2023;19(3): 168-84.
3. TODAY Study Group; Bjornstad P, Drews KL, Caprio S, Gubitosi-Klug R, Nathan DM, Tesfaldet B, et al. Long-term complications in youth-onset type 2 diabetes. N Engl J Med. 2021;385(5):416-26.
4. Cioana M, Deng J, Nadarajah A, Hou M, Qiu Y, Chen SSJ, et al. The prevalence of obesity among children with type 2 diabetes: a systematic review and meta-analysis. JAMA Netw Open. 2022;5(12):e2247186.
5. Arslanian SA, Bacha F, Grey M, Marus MD, White NH, Zeitler P. Evaluation and management of youth-onset type 2 diabetes: a position statement by the American Diabetes Association. Diabetes Care. 2018;41(12):2648-68.
6. Asif M. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. J Educ Health Promot. 2014;3:1.
7. Hattersley AT, Greeley SAW, Polak M, Rubio-Cabezas O, Mlynarski W, Castano L, et al. ISPAD Clinical Practice Consensus Guidelines 2018: The diagnosis and management of monogenic diabetes in children and adolescents. Pediatr Diabetes. 2018;19 Suppl 27:47-63.
8. Bajpai A, Shenoy MT, Karia-Shah P. Standard treatment guidelines for childhood obesity 2022. Indian Academy of Pediatrics. Available at: https://iapindia.org/pdf/Ch-026-Childhood-Obesity.pdf
9. American Diabetes Association. 2. Classification and diagnosis of diabetes. Diabetes Care. 2015;38 Suppl 1:S8-S16.
10. Klingensmith GJ, Pyle L, Arslanian S, Copeland KC, Cuttler L, Kaufman F, et al; TODAY Study Group. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study. Diabetes Care. 2010;33(9):1970-5.

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Dual Left Circumflex Artery

MONIKA MAHESHWARI*, VISHWAS†, RAKESH MAHLA‡

Dual left circumflex (LCx) arteries represent a very rare congenital anomaly with only few reported cases in literature. Herein, we present a case of dual LCx arteries originating from the left main coronary artery (LMCA) and right coronary artery (RCA), respectively.

A 40-year-old male presented in emergency department with complaint of chest pain. On examination, his pulse rate was 90 beats/min and blood pressure 120/70 mmHg. Electrocardiogram (ECG) showed ST depression in inferior leads. Cardiac markers creatine phosphokinase-MB and troponin I was within normal limits.

Echocardiography revealed hypokinetic inferolateral wall. Elective coronary angiography was then planned, which showed twin LCx arteries: one originating from LMCA and the other from the proximal RCA (Figs. 1 and 2). Patient was discharged on optimal medical therapy and he remained asymptomatic in follow-up period.

Coronary anomalies are rare. The most frequently found anomalies include a LCx artery with a separate origin of the left anterior descending (LAD), followed by a LCx artery arising from the right sinus of Valsalva or the RCA.[1] Only a few cases of twin circumflex arteries originating from both left and right coronary systems have been reported in the literature.[2-4] It may cause chest pain, heart failure, arrhythmia and sudden death as a consequence of the repeated compression of the anomalous artery by a dilated aortic root or of slit-like ostia or of unusual angling as a result of the retroaortic course of the LCx.[5]

The clinical significance of this anomaly may be important in patients undergoing coronary intervention or cardiac surgery. It is important to inform the surgeons so as to accidentally avoid cross-clamping or transecting the artery during surgery.

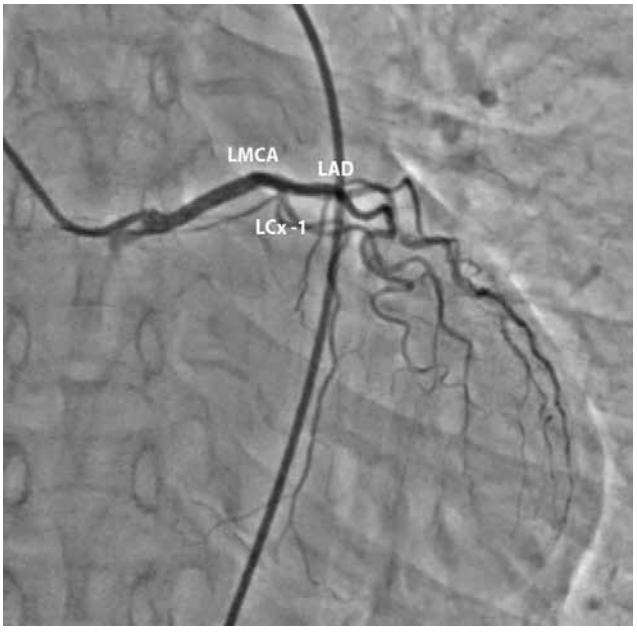

Figure 1. Left coronary angiogram showing small, left circumflex artery (LCx-1) arising from left main coronary artery (LMCA).

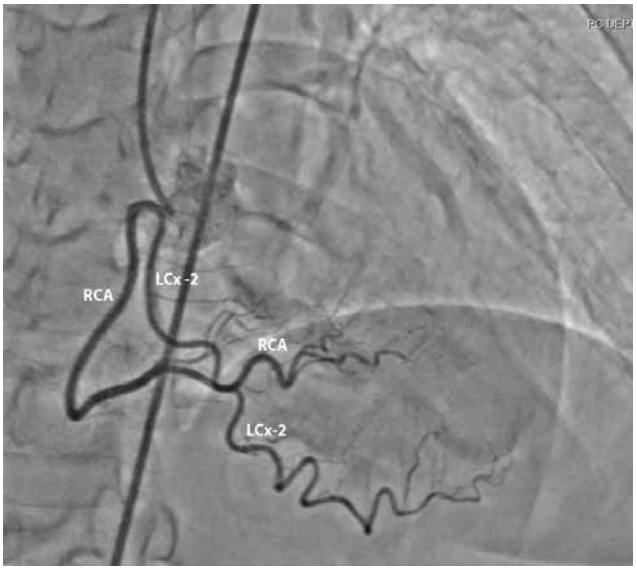

Figure 2. Right coronary angiogram showing second left circumflex artery (LCx-2) arising from right coronary artery (RCA).

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REFERENCES

1. Angelini P, Villason S, Chan AV, Diez RJG. Normal and anomalous coronary arteries in humans. In: Angelini P (Ed.). Coronary Artery Anomalies: A Comprehensive Approach. Philadelphia, PA: Lippincott Williams & Wilkins; 1999. pp. 27-79.
2. Karabay KO, Uysal E, Bağırtan B, Vural M. A case of twin circumflex arteries associated with acute myocardial infarction. Turk Kardiyol Dern Ars. 2010;38(7): 496-8.
3. Uluçay A. A case of twin circumflex arteries associated with acute myocardial infarction. Turk Kardiyol Dern Ars. 2011;39(4):348; author reply 349-50.
4. Uğuz B, Tiryakioğlu SK, Öztaş S, Karakuş A. A very rare coronary artery anomaly: twin circumflex arteries associated with acute coronary syndrome - two cases report. Arch Clin Cases. 2021;7(2):22-7.
5. Aydin M, Ozeren A, Peksoy I, Cabuk M, Bilge M, Dursun A, et al. Myocardial ischemia caused by a coronary anomaly: left circumflex coronary artery arising from right sinus of valsalva. Tex Heart Inst J. 2004;31(3):273-5.

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Benefits of COVID-19 Vaccine and Booster during Pregnancy

Pregnant women are at risk of developing severe coronavirus disease (COVID-19), which is associated with adverse maternal and neonatal outcomes. Taking a COVID-19 mRNA vaccine and a booster dose during pregnancy protects both the mother and her child against COVID-19, according to results of the Multisite Observational Maternal and Infant Study for COVID-19 (MOMI-VAX) study published in the journal *Vaccine*.[1,2]

This observational study of COVID-19 vaccination during pregnancy and postpartum was launched in 2021 by the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH).

Researchers enrolled 240 women who had been vaccinated with COVID-19 mRNA vaccine (Pfizer/Moderna) during pregnancy in this study conducted at 9 centers in the United States from July 2021 to January 2022. Of these, 167 had completed their primary 2-dose series and 73 had also taken one booster dose (as recommended at the time of this study). The objective of the study was to estimate the levels of the binding and neutralizing antibodies to the COVID-19 mRNA vaccines in the pregnant women and also to measure the antibody levels in cord blood.

Binding and neutralizing antibodies against the D614G variant of SARS-CoV-2, including its Delta and Omicron (BA.1) subvariants were detected in all pregnant women at delivery who had completed their primary vaccination series against COVID-19 and also in all cord blood samples of the vaccinated women. The serum antibody levels, including in the cord blood, were found to be further increased among pregnant women, who had also taken the booster dose of the vaccine compared to those who had taken just the two vaccine doses. Nine percent of women who had taken the primary series of the Pfizer vaccine had neutralizing antibodies to Omicron compared to 22% of those who had received two doses of the Moderna primary series. Seventy-three percent of the boosted women had antibody levels "although titers were significantly lower than to the D614G strain".

An efficient transplacental transfer of antibodies was seen with primary vaccination as well as booster vaccination during pregnancy. The antibody transfer ratio ranged from 1.55 to 1.77 for binding IgG, 1.00 to 1.78 for live virus neutralizing antibodies and 1.79 to 2.36 for pseudovirus neutralizing antibodies.

This study demonstrates the robust maternal immune response generated after COVID-19 mRNA vaccination during pregnancy, especially following the booster dose as well as the transplacental transfer of antibodies. It illustrates the protective effect of the vaccine on the newborns and supports the use of COVID-19 vaccine, especially its booster dose during pregnancy as "newborns are too young to be vaccinated". The researchers advocate further research to ascertain the optimal time of vaccination during pregnancy to gain the maximum benefit for both the mother and her child.

References

1. Munoz FM, et al; DMID 21-0004 Study Group. COVID-19 booster vaccination during pregnancy enhances maternal binding and neutralizing antibody responses and transplacental antibody transfer to the newborn. Vaccine. 2023;41(36):5296-303.
2. NIH News Release. August 11, 2023. Available at: https://www.nih.gov/news-events/news-releases/covid-19-vaccination-boosting-during-pregnancy-benefits-pregnant-people-newborns Accessed August 16, 2023.

EXPERT OPINION

Nutrition and COPD

VIJAY KUMAR

INTRODUCTION

- Changes in diet like decreased consumption of fruits, vegetables, whole grains and fish, and increased consumption of processed and refined foods, have increased the prevalence of chronic diseases, including chronic obstructive pulmonary disease (COPD), in the past few decades.[1]
- Advanced COPD patients demonstrate an abnormal nutritional status with unintended weight loss, muscle loss, low-fat and fat-free mass associated with the presence of emphysema, which serves as an independent determinant of COPD outcomes and thus demands nutritional interventions.[1]
- Scientific evidence suggests that some foods and nutrients, particularly those nutraceuticals enriched with antioxidant and anti-inflammatory properties, when consumed in combinations in the form of balanced dietary patterns, render better pulmonary function, less lung function decline and reduced risk of COPD.[1]

WHY DIETARY MANAGEMENT AND NUTRITIONAL SUPPLEMENTATION IS IMPORTANT IN COPD?

It Treats Weight Loss in COPD

- A patient with a negative energy balance or losing weight rapidly will require increased energy intake since an additional reduction of energy expenditure is not desirable in COPD.[2]
- Several small portions of diet spread throughout the whole day will give optimum energy- and protein-enriched diet.[2]
- Current guidelines recommend protein must provide 20% of the total energy intake.[2]
- Low energy intakes make it hard to fulfill the vitamins, minerals and trace elements requirements. Thus, oral nutritional supplements can prove beneficial to fulfill nutrient requirements when supplemented along with food.[2]
- There is moderate-quality evidence that suggests nutritional supplementation promotes weight gain among patients with COPD, particularly undernourished.[2]
- Undernourished patients have shown significant weight gain, improvement in anthropometric measures (fat-free mass, mid-arm muscle circumference and triceps skin folds), 6-min walk distance, respiratory muscle strength (maximal inspiratory and expiratory pressures) and overall health-related quality of life as measured by the St George's Respiratory Questionnaire after nutritional supplementation.[2]

Nutrition Acts as an Ergonic Aid in COPD

- Enhancing physical performance is a key therapeutic goal in COPD, which can be achieved by nutritional intervention.[2]
- Nutritional therapy in this population can improve performance as well as enhance the outcome of exercise training that provides clinical and physiological benefit in COPD.[2]
- Carbohydrate-rich supplements and polyunsaturated fatty acids (PUFAs) have been shown to improve outcomes or exercise training in selected COPD patients.[2]

It is Cost-effective

Undernourishment in COPD is likely to be associated with:

- Longer in-patient hospital stays[2]
- A higher probability of being readmitted[2]
- An increase in health care utilization.[2]

THERE IS PRESENCE OF INAPPROPRIATE DIETARY QUALITY AND NUTRIENT DEFICIENCIES IN COPD

COPD is frequently associated with vitamin D deficiency and insufficient intake of vitamin with antioxidant capacity (vitamins A, C and E).[2]

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Vitamin D

- Vitamin D status serves as an independent predictor of all-cause mortality, upper airway respiratory infections and pulmonary function in the general population.[2]
- But for COPD, the evidence is conflicting on whether 25-hydroxyvitamin D (25[OH]D) levels correlate with lung function decline, infectious exacerbations and muscular function.[2]
- Vitamin D deficiency is common in COPD because of smoke-induced skin aging, reduced outdoor activity and low-quality dietary intake.[2]
- Daily intakes along with a minimal amount of ultraviolet radiation exposure vary with age but a dose of 800 IU with 1 g calcium is considered optimum.[2]

Vitamin E

Long-term supplementation with vitamin E has shown to reduce the risk of COPD but no evidence exists on the positive effects of additional vitamin intake on clinical outcomes in a COPD population.[2]

Prudent Diet

A prudent diet in COPD is linked with better pulmonary function, less lung function decline and reduced risk of COPD.[2]

Iron

Iron deficiency also frequently occurs in COPD due to several factors including systemic inflammation, malabsorption of iron from the gut, renal failure (as a consequence of concomitant chronic kidney disease or diabetes mellitus), and medications such as angiotensin-converting enzyme inhibitors and corticosteroids.[2]

Dietary Fiber

Greater intake of dietary fiber is linked with a reduced COPD risk, better lung function and reduced respiratory symptoms.[2]

Meat

Frequent or high consumption of cured meats is associated with an increased risk of developing COPD and a higher risk of readmission to hospitals with COPD.[2] Thus, a well-balanced with a sufficient intake of fresh fruits and vegetables is advantageous for COPD patients due to their potential benefits on the lung and their proven benefits on metabolic and cardiovascular risk.[2]

NUTRITION IS A PART OF INTEGRATED DISEASE MANAGEMENT

The efficacy of nutritional supplementation can be intensified by additional interventions like:

- Smoking cessation[2]
- Correction of hypoxemia and/or hypercapnia with long-term oxygen therapy and/or noninvasive ventilation[2]
- Reduction of static and dynamic hyperinflation by long-acting bronchodilators or lung volume reduction, or androgens either to correct hypogonadism or to boost muscle anabolism.[2]

Multimodal rehabilitation program including nutritional supplementation, androgens and exercise training improves clinical outcome and survival in malnourished patients with advanced COPD.[2]

EFFECT OF DIETARY PATTERN IN COPD OUTCOME

Numerous epidemiological studies linking dietary patterns to adult lung function and COPD (incidence, prevalence and severity) have shown:[1]

Meat-Dim-Sum Pattern and Vegetable-Fruit-Soy Pattern

The meat-dim-sum pattern is associated with increased incidence of cough with phlegm.[1]

Prudent Pattern and Western Pattern

The prudent pattern is negatively, while the Western pattern is positively associated with COPD risk.[1]

Prudent Pattern and Traditional Pattern

The prudent pattern is positively associated with forced expiratory volume in 1 second (FEV1) in males and females, and negatively with COPD in males.[1]

Prudent Pattern, High-carbohydrate Diet, Western Pattern

The prudent pattern is positively associated with lung function and negatively with COPD prevalence.[1]

Western Pattern and Prudent Pattern

The Western pattern is associated with a higher prevalence of COPD, respiratory symptoms and worse lung function.

The prudent pattern is associated with a lower prevalence of COPD, cough and higher lung function.[1]

Alcohol-consumption Pattern, Westernized Pattern and Mediterranean-like Pattern

Alcohol-consumption pattern and Westernized pattern (in female) are associated with impaired lung function; a nonsignificant trend for preserved lung function is found for Mediterranean-like pattern.[1]

Cosmopolitan Pattern, Traditional Pattern and Refined Food Dietary Pattern

The traditional pattern is associated with lower FEV1 and increased prevalence of COPD; the cosmopolitan pattern is associated with increased prevalence of asthma and wheeze.[1] The refined food pattern is associated with a nonsignificant greater decline in lung function.[1]

REFERENCES

1. Scoditti E, Massaro M, Garbarino S, Toraldo DM. Role of diet in chronic obstructive pulmonary disease prevention and treatment. Nutrients. 2019;11(6):1357.
2. Schols AM, Ferreira IM, Franssen FM, Gosker HR, Janssens W, Muscaritoli M, et al. Nutritional assessment and therapy in COPD: a European Respiratory Society statement. Eur Respir J. 2014;44(6):1504-20.

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History of Infertility and Severity of Menopausal Symptoms

Middle-aged women with a history of infertility have higher odds of experiencing more severe menopausal symptoms compared to those who do not have infertility, according to the results of a recent study published in the journal *Menopause*.[1] They had higher incidence of depressive mood, irritability and difficulties in sleeping.

A secondary analysis of data from Project Viva was conducted by Fitz et al in order to investigate if history of infertility in women had any impact on menopausal symptoms. Project Viva included 695 women aged ≥45 years with amenorrhea for ≥1 year. They had been enrolled during pregnancy from 1999 to 2002 and followed for 18 years. If time taken to become pregnant was 12 months or more or the participants had used medical treatments to conceive or had infertility consultation or had taken infertility treatment in the preceding 6 months was considered as infertility by the researchers. The severity of menopausal symptoms was evaluated with the Menopause Rating Scale (MRS). A score above or below the median was defined as the primary outcome of the study. The individual symptom score on the MRS and self-reported age at which menopause was attained were the secondary outcomes of the study.

Nearly 37% of women included in the study had a history of infertility. Women with a history of infertility were older in age than those with no infertility; 53.4 vs. 51.2 years. Little over 60% of them had attained menopause compared to 40% without infertility. Women with infertility had higher chances of having scores above the median on the MRS scale with adjusted odds ratio (aOR) of 1.45. They were 1.5 times more likely to report depressive mood and irritability with aOR of 1.56 and 1.57, respectively. The probability of sleep problem severity was nearly doubled in women with infertility with aOR of 1.91. However, infertility and other symptoms or age of menopause had no correlation.

These findings suggest a history of infertility as a red flag to screen menopausal women for symptoms of depression.

Reference

1. Fitz VW, et al. Exploring the relationship between history of infertility and the experience of menopausal symptoms. Menopause. 2023;30(9):913-9.

Medicolegal Insights

CAN DOCTOR/SURGEON/CONSULTANT BE HELD LIABLE FOR NOT RENDERING A SERVICE OR FACILITY, WHICH IS NOT AVAILABLE IN THE HOSPITAL?

The doctor cannot be held liable for not rendering a facility, which was not available in the hospital. If the hospital knowingly fails to provide some amenities that are fundamental for the patients, then it would certainly amount to medical malpractice; but for the same, the doctor cannot be held liable for medical negligence.

In the matter of **Malay Kumar Ganguly vs. Sukumar Mukherjee & Ors. AIR 2010 SC 1162, the Hon'ble Supreme Court of India** has held that:

"We must bear in mind that negligence is attributed when existing facilities are not availed of. Medical negligence cannot be attributed for not rendering a facility which was not available. In our opinion, if hospitals knowingly fail to provide some amenities that are fundamental for the patients, it would certainly amount to medical malpractice. As it has been held in Smt. Savita Garg (supra), that a hospital not having basic facilities like oxygen cylinders would not be excusable. Therein this Court has opined that even the so-called humanitarian approach of the hospital authorities in no way can be considered to be a factor in denying the compensation for mental agony suffered by the parents. The aforementioned principle applies to this case also in so far as it answers the contentions raised before us that the three senior doctors did not charge any professional fees."

In the matter of **Savita Garg vs. Director, National Heart Institute AIR 2004 SC 5088, the Hon'ble Supreme Court of India** has held that:

"The patients once they are admitted to such hospitals, it is the responsibility of the said hospital or the medical institutions to satisfy that all possible care was taken and no negligence was involved in attending the patient. The burden cannot be placed on the patient to implead all those treating doctors or the attending staff of the hospital as a party so as to substantiate his claim. Once a patient is admitted in a hospital it is the responsibility of the Hospital to provide the best service and if it is not, then hospital cannot take shelter under the technical ground that the concerned surgeon or the nursing staff, as the case may be, was not impleaded, therefore, the claim should be rejected on the basis of non-joinder of necessary parties. In fact, once a claim petition is filed and the claimant has successfully discharged the initial burden that the hospital was negligent, as a result of such negligence the patient died, then in that case the burden lies on the hospital and the concerned doctor who treated that patient that there was no negligence involved in the treatment. Since the burden is on the hospital, they can discharge the same by producing that doctor who treated the patient in defence to substantiate their allegation that there was no negligence. In fact, it is the hospital who engages the treating doctor thereafter it is their responsibility. The burden is greater on the Institution/Hospital than that of the claimant. The institution is private body and they are responsible to provide efficient service and if in discharge of their efficient service there are couple of weak links which has caused damage to the patient then it is the hospital which is to justify the same and it is not possible for the claimant to implead all of them as parties."

IS IT OBLIGATORY FOR HOSPITALS TO PROVIDE COPY OF THE CASE RECORD TO PATIENT OR HIS LEGAL REPRESENTATIVE?

Yes, it is obligatory for doctors, hospitals to provide the copy of the case record or medical record to the patient or his legal representative.

The Medical Council of India (MCI) has imposed an obligation on doctors as per the Indian Medical Council (Professional Ethics, Etiquette & Conduct) Regulations, 2002 notified on 11th March 2002, amended up to December 2010 to maintain the medical record and provide patient access to it.

Maintenance of Medical Records:

1.3.1. Every physician shall maintain the medical records pertaining to his/her indoor patients for a ***period of three years*** *from the date of commencement of the treatment in a standard proforma laid down by the Medical Council of India and attached as Appendix 3.*

1.3.2. If any request is made for medical records either by the patients/authorized attendant or legal authorities involved, the same may be duly acknowledged and documents ***shall be issued within the period of 72 hours.***

With the enforcement of the MCI Regulations, 2002 it is made clear that the patient has a right to claim medical records pertaining to his treatment and the doctors/ hospitals are under obligation to maintain them and provide them to the patient on request.

In **Kanaiyalal Ramanlal Trivedi vs. Dr Satyanarayan Vishwakarma I (1997) CPJ 332 (Guj), The Hon'ble High Court of Gujarat** has held that the hospital and doctor were held guilty of deficiency in service as case records were not produced before the court to refute the allegation of a lack of standard care.

In **Raghunath Raheja vs. Maharashtra Medical Council, AIR 1996 Bom 198, Bombay High Court** upheld the right of patient to medical record very emphatically.

In the matter titled as **P.P. Ismail v K.K. Radha 1999 CPJ 99 (NC), the Hon'ble National Commission for Consumer Dispute Redressal Forum** has held the hospital vicariously liable for the negligent action of the doctor on the basis of the bill showing the professional fees of the doctor and the discharge certificate under the letterhead of the hospital signed by the doctor

In **S.A. Quereshi vs. Padode Memorial Hospital and Research Centre II 2000. CPJ 463** (Bhopal) it was held that the plea of destroying the case sheet as per the general practice of the hospitals appeared to the court as an attempt to suppress certain facts that are likely to be revealed from the case sheet.

In case of **Dr Shyam Kumar vs. Rameshbhai, Harmanbhai KachiyaI (2006) CPJ 16 (NC), the Hon'ble National Commission of Consumer Dispute Redressal Forum** has held that not producing medical records to the patient prevents the complainant from seeking an expert opinion and it is the duty of the person in possession of the medical records to produce it in the court and adverse inference could be drawn for not producing the records.

In **Medi. Supri. Loknayak Jaiprakash Narayan Hospital & Ors. V/s. K.M. Santosh. F.A. No. 244/2008, decided on 14/03/2016, the National Consumer Disputes Redressal Commission** has observed that it is the primary responsibility of the hospital to maintain and produce patient records on demand by the patient or appropriate judicial bodies. The patient or their legal heirs can ask for copies of the treatment records that have to be provided within 72 hours. The hospital can charge a reasonable amount for the administrative purposes including photocopying the documents. Failure to provide medical records to patients on proper demand will amount to deficiency in service and negligence.

■■■■

Lancet: Nutrition Support Cuts TB, Deaths in India

A study published in the global health journal *The Lancet* found that a monthly food basket with enough protein and efficient treatment can cut the number of new tuberculosis (TB) cases among family members of TB patients in India by almost half.

The study conducted in household contacts of 2,800 patients with confirmed pulmonary tuberculosis in 28 TB units of the National Tuberculosis Elimination Programme in four districts of Jharkhand showed that these patients gained more weight when they received a monthly food basket with enough protein and effective treatment.

A group in the trial with a high frequency of severe undernutrition received nutritional supplementation. The researchers discovered that weight increase was significantly connected with a lower risk of TB death, especially in the first 2 months. The control group got a control group, whereas the intervention group received monthly food rations and micronutrients.

Results showed a relative decrease in TB incidence from 39% (all types) to 48% (pulmonary TB proven by microbiology) in the intervention group. To stop one case of TB, nutritional supplements would need to be given to 30 homes (111 household contacts). In these circumstances, nutritional assistance is crucial to patient-centered care to enhance treatment success.

In India, HIV-negative people contracted TB at a rate of 3 million cases per year and died from the disease at a rate of 4,94,000. According to India's National Strategic Plan for TB Elimination, the incidence of TB would decrease by 80% by 2025, and the mortality rate will decrease by 90%.

(*Source: https://www.tribuneindia.com/news/health/nutrition-support-shown-to-prevent-tb-related-deaths-in-india-lancet-study-533582*)

HCFI Dr KK Aggarwal Research Fund

Minutes of an International Weekly Meeting on "Nonobstetric Surgical Emergencies"

Speaker: Dr Avinash Parmar, *MBBS, MS (General Surgery), FMAS, FIAGES. Consultant General & Laparoscopic Surgeon, PD Hinduja Hospital and Medical Research Centre, Mumbai, India*

April 1, 2023 (Saturday, 9.30-10.30 am)

- Pregnancy can be complicated with different surgical emergencies, which may potentially endanger mother as well as fetus.
- Diagnosis and treatment both carry a dilemma followed by a debate on the safest surgical approach during pregnancy, which still continues.
- Appropriate early intervention is essential to decrease the morbidity and mortality.
- Nonobstetric pathologies during pregnancy can be seen in 1% to 2% of all cases. During pregnancy, 0.2% to 1.0% of women require general surgery for nonobstetric problem. Acute abdomen develops during 1 in 500 to 635 pregnancies.
- Gastrointestinal (GI) disorders account for 0.5% to 1% of presentations requiring surgery during pregnancy.
- Pregnancy causes several changes that affect presentation of acute abdominal pain.
- Heartburn and constipation are frequent because of decreased gastric motility.
- Gravid uterus approximately 12 weeks of gestational age compresses and displaces the underlying and surrounding abdominal viscera.
- The expanding uterus makes it difficult to localize pain and can mask or delay the emergence of peritoneal signs.
- Increased laxity of the anterior abdominal wall can also further delay peritoneal signs during pregnancy.
- Progesterone prepares the body for pregnancy by relaxing smooth muscles but also affects the GI tract. It relaxes the lower esophageal sphincter and decreases gastric motility, which increases frequency of heartburn, gastroesophageal reflux and nausea during pregnancy. Progesterone causes bile stasis and increases the incidence of cholelithiasis and resultant cholecystitis. Additionally, elevated levels of estrogen increases bile concentration, which also increases formation of cholelithiasis and risk of acute cholecystitis.
- The most frequent indications for surgery during pregnancy are infections such as acute appendicitis and cholecystitis. Other indications are infected cysts, carbuncles, hemorrhoids (external thrombosed), hernia (strangulated, incarcerated or obstructed).
- Pregnant women may also require acute surgical intervention for ovarian disorders and bowel obstruction, as well as for traumatological or oncological indications.
- Managing such scenarios can be equally challenging for both obstetricians and general surgeons.
- The nongynecological and nonobstetric causes include acute appendicitis, symptomatic cholecystitis, intestinal obstruction, cholangitis, acute pancreatitis and peptic ulcer perforation.
- The gynecological and nonobstetric causes include twisted or ruptured ovarian cyst and torsion of pedunculated subserosal fibroid.
- The obstetric causes are acute ectopic pregnancy, ruptured uterus (spontaneous or with risk factors).
- Appendicitis is one of the most common problems in pregnant women with acute abdomen. The incidence of acute appendicitis is the same in pregnant and nonpregnant women. It occurs most commonly during the second trimester.
- Appendicitis occurs in one of every 1,500 pregnancies. Perforated appendix increases fetal morbidity and mortality rates, which are as high as 20% to 35% with perforation and as low as 0% to 1.5% in uncomplicated appendicitis.
- The classic scenario of appendicitis entails periumbilical pain radiating to right lower quadrant. Following the onset of pain, anorexia, nausea, vomiting, fever may develop.
- Anorexia, nausea and vomiting can also occur in early pregnancy, but differential diagnosis can be done by lab investigations and imaging.
- Abdominal examination usually reveals tenderness, rebound tenderness and involuntary guarding classically over the McBurney's point.

- Diffuse peritonitis or abdominal wall rigidity are suggestive of appendicular perforation.
- When the appendix is in the retrocecal region, pain is usually described as dull rather than localized, elicited more likely by rectal/vaginal examination than by abdominal examination. Accordingly, pelvic appendix may cause tenderness below McBurney's point, urinary frequency, dysuria, tenesmus and diarrhea.
- Pregnant women are less likely to have a classic presentation of appendicitis versus nonpregnant women, especially in late pregnancy.
- However, location of appendix migrates a few cms cephalad (above) towards the liver, with the enlarged uterus, so in the third trimester, the pain may localize to mid or even upper right abdomen.
- McBurney's point tenderness may be less prominent because gravid uterus lifts and stretches anterior abdominal wall away from the inflamed appendix.
- Since direct contact between area of inflammation and parietal peritoneum is impeded, there is less rebound tenderness or guarding.
- Gravid uterus may also inhibit contact between the omentum and the inflamed appendix.
- Around 80% of nonpregnant patients with appendicitis have a preoperative leukocytosis (total leukocyte count [TLC] >10,000) with left shift. But mild leukocytosis can be a normal finding in pregnant individuals; TLC may be as high as 16,900 in the third trimester, rising as high as 29,000 during labor.
- If the inflamed appendix is close to the ureter or bladder, microscopic hematuria and pyuria may occur.
- Mild elevations in serum bilirubin may be a marker for appendicular perforation with sensitivity of 70% and specificity of 86%.
- C-reactive protein (CRP) may be elevated in appendicitis, but it is a nonspecific sign of inflammation.
- Ultrasound during pregnancy is safe and is effective in identifying the etiology of acute abdominal pain in many patients and should be the initial imaging modality of choice.
- Magnetic resonance imaging (MRI) is preferred over computed tomography (CT) scan for diagnosis of nonobstetric pain in the gravid patient.
- Abdominal CT scan may be used in emergency situations during pregnancy. CT scan should not be the initial imaging test of choice.
- The first imaging test is USG, 2nd is MRI and third is CT scan.
- Antibiotic therapy alone for pregnant women with appendicitis should be considered experimental as available data are limited.
- Patients should be counseled about the possible increase in maternal morbidity.
- In a study involving over 7,000 pregnant women with uncomplicated appendicitis, medical management was associated with increased risk of complications compared with appendectomy viz. peritonitis, venous thromboembolism, sepsis syndrome and septic shock.
- Appendectomy is usually the curate treatment of acute appendicitis. Delaying surgery for >24 hours after the onset of symptoms increases risk of perforation.
- Approaches for appendectomy include laparoscopic and open techniques. The choice of technique should be based on the patient's clinical status and preferences, gestational age and the experience of the surgeon.
- Earlier there were concerns of uterine injury from trocar placement and fetal malperfusion due to pneumoperitoneum during laparoscopy.
- However, current guidelines state that laparoscopic surgery is standard of care in pregnant women as it is safe, allows easier identification of appendix and offers an opportunity for evaluation of abdomen for any associated pathology.
- When performing open appendectomy in a pregnant woman, a transverse incision is made at McBurney's point. But when the diagnosis is less certain, lower midline vertical incision can be used as it permits adequate exposure of abdomen for diagnosis and treatment of surgical conditions that mimic appendicitis.
- Vertical incision can also be used for a cesarean delivery, if subsequently required for the usual obstetric indications.
- It is prudent to minimize traction on the uterus and uterine manipulation, although an association between these maneuvers and preterm birth is unknown.
- Laparoscopic appendectomy can be performed successfully during all trimesters with very few complications as shown in many case reports, case series and cohort studies in pregnancy.

- Decision to proceed is based on skill and experience of surgeon and clinical factors such as size of the gravid uterus.
- Adopt slightly left lateral position of the patient in the second trimester during laparoscopic surgery.
- Use of open entry techniques or placement of trocars under direct visualization and limiting intra-abdominal pressure to <12 mmHg.
- Concerns have however been raised that laparoscopic appendectomy appears to be associated with higher rates of preterm delivery and fetal loss.
- After appendicitis, cholecystitis is the second most common surgical condition during pregnancy. Acute acalculous cholecystitis seems to be more common during pregnancy vs. nonpregnant women.
- The incidence of gallstone disease complicating pregnancy is 0.05% to 0.8%.
- Hormonal changes during pregnancy increase the risk of cholecystitis. An elevated estrogen level causes aggregation of cholesterol crystals and thus leads to increased viscosity of bile and gallstone formation. Progesterone causes smooth muscle relaxation and bile sludging creating a good environment for development of cholelithiasis.
- The signs and symptoms of acute cholecystitis are similar to those in nonpregnant population and include nausea, vomiting, fever and right upper quadrant pain.
- Laboratory tests are not useful as the TLC, amylase and alkaline phosphatase are elevated during normal pregnancy.
- Diagnostic test of choice for all patients with right upper quadrant pain is ultrasound, which has 95% to 98% accuracy: wall thickness >3 mm, presence of pericholecystic fluid/gallstones/Murphy sign.
- If diagnosis and surgical evaluation are delayed, the risk of complication increases, which may include gallbladder rupture, peritonitis, sepsis. They can cause preterm labor and contribute to fetal death and increase maternal mortality.
- Either conservative management or cholecystectomy may be chosen for management of acute cholecystitis.
- Conservative management includes hydration, supportive care and antibiotic therapy with a beta-lactamase inhibitor. Alternatively, third-generation cephalosporin may be given along with metronidazole.
- Acute pancreatitis presents as sudden onset, dull aching, rapidly progressive epigastric pain radiation towards back, refractory to usual doses of analgesics. It improves with stooping forwards.
- Ultrasound helps to exclude possible differential diagnoses and to diagnose gallstone pancreatitis, but it does not establish diagnosis. CT is reserved for particular indications.
- Acute pancreatitis should always be diagnosed with both clinical features and biochemical tests.
- Acute pancreatitis should initially be managed conservatively after resuscitation, preferably in intensive care unit (ICU). Prognosis is assessed by APACHE-II or CTSI (CT scan Severity Index). Necrosectomy can be done in laparoscopic approach by an experienced hepatopancreatobiliary surgeon.
- Laparoscopic cholecystectomy is very safe. Port placement should be above the umbilicus depending on the size of the gravid uterus. Trocar entry should be guided, under direct vision, should be tailored.
- Intestinal obstruction is characterized by colicky abdominal pain, vomiting, constipation and abdominal distension.
- Clinical presentation may be confusing since vomiting, constipation both can be present due to physiological changes of pregnancy.
- Abdominal distension and visible peristalsis are difficult to assess because of the growing uterus.
- Intestinal obstruction complicates as many as 1 in 1,500 to 3,000 pregnancies.
- They most often occur in the third trimester because of the mechanical effects of the rapidly growing gravid uterus on the GI tract.
- Obstructions also occur in the immediate post-partum period from the rapidly decreasing size of the uterus.
- Among patients with bowel obstruction, the maternal mortality rate can be as high as 6% and the fetal mortality rate as high as 26%.
- Risk increases in the third trimester, where maternal mortality rate can reach 10% to 20%, especially if the diagnosis is delayed.
- The incidence of bowel obstruction increased recently, perhaps because of an increase in number of abdominal procedures, an increased incidence of pelvic inflammatory disease (PID) and an increase in the number of older women becoming pregnant.
- Adhesions are thought to cause 60% to 70% of small bowel obstructions during pregnancy.

- Diagnosing intestinal obstruction in pregnancy is challenging as clinical symptoms mimic morning sickness in first trimester. Ideally MRI should be investigation of choice in pregnancy. But if unavailable, X-ray abdomen can be done. Supine X-ray is better than erect posture. However, due to superimposed images of the fetal skeleton identification of dilated bowel loops can be difficult.
- X-ray during organogenesis should be done with caution.
- Decision should be taken after assessing the risk and benefits. Explain clearly to the patient and the family.
- USG might show a hernia defect if an incarcerated hernia is suspected based on physical examination or patient history.
- Majority of other bowel obstruction improve with resuscitation. No improvement of symptoms should be managed by laparoscopic or open surgery.
- Surgical evaluation should not be delayed once the diagnosis is suspected.
- Colonoscopy allows identification and treatment of sigmoid volvulus.
- Surgery during pregnancy for hernia is indicated only when obstruction, strangulation or incarceration is suspected.
- Resection of nonviable gut followed by stoma formation or primary anastomosis can be attempted.
- Any kind of pathology can occur in pregnant women and requires immediate surgical treatment and optimized interdisciplinary management to achieve maximum safety for both mother and fetus, to avoid teratogenous mediation, fetal acidosis and hypoxemia, stillbirth or premature birth.
- It is possible that the physiological changes of pregnancy including the gravid abdomen with displacement of abdominal structures and respiratory changes may increase the risk of perioperative complications. Despite the paucity of data, there have been concerns that nonobstetric surgery may increase the risk of surgical complications as well as adverse obstetrical outcomes.
- A study by Fong et al focused on surgical interventions during the third trimester, giving the general recommendation that they should be avoided whenever possible.
- There are no clear recommendations as to the circumstances in which laparoscopy should be used in pregnant women or open surgery is preferred.
- The decision to choose either laparoscopy or open surgery is mostly taken at the surgeon's discretion.
- Only for unclear acute abdomen with suspected acute appendicitis does the Society of American Gastrointestinal Endoscopic Surgeons recommend laparoscopy.
- In a systemic review, the rate of elective termination of pregnancy following nonobstetric surgery was 1.3%. The prematurity rate was 8.2%. Fetal loss associated with appendectomy was 2.6%; however, the rate was increased when peritonitis was present (~11%).
- Pregnant women had higher risks of postoperative septicemia, pneumonia, urinary tract infection and in-hospital mortality compared with nonpregnant women. Pregnant women also had longer hospital stays and higher medical expenditures.
- The most commonly reported complications include reoperation, infection, wound morbidity, prolonged mechanical ventilation or reintubation, venous thromboembolism and death.
- Withholding indicated surgery during pregnancy is not recommended by either the American Society of Anesthesiologists (ASA) or the American College of Obstetricians and Gynecologists (ACOG).
- Pregnancy does not increase the risk of postoperative complications after cholecystectomy and appendectomy. ACOG states: "Because of the difficulty of conducting large-scale randomized trials in this population, there are no data to allow for specific recommendations."
- When there is need for nonobstetric surgery during pregnancy arises, risk stratification, risk mitigation and maternal counseling regarding anticipated outcomes can be challenging.
- Modern surgical and anesthesia techniques appear to diminish the rate of maternal death and neonatal morbidity.
- With a proper multidisciplinary approach, nonobstetric surgery during pregnancy should only be considered to achieve maximum safety for both mother and fetus.

Participants – Member National Medical Associations: Dr Wasiq Qazi, Pakistan, President-CMAAO; Dr Alvin Yee-Shing Chan, Hong Kong, Treasurer-CMAAO; Dr Akhtar Hussein, South Africa

Invitees: Dr Monica Vasudev, USA; Dr Colin Goldberg; Dr Toran Scythe; Dr Bimla Kapoor; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal

India Live 2023

OCT FOR CHRONIC TOTAL OCCLUSIONS

Dr Selvamani S, Madurai

Percutaneous coronary intervention (PCI) of chronic total occlusions (CTOs) is challenging. It is associated with low success rates, increased restenosis and reocclusion. CTOs of arteries are more challenging lesions to treat with angioplasty and stenting than stenotic vessels, primarily due to the difficulty in guiding the wire across the lesion. Angiography alone cannot differentiate between the occluded lumen and the vessel wall and characterize the content of the occlusion. Angiography provides a two-dimensional image of the contrast-filled lumen and does not allow an accurate assessment of the plaque.

Optical coherence tomography (OCT) is a high-resolution imaging technique that can improve the understanding of the vascular response after stenting of chronically occluded vessels. OCT correctly identifies tissue composition within the CTO, such as collagen and calcium can identify intraluminal microchannels. OCT imaging of CTO anatomy and tissue characteristics can significantly improve PCI by providing novel guiding capabilities.

In the ACE-CTO study, OCT was performed 8 months post-stenting. High rates of stent strut malapposition and incomplete stent strut coverage were observed after CTO PCI using everolimus-eluting stent (EES). The study highlighted unique challenges associated with stent implantation in CTOs.

The PRISON-IV trial showed inferior outcomes in patients with CTOs treated with the ultrathin-struts (60 μm for stent diameter ≤3 mm, 81 μm >3 mm) hybrid sirolimus-eluting stents (SES) compared with EES (81 μm). Another recent study evaluated if using smaller stents (≤3 mm) was responsible for the inferior outcome reported in the trial. The study population was divided according to the different sizes of stents implanted in those receiving only stents with a diameter of ≤3 mm (Group-A, 178 patients), only stents >3 mm (Group-B, 59 patients) and those receiving stents of both sizes (Group-C, 93 patients). OCT was performed in 60 patients at follow-up and documented a mild trend toward lower values of minimum in stent area in the hybrid-SES arm of Group A (4.4 ± 1.02 mm^2 vs. 5.0 ± 1.28 mm^2, respectively, p = 0.16). OCT can thus provide important information in CTOs.

FRACTIONAL FLOW RESERVE AND NONHYPEREMIC PRESSURE RATIOS – BE METICULOUS IN ACQUISITION AND INTERPRETATION

Dr Harikrishnan S, Trivandrum

Fractional flow reserve/Nonhyperemic pressure ratios (FFR/NHPR) exposes the 'functional' aspect of a stenosis and is affected by the following parameters: a) Epicardial coronary artery anatomy, b) extent of perfused territory, c) microvascular function (RESISTANCE) and d) collateral flow.

The anatomic severity of stenosis which we assess by coronary angiography is just one component only. That is why coronary physiology assessment scores over angiography. We have to be meticulous in assessing FFR/NHPR. Minor errors in techniques can lead to erroneous values and can influence the management of the patient.

Rules in measuring FFR

- Pressure zeroing of both Pa and the Wire (Pd) should be done meticulously.
- Once zeroing done, the level of the Pa transducer should not be changed.
- Equalization of Pa and Pd should be done with the transducer (located at the proximal part of the dark end of the wire) just inside the proximal coronary.
- Look for Tuohy Borst leak while equalizing and also the introducer needle should be out of the Tuohy.
- For osteal lesions – Equalization to be done with the transducer in the aortic sinus rather in the coronary.
- The guiding catheter should be frequently flushed with normal saline before any measurement to avoid contrast induced damping of Pa.
- The wire to be placed 2-3 cm distal the lesion which is assessed to avoid error due to pressure recovery.
- Nitroglycerin (NTG) should be given for epicardial vessel dilation and adenosine for microvascular dilation.
- Guide catheter should be carefully positioned in osteal lesions and FFR should be measured only when guide is disengaged. Always look for wedging of Pa.
- Measure the FFR during steady state hyperemia and 3-5 beat average measurement is better.

- Pull back verification is **THE MOST IMPORTANT STEP.** Once measurement is over pull back the wire to the position where it was equalized and check whether the value is 1. If >5 mmHg difference, repeat the measurement.
- Pullback verification is done to assess – DRIFT- A phenomenon inherent to piezoelectric systems like the FFR wires.
- Scar tissue can give higher FFR values (negative) as FFR correlates with the perfused myocardial territory.
- Left ventricular hypertrophy, high left ventricular end-diastolic pressure and presence of collaterals can affect FFR.
- For measurement of NHPR – Techniques are the same, but it has to be measured in "true" resting state. Wait 30-45 seconds after contrast/NTG.

ANATOMY CONSIDERATIONS IN PLANNING THE FIRST TAVR

Dr Raj Makkar, USA

Transcatheter aortic valve replacement (TAVR) is a minimally invasive heart procedure to replace a thickened aortic valve that cannot fully open. In the US TVT Registry, 3% to 7% of the TAVRs are for bicuspid AS. It indicated that TAVR is being used selectively in bicuspid AS, and the related data should be interpreted accordingly.

The acceptance of the use of TAVR in high-risk patients was based on evidence from clinical trials that used early-generation TAVR devices. However, these procedures were associated with considerable procedure-related complications. Increased operator experience and enhanced transcatheter valve systems have led to a worldwide trend to use TAVR in patients at low or intermediate risk. This trend has been evaluated in small observational studies, but most patients who are currently recommended for surgery are at low or intermediate risk.

Hence, some of the important inferences drawn from several small studies are:

- Favorable outcomes with TAVR in carefully selected patients with Sapien and Evolut on real-life TVT and sponsored prospective registries.
- CT phenotyping is important in patients' selection and procedure planning.
- While bicuspid TAVR is justifiable irrespective of surgical risk, high-risk anatomical features and/or concomitant aortopathy should prompt consideration for surgical aortic valve replacement (SAVR) in low-risk patients.
- Randomized trials/prospective registries are needed, especially in patients with lower surgical risk.
- Important to consider the lifetime management of patients when deciding between TAVR and SAVR in younger patients who are likely to require multiple procedures over a lifetime.

DEDICATED SIDE BRANCH STENT: WHEN, WHERE AND HOW TO USE?

Dr NK Mahesh, Kerala

Bifurcation lesions are complex, technically tricky and have a higher rate of adverse events and lower success rates. It has been seen that bifurcation intervention is required in approximately 20% of PCIs.

While current guidelines and expert consensus recommend provisional stenting for managing bifurcation lesions, a two-stent strategy must be considered if the side branch (SB) displays a diameter ≥2.5 mm and if the lesion exhibits significant stenosis within the SB ostium.

This has led to the introduction of dedicated bifurcation stents, generally deployed along with main-vessel (MV) stents. Therefore, the important steps to remember in the deployment of the stent are:

- Prepare and pre-dilate the SB lesion with a balloon
- Deployment of BIOMIME branch
- Post-dilation with a balloon
- Prepare the main branch (MB) lesion and position the workhorse stent
- Kissing balloon technique in both MB and SB.

On the other hand, if one faces any difficulty in wiring the SB, there are two approaches to resolving the issue:

- Wire-based option
  - Create or increase the secondary bend
  - Try a different wire after considering Torquability, hydrophilic
  - Pullback of angulated MB wire or dedicated hairpin technique
- Microcatheter-based approach
  - Direct highly angulated wire from straight tip MC
  - Use of angulated MC to direct wire
  - Use of dual lumen MC to direct wire.

News and Views

Landmark SELECT Trial Shows Exciting Results: Will Semaglutide be the Game Changer in Obesity Management?

Use of semaglutide 2.4 mg reduced the risk of major adverse cardiovascular (CV) events in patients with overweight or obesity and known cardiovascular disease (CVD) but no diabetes by 20%, according to headline results from the landmark Semaglutide Effects on Heart Disease and Stroke in Patients with Overweight or Obesity (SELECT) CV outcomes trial (CVOT), released early this week. The trial involved participants across a wide range of clinically relevant risk categories.

According to the top-line results, a 20% reduction in the incidence of composite of major adverse cardiovascular event (MACE) was noted in patients treated with semaglutide compared with placebo, which was statistically significant. All the three components of MACE contributed to the decline with MACE seen with semaglutide. Moreover, it was also safe and well-tolerated.

Once weekly subcutaneous semaglutide 2.4 mg was the first glucagon-like peptide 1 (GLP-1) receptor agonist to be Food and Drug Administration (FDA) approved in June 2021 for management of weight in adult patients with a body mass index (BMI) of ≥27 kg/m^2 who have at least one weight-related ailment or in patients with a body mass index (BMI) of ≥30 kg/m^2. It is intended to be used as an adjunct to increased physical activity and a low-calorie diet.

About the SELECT trial

The SELECT study, initiated in 2017 was a multicenter, multicountry trial conducted in 41 countries and enrolled 17,604 adults aged ≥45 years (average age 61.6 years) with BMI of 33.34 kg/m^2. The trial compared the CV outcomes of treatment with subcutaneous once-weekly semaglutide 2.4 mg (vs. placebo) for prevention of MACEs over a period of up to 5 years in persons with overweight or obesity and past history of CV event, but without diabetes.

The study population was subgrouped into three pre-determined categories according to baseline glycated hemoglobin (HbA1c) (<5.7%, ≥5.7% to <6.0% and ≥6.0 to <6.5%), tertiles of waist-to-height ratio and type of pre-existing CV event namely myocardial infarction (MI), stroke or peripheral artery disease (PAD). The primary endpoint of the trial was the impact of semaglutide on the new-onset MACE comprising of nonfatal MI, nonfatal stroke and CV death. The effect on mortality, CV risk factors, glucose metabolism, body weight and renal function were selected as secondary outcomes. SELECT is the only CVOT till date, which examines the superiority of an antiobesity drug on 3-point MACE.

However, at this point of time, we do not have enough details to further characterize the results in terms of the magnitude of the reduction. The detailed results are likely to be presented at a conference later this year and make a strong case for regulatory approval of addition of a new indication in the label of semaglutide.

References

1. Novo Nordisk press release. August 8, 2023. Available from: https://www.globenewswire.com/news-release/2023/08/08/2720343/0/en/Novo-Nordisk-A-S-Semaglutide-2-4-mg-reduces-the-risk-of-major-adverse-cardiovascular-events-by-20-in-adults-with-overweight-or-obesity-in-the-SELECT-trial.html. Accessed August 10, 2023.
2. Lingvay I, et al; SELECT Study Group. Semaglutide for cardiovascular event reduction in people with overweight or obesity: SELECT study baseline characteristics. Obesity (Silver Spring). 2023;31(1):111-22.

Beneficial Effects of Vegetarian Diet on Cardiometabolic Risk in Heart Disease Patients

The role of vegetarian diet in prevention of cardio-metabolic diseases is well-established. The American Heart Association (AHA) emphasizes on eating a diet rich in fruits and vegetables and whole grains. It also recommends proteins from plants as healthy sources of protein, in addition to fish/seafood and low-fat dairy products.[1]

The American Diabetes Association (ADA) also advocates consumption of a fiber-rich diet containing plenty of vegetables, pulses, fruits and whole intact grains.[2]

But does a vegetarian diet exhibit similar beneficial effects in persons with heart disease or those at high risk of heart disease? To find an answer to this, a meta-analysis examined the effect of vegetarian diet on low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), systolic blood pressure (SBP) and body weight in people with or at high risk of CVDs.[3] After a comprehensive search of Embase, MEDLINE, CINAHL and CENTRAL databases, from their commencement

to July 2021, 20 randomized controlled trials were found to be eligible for the meta-analysis. These trials were conducted in New Zealand, USA and countries in Asia and Europe and involved a total of 1,878 participants comprising people with CVDs, diabetes and those with a minimum of two CVD risk factors.

Results published in *JAMA Network Open* showed that eating a vegetarian diet for 6 months (average) led to significant reduction in LDL-C and HbA1c beyond that achieved with standard therapy. Analysis of data from 19 studies showed reduction in LDL-C levels by 6.6 mg/dL in participants who consumed a vegetarian diet. "The most consistent reduction was observed among people at high risk of CVDs (–9.1 mg/dL)". The HbA1c was also found to decrease by 0.24% when data from 10 studies that had examined HbA1c were analyzed. Analysis of 16 trials observed a decrease of 3.4 kg in body weight in subjects in the vegetarian diet group. However, no statistically significant impact of the vegetarian diet on SBP in pooled analysis of 14 studies, which showed a decrease of –0.1 mmHg. "The GRADE assessment showed a moderate level of evidence for LDL-C and HbA1c reduction", write the authors.

According to the authors, theirs is the first study to analyze data from randomized controlled trials to investigate the association of vegetarian diets with outcomes in people with heart disease. In this study, eating a vegetarian diet was associated with significant improvement in LDL-C, HbA1c and body weight, which are traditional major risk factors for CVD. The beneficial effects relating to glycemic control were most pronounced in patients with type 2 diabetes. The weight changes were also favorable in those with type 2 diabetes and those at high risk of CVD. These results show that consuming a vegetarian diet can enhance the effect of pharmacotherapy in management of cardiometabolic diseases. "Additional high-quality trials are warranted to further elucidate the effects of healthy plant-based diets in people with CVDs" concluded the authors.

References

1. Lichtenstein AH, et al. 2021 dietary guidance to improve cardiovascular health: a scientific statement from the American Heart Association. Circulation. 2021;144(23):e472-e487.
2. Evert AB, et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care. 2019;42(5):731-54.
3. Wang T, et al. Vegetarian dietary patterns and cardiometabolic risk in people with or at high risk of cardiovascular disease: a systematic review and meta-analysis. JAMA Netw Open. 2023;6(7):e2325658.

Increased Sedentary Screen Time during Childhood Increases Risk of Future Metabolic Syndrome

Children who watch television (TV) frequently are likely to develop metabolic syndrome as adults, suggests a study published in the journal *Pediatrics*.[1]

Researchers from the Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago in New Zealand examined the impact of TV viewing time during childhood on health outcomes at 45 years of age. Subjects born in Dunedin, New Zealand in 1972 and 1973 were selected for the study. They were enquired about the time they spent watching TV at ages 5, 7, 9, 11, 13, 15 and 32 years. The blood pressure, blood sugar levels, body weight, waist circumference, blood cholesterol (HDL-C) and triglycerides were measured at 45 years of age. Presence of any 3 or more (high levels of A1c, BP, triglycerides, waist circumference and low HDL-C) of these were defined as metabolic syndrome, which was the primary endpoint of the study. Out of the 997 participants, data for TV viewing time and metabolic syndrome was available for 870.

Results showed an association between mean TV viewing time, from 5 to 15 years of age, with metabolic syndrome. After adjusting for confounding variables such as sex, socioeconomic status and BMI at 5 years of age, the odds ratio (OR) for this association was 1.30. This association was seen to persist even after adjusting for TV watching as adults with OR of 1.26. Children who watched TV for a longer duration of time were found to have higher BMI and lower cardiorespiratory fitness at 45 years of age.

This study highlights the adverse effects of childhood television watching on long-term metabolic health as children and adolescents who spent longer hours watching TV were at higher risk of developing obesity and metabolic syndrome by middle age. They were also more likely to have poor cardiorespiratory fitness. Hence, TV viewing including other screen time should be limited for children and adolescents for better future health.

The World Health Organization (WHO) does not recommend any sedentary screen time for children younger than 1 year of age. For children under 5 years of age, WHO restricts screen time to maximum of 1 hour.[2] The American Academy of Pediatrics (AAP) the age for no screen time to under 2 years of age. For children aged 2 to 12 years, AAP recommends 1 hour of screen time per day and for teenagers, 2 hours per day. The Indian Academy of Pediatrics (IAP) recommends that children below 2 years age should not be exposed to

any type of screen, whereas exposure should be limited to a maximum of 1 hour of supervised screen time per day for children 24 to 59 months age, and less than 2 hours per day for children 5 to 10 years age.[3]

References

1. MacDonell N, Hancox RJ. Childhood and adolescent television viewing and metabolic syndrome in mid-adulthood. Pediatrics. 2023;152(2):e2022060768. doi: 10.1542/peds.2022-060768.
2. WHO News Release. April 24, 2019. Available from: https://www.who.int/news/item/24-04-2019-to-grow-up-healthy-children-need-to-sit-less-and-play-more, Accessed August 12, 2023.
3. Gupta P, et al; IAP Guideline Committee on Digital Wellness and Screen Time in Infants, Children, And Adolescents. Indian Academy of Pediatrics Guidelines on screen time and digital wellness in infants, children and adolescents. Indian Pediatr. 2022;59(3):235-44.

COVID's Effects: Researchers Identify Mitochondrial Dysfunction in Heart and Organs

A recent study published in the journal *Science Translational Medicine* showed a link between the coronavirus and mitochondrial genes, which are crucial in generating energy within human cells. The study highlighted that the coronavirus can adversely affect these genes, leading to dysfunction in various organs beyond just the lungs.

To determine the impact of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus on mitochondria, scientists analyzed tissues of different organs collected from individuals affected by the virus. The scientists observed that while mitochondrial gene expression recovered in the lungs, its functionality in other vital organs, such as the heart, kidneys, and liver, was compromised.

They also observed that the period of highest viral load in the lungs also did not coincide with the presence of the virus in the brain. However, even in the cerebellum, a part of the brain, the expression of mitochondrial genes appeared to be suppressed.

These findings indicated that the body's cells primarily respond through lung involvement upon initial infection. However, over time, mitochondrial function recovers only in the lungs, while other organs, particularly the heart, maintain impaired mitochondrial function.

Dr Douglas C Wallace, PhD, co-senior author of the study, emphasized the significance of these findings, suggesting a paradigm shift in the understanding of coronavirus disease (COVID-19). He added that instead of solely categorizing it as an upper respiratory disease, perceiving COVID-19 as a systemic disorder capable of affecting multiple organs is crucial.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1108590*)

AI-Powered Microscope Triumph: Effective Detection of Malaria in Travelers

A multinational group of researchers has conducted a rigorous evaluation of the precision of an automated microscope coupled with advanced AI software. This technology was employed to detect malaria parasites within blood samples from travelers, a method tested in an authentic clinical environment, presenting an innovative approach to disease identification.

Malaria afflicts over 200 million individuals annually, with over 5,00,000 of these cases resulting in fatalities. The WHO advocates for parasite-centered diagnosis as a prerequisite before commencing treatment for diseases attributed to Plasmodium parasites.

Published in the journal "*Frontiers in Malaria*", the recent study scrutinized more than 1,200 blood samples obtained from travelers who had returned to the United Kingdom from nations where malaria is prevalent.

The researchers meticulously gauged the precision of the AI-augmented microscope setup in an authentic clinical context, carefully emulating ideal conditions. The achieved level of performance in this clinical setup stands as a notable feat for AI algorithms aimed at addressing malaria. The research team meticulously assessed samples through conventional manual light microscopy and the innovative AI-microscope fusion.

Through manual examination, 113 samples were diagnosed as harboring malaria parasites. In comparison, the AI-integrated system accurately detected 99 of these cases as positive, culminating in an impressive 88% precision rate. The researchers highlighted multiple potential advantages stemming from automated malaria diagnosis.

(*Source: https://indiatribune.com/ai-based-automated-microscope-successfully-detects-malaria-in-travellers/*)

■■■■

Do Your Duty with Discipline and Devotion

"Vasudhaiva Kutumbakam" (the whole world is one family) and "Ekam Sat Viprah Bahudavanti" (truth is one but the wise call it by various names) are two basic statements, which come from the ancient Rig Veda and form the fundamentals of Vedic philosophy.

One should do one's duty with devotion and discipline. This principle can be remembered as the principle of three Ds.

In daily routine 'one should remember the purpose for which one is born, which is to fulfil *Dharma* (duty), *Artha* (wealth), *Kama* (desire) and *Moksha* (liberation). To achieve them, one needs to follow the four Fs: (i) Follow the teacher, (ii) Face the negative devils of the mind, (iii) Fight till the end and (iv) Finish at the goal.

The essence of Bhagwad Gita can be summarized in one shloka (Chapter 2.48) where Krishna says to Arjuna "*yogastha kuru karmani*", which means 'concentrate on actions' (do all actions while remaining in yoga). He further says that one should take success and failure in the same stride. (yogastha = steadfast in yoga, kuru = perform, karmani = duties or action).

To acquire spiritual health, one should follow three Ss which are: (i) *Satsang* (company of good people), (ii) *Sadhana* (hard work) and (iii) *Sanskar* (good deeds). Adi Shankaracharya in Bhaj Govindam describes them as Satnam or Simran (bhakti, or reciting the name of their God), Satsang (company of good people) and Seva (good karmas).

Before doing any work, one should follow the principles of three Hs: (i) listen with the Head, (ii) follow the Heart to choose one of the choices and (iii) order the Hands to take an action.

The ABCs of a good professional are Availability, Behavior and Competence. Competence comes last; the first is the availability of the professional.

An action should be based on Truth; it should be coming from consciousness and should end in internal bliss. Various Vedic literatures have termed this triad by different names like *satha, chitha, ananda,* and *satyam, shivam sundaram.*

■■■■

Microplastics Discovered in Human Heart Tissues Pre- and Post-Surgical Procedures, Study Finds

A recent study has revealed that microplastics have been discovered in the heart tissues of individuals who underwent heart surgery. Microplastics are tiny fragments of plastic, typically <5 mL in size, comparable to the dimensions of a pencil eraser.

Evidence suggests that these minuscule plastic particles can infiltrate the human body through entry points such as the mouth, nose and other bodily openings connected to the external environment.

However, many organs and tissues are enclosed within the body, and there is a dearth of knowledge about their potential interaction with and impact from microplastics. This information gap is highlighted in a study by the American Chemical Society. In an initial trial, scientists procured heart tissue samples from 15 individuals during cardiac surgeries.

Additionally, they obtained pre- and postoperative blood samples from half of the participants. These samples were then subjected to analysis using laser direct infrared imaging. The investigation revealed particles measuring 20 to 500 μm in width, composed of eight distinct types of plastic, including polyethylene terephthalate, polyvinyl chloride and poly(methyl methacrylate).

While the quantity and composition of these particles varied among participants, all blood samples contained plastic particles. Notably, the size of these particles diminished after surgery, and they originated from a broader array of plastic materials.

(*Source: https://www.punjabnewsexpress.com/health/news/researchers-find-microplastics-in-human-heart-tissues-before-after-surgical-procedures-218974*)

INSPIRATIONAL STORY

Power of Thought: Hitting Unseen Target

Yogi Raman was a true master of the art of archery. One morning, he invited his favorite disciple to watch a display of his skill. The disciple had seen this more than a hundred times before, but he nevertheless obeyed his teacher. They went into the wood beside the monastery and when they reached a magnificent oak tree, Raman took a flower, which he had tucked in his collar and placed it on one of the branches. He then opened his bag and took out three objects: his splendid bow made of precious wood, an arrow and a white handkerchief embroidered with lilacs. The yogi positioned himself one hundred paces from the spot where he had placed the flower. Facing his target, he asked his disciple to blindfold him with the embroidered handkerchief.

The disciple did as his teacher requested. "How often have you seen me practice the noble and ancient sport of archery?" Raman asked him. "Every day," replied his disciple. "And you have always managed to hit the rose from three hundred paces away." With his eyes covered by the handkerchief, Yogi Raman placed his feet firmly on the ground, drew back the bowstring with all his might – aiming at the rose placed on one of the branches of the oak tree – and then released the arrow.

The arrow whistled through the air, but it did not even hit the tree, missing the target by an embarrassingly wide margin. "Did I hit it?" said Raman, removing the handkerchief from his eyes. "No, you missed completely," replied the disciple. "I thought you were going to demonstrate to me the power of thought and your ability to perform magic."

"I have just taught you the most important lesson about the power of thought," replied Raman. "When you want something, concentrate only on that: no one will ever hit a target they cannot see."

■■■■

Worldwide Surge in Cardiovascular Deaths Due to Particulate Matter Air Pollution

Research published in the *Journal of the American Heart Association* showed that particle matter air pollution (PM) is having a greater worldwide influence on death and disability.

PM pollution is made up of tiny particles floating in the air. The researchers examined PM pollution as a risk factor for mortality and disability by using information from 204 nations gathered between 1990 and 2019.

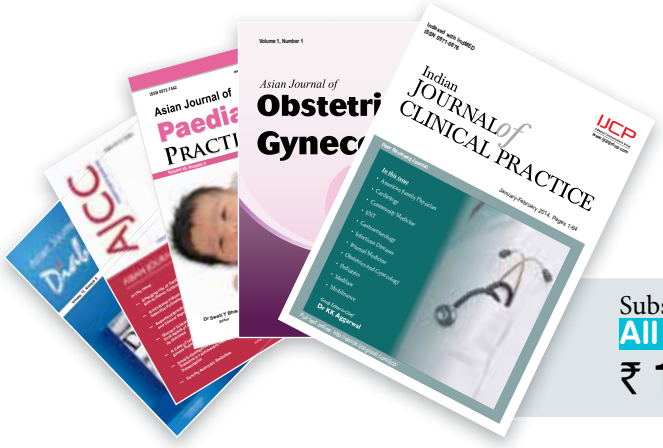
Data revealed that PM air pollution causes a 31% rise in premature deaths and years of cardiovascular impairment globally. The surge in fatalities overall was unequally distributed, with men seeing a 43% increase and women experiencing a 28.2% increase.

During the study period between 1990 and 2019, there was a 36.7% decline in age-standardized premature mortality linked to PM pollution, which means fewer individuals passed away from CVD but lived longer with disabilities. While regions with poorer socioeconomic circumstances lost more lives and saw fewer years of impairment, those with higher socioeconomic conditions experienced the lowest number of years lost to CVD related to PM pollution.

Men and women saw different changes in the CV effects of ambient PM pollution in the same study period, with increased disability and mortality from this pollution being larger in men than in women.

The study results can assist decision-makers in examining hundreds of illnesses, their risk factors, and their effects on mortality and disability throughout the globe.

(*Source: https://www.news-medical.net/news/20230809/Particulate-matter-air-pollution-linked-to-increased-cardiovascular-disease-death-and-disability-worldwide.aspx*)



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Lighter Side of Medicine

HUMOR

THE PAINTINGS

A man was standing in a gallery, studying two near-identical pictures by the same artist. Both showed a glass of wine, a basket of bread rolls, a bowl of salad and a plate of smoked salmon.

Yet one painting was priced $150, the other at $125.

So, he asked the gallery owner to explain why one was more expensive than the other.

"It's simple," said the gallery owner, indicating the more expensive painting.

"You get two extra slices of smoked salmon in that one."

21ST CENTURY MARRIAGE

I stopped at a florist shop after work to pick up roses for my wife. As the clerk was putting the finishing touches on the bouquet, a young man burst through the door, breathlessly requesting a dozen red roses.

"I'm sorry," the clerk said. "This man just ordered our last bunch."

The desperate customer turned to me and begged, "May I please have those roses?"

"What happened?" I asked. "Did you forget your wedding anniversary?"

"It's even worse than that," he confided. "I crashed my wife's hard drive!"

SALES PRACTICE

The out-of-work newlywed took a temporary job as a vacuum cleaner salesman to make ends meet. After 3 days of intensive training, the sales manager told him to go home and practice his pitch on his wife.

The next morning, the manager asked the novice how he made out.

"Well," the man began, "I did what you said, and after I finished, I asked her if she would buy the vacuum cleaner from me. She said 'Yes.' Then I asked her 'Why?' She replied, 'Because I love you.'"

OLD AGE SECRET

Grandpa was celebrating his 100th birthday and everybody complimented him on how athletic and well-preserved he appeared.

"Gentlemen, I will tell you the secret of my success," he cackled. "I have been in the open air day after day for some 75 years now."

The celebrants were impressed and asked how he managed to keep up his rigorous fitness regime.

"Well, you see my wife and I were married 75 years ago. On our wedding night, we made a solemn pledge. Whenever we had a fight, the one who was proved wrong would go outside and take a walk."

I'M NOT GOING TO DO THAT!!

Tech support: "Okay Colin, let's press the control and escape keys at the same time. That brings up a task list in the middle of the screen. Now type the letter "P" to bring up the Program Manager."

Customer: I don't have a P.

Tech support: On your keyboard, Colin.

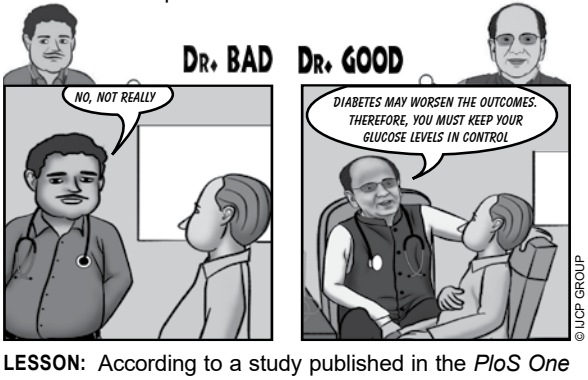
Customer: What do you mean?

Tech support: "P" on your keyboard, Colin.

Customer: I'm not going to do that!!

Dr. Good and Dr. Bad

SITUATION: A known case of diabetes mellitus was diagnosed with COPD in the recent past. He was worried if his diabetes would have an impact on this disease.



LESSON: According to a study published in the *PloS One* journal, diabetes mellitus, either pre-existing or incident, often worsens the outcomes in patients with COPD. Thus, targeted surveillance and management of diabetes hold great importance in the care of COPD population.

PLoS One. 2017;12(4):e0175794.

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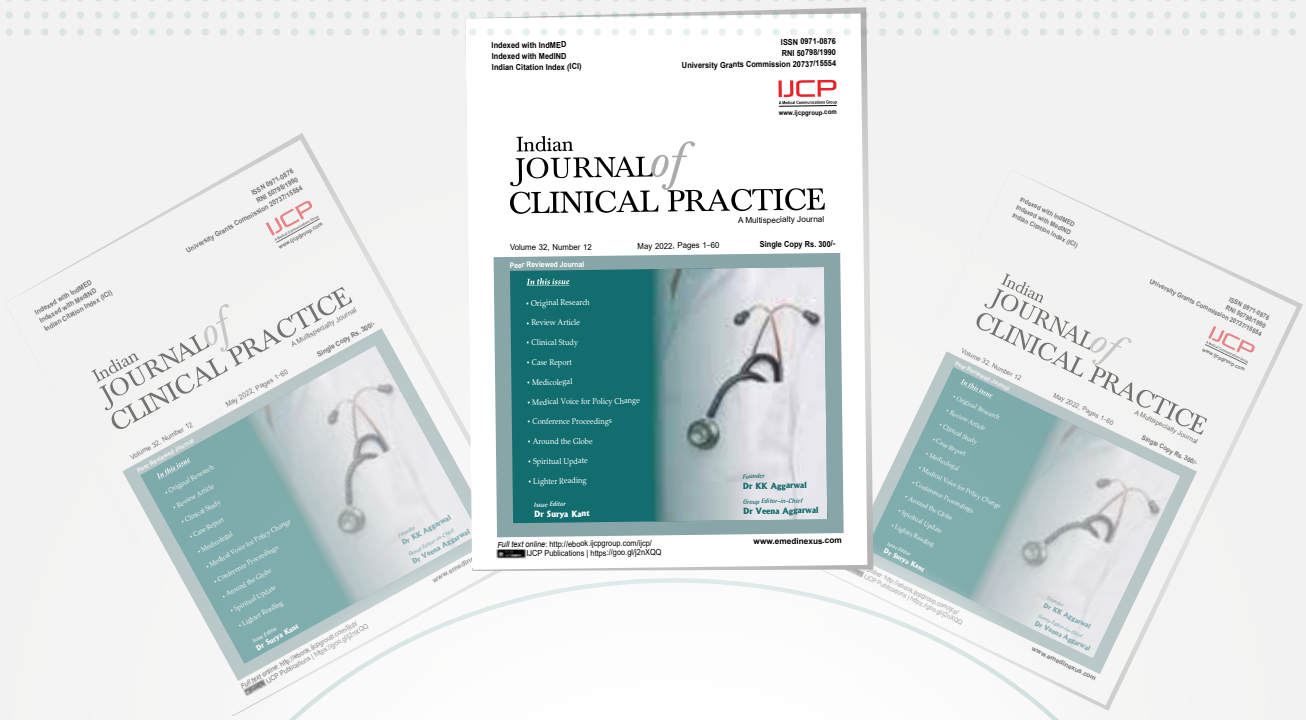

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– This should consist of a review of the literature and relate the major findings of the article to other publications on the subject. The particular relevance of the results to healthcare in India should be stressed, e.g., practicality and cost.

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

Books

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

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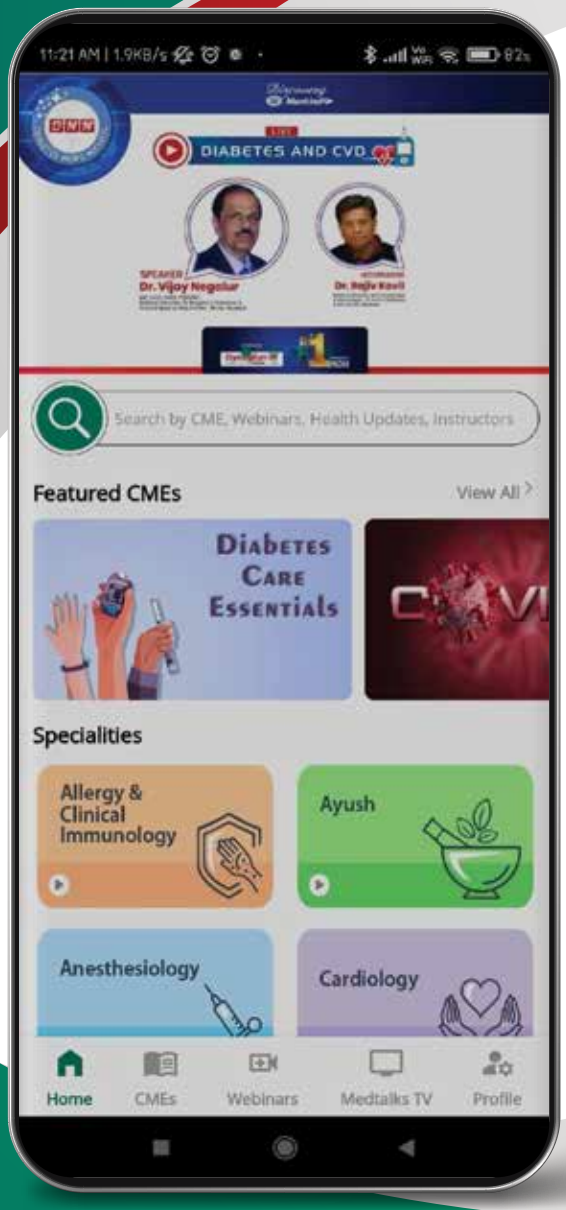

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