



## Editorial commentary on the Indian Journal of Gastroenterology - March–April 2021

Jimmy K Limdi<sup>1,2,3</sup> 

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### Respiratory function and comfort levels in three different defecatory simulation postures in the elderly

Constipation is common in the elderly and maintaining a sitting position for long durations during defecation increases fatigue. The availability of handrails that enable the arm-supported, forward-leaning position has shown positive effects, on respiratory function reducing dyspnea and decreasing the work of breathing [1]. Tashiro and colleagues from the Kobegakuin University, and International University of Health and Welfare Graduate School of Medical Welfare Graduate School of Health and Medical Science, Japan compared the respiratory function in traditional defecation postures and the arm-supported, forward-leaning position using the handrail in 57 community-living elderly self-caring individuals [2]. Three sitting defecation postures (the upright, forward-leaning, and arm-supported forward-leaning positions) were compared.

They found higher values for vital capacity, expiratory reserve volume and forced vital capacity in the arm supported, forward-leaning position than in the forward-leaning position, which was also ranked as the most comfortable posture. The authors discuss how this position improves the mechanics of breathing during defecation and improves stability. Further research on elderly individuals with constipation will be of interest.

### The effect of a low nickel diet and nickel sensitization on gastroesophageal reflux disease: A pilot study

Food allergies and sensitization of the esophageal mucosa to allergens are implicated in the etiopathogenesis of gastroesophageal reflux disease (GERD), with some studies suggesting that patients with GERD are more likely to have nickel sensitization than matched controls [3]. Although foods rich in nickel have been associated with GERD, the relationship between nickel allergy and GERD remains unclear.

Yousaf and colleagues from West Virginia University, Morgantown, USA report a prospective study on 20 patients with refractory GERD and confirmed by a symptom score of  $\geq 30$  on the validated GERD Health-Related Quality of Life (GERD-HRQL) questionnaire [4]. Nineteen of 20 patients reported reduced GERD symptoms after 8 weeks on a low-nickel diet with a reduction in mean total GERD-HRQL, regurgitation, and heartburn scores. Participants with positive vs. negative patch testing to nickel responded equivalently to a low-nickel diet. Larger placebo-controlled studies are needed to validate these findings, but the implications are interesting.

### Prevalence, overlap and risk factors for Rome IV functional gastrointestinal disorders among college students in northern India

Data on the prevalence of functional gastrointestinal disorder (FGID) subtypes in an adult Indian population are scarce. Goyal et al. from Dayanand Medical College and Hospital, Ludhiana, India report on the prevalence and overlap of Rome IV FGIDs among college students (medical, nursing, and humanity courses), risk factors for FGIDs and the impact of changes in the Rome IV diagnostic criteria on the prevalence of irritable bowel disease (IBS), functional diarrhea and constipation compared with Rome III criteria [5].

✉ Jimmy K Limdi  
Jimmy.Limdi@nhs.net

<sup>1</sup> Head- Section of Inflammatory Bowel Diseases, Division of Gastroenterology, The Pennine Acute Hospitals NHS Trust, Manchester, UK

<sup>2</sup> MAHSC Hon Clinical Professor, Manchester Academic Health Sciences, University of Manchester, Manchester, UK

<sup>3</sup> Visiting Professor-Manchester Metropolitan University, Manchester, UK

Among 1309 college students, the prevalence of Rome IV FGIDs was 26.9%, significantly higher among females and medical (34.4%) and nursing students (29.2%) compared with humanity students (18.6%). Functional dyspepsia (15.2%) was most common followed by IBS (6.2%), reflux hypersensitivity (3.5%), functional diarrhea (2.9%) and functional constipation (2.1%). Female gender, medical student, non-vegetarian diet, junk food, tea/coffee, poor physical activity, anxiety, and insomnia were all independent predictors of FGID. Larger and more representative population-based studies are needed. This study also highlights the need for psychosocial and dietary modifications in addressing FGID's.

### Low prevalence of gastroesophageal reflux symptoms in vegetarians

Wenzel et al. from Medical University of Graz, Graz, Austria studied the prevalence of gastroesophageal reflux symptoms (GERS) in a cross-sectional survey of 350 individuals (100 vegetarians) from the general population [6]. "Any" GERS was experienced by 19% vegetarians and 39.2% non-vegetarian controls ( $p < 0.001$ ). Frequent GERS, ( $\geq 1$  day per week) were noted in 3% of vegetarians and in 12.8% of controls ( $p = 0.006$ ). Reflux symptoms were significantly less severe in vegetarians than in non-vegetarians. Independent predictors of GERS included male sex, current smoking, body mass index (BMI)  $\geq 25$  and a non-vegetarian diet. The study supports the hypothesis that GERS occurs less frequently in vegetarians than among non-vegetarians, but the results must be interpreted with caution. A number of confounders such as higher fiber intake, antioxidants and a healthier lifestyle are linked to vegetarianism and may influence results. Furthermore, a small sample size, recall bias and indeed other confounders such as social status, alcohol consumption, physical activity, were not considered. The data, however, are interesting and prospective controlled studies mitigating against potential confounders are needed to provide further insights into this intriguing observation.

### The water load test in school children and adolescents with functional gastrointestinal disorders

Patients with functional dyspepsia often have gastric dysmotility, which could include impaired gastric accommodation, visceral hypersensitivity, and delayed gastric emptying [7]. In this study from Universidad Nacional de Colombia, Bogotá, Columbia, investigators tested their hypothesis that patients with FGID drink less water volume than healthy

subjects during a water load test in 142 students from two schools [8]. Students drank water and libitum for 3 min or until pain, satiety, or vomiting occurred. Investigators correlated anthropometric variables with water volumes drunk. There was no significant difference between water volume drunk by students with and without FGID. Despite this, those with FGID reported nausea and abdominal pain more often suggesting alterations in gastric motility. Gastric motility is complex, and the nuances of testing are discussed along with limitations in this study.

### Cognitive dysfunction in ulcerative colitis patients in remission and its comparison with patients with irritable bowel syndrome and healthy controls

Patients with ulcerative colitis (UC) may experience chronic fatigue, mood disturbances and chronic pain among other psychosocial and extraintestinal manifestations [9]. Cognitive dysfunction, particularly in quiescent UC is less studied. Sharma and colleagues from Indira Gandhi Medical College, Shimla, India report a single-centre cross-sectional observational study on 90 participants (29 UC in remission; 31 with IBS and 30 healthy controls) [10]. A mini-mental state examination, Montreal Cognitive Assessment and mean peak latency p300 were performed in all participants; statistically significant impairment in cognitive functioning was observed in the UC in remission group, compared to the IBS and control group across all scales of cognitive function assessment. Larger, controlled prospective studies and deeper mechanistic insights are needed to understand, address and mitigate against this likely association.

### The prevalence of uninvestigated dyspepsia and the association of physical exercise with quality of life of uninvestigated dyspepsia patients in Indonesia: An internet-based survey

The adverse effect of dyspepsia on health-related quality of life (HRQOL) is well known but the association of physical exercise and its impact on HRQOL in patients with uninvestigated dyspepsia (UD) has not been studied. Huang et al. from the Universitas Pelita Harapan, Tangerang, Banten, Indonesia report an internet-based questionnaire study to assess prevalence of UD, its association with physical exercise, and impact on HRQOL in Indonesian patients with UD [11]. Data on sociodemographic factors, exercise levels, Rome III criteria for dyspepsia, and Short Form-Nepean Dyspepsia Index were collected. The overall prevalence of UD from 2725 valid responses was 49.75% [12]. Female gender and

lack of exercise were independently associated with UD whilst physical exercise was associated with better HRQOL. Authors acknowledge the multiple variables (body mass index, diet, nonsteroidal anti-inflammatory drug [NSAID] use, smoking and comorbidities, among others) as risk factors for UD; though the data are interesting but have limitations but should stimulate controlled studies to understand this association further.

### **Diagnostic utility of alarm features in predicting malignancy in patients with dyspeptic symptoms**

Patients with new-onset dyspepsia with alarm features should be suspected to have malignancy [13]. The diagnostic utility of dyspeptic alarm symptoms in predicting malignancy is unclear. In a prospective observational study on consecutive patients undergoing esophagogastroduodenoscopy (EGD) for dyspeptic symptoms, Shetty and colleagues from Kasturba Medical College, Mangalore, India studied the diagnostic accuracy of alarm features in predicting malignancy [14].

Among 900 patients, the diagnosis was functional and benign lesions were noted in approximately a third each and 5.5% had a malignancy (gastric in 56% and esophageal in 40%). Alarm features were present in 22.9%, of which malignancy was diagnosed in 22.3% patients. Alarm features had a sensitivity of 92% and specificity of 81.2% for predicting malignancy. In particular, sensitivity and specificity for weight loss was 76% and 90.8%, respectively. Alarm features taken together had a high (99.4%) negative predictive value. The authors noted an optimal age for screening of malignancy on receiver operator characteristic (ROC) curve analysis of 46.5 years. Notably, this study excluded patients with predominant dysphagia but without associated dyspepsia.

### **Effect of moderate aerobic exercises on symptoms of functional dyspepsia**

The management of functional dyspepsia is challenging and the role of mental and physical stress in functional dyspepsia is well recognized [15]. Although proton pump inhibitors (PPIs) are used, most patients remain refractory to treatment. Rane and colleagues from Topiwala National Medical College and B.Y.L. Nair Charitable Hospital, Mumbai, India report their study on the effects of moderate aerobic exercise on symptoms of functional dyspepsia and compared the effect of conventional treatment (using pantoprazole 40 mg daily for 6 weeks) alone vs. exercise plus conventional treatment [16]. The aerobic exercise programme consisted of 30 min supervised exercise, 5 times a week for 6 weeks. Response was

assessed using the Glasgow dyspepsia severity score (GDSS), Depression Anxiety Stress Scale-42 (DASS-42) and visual analogue scale (VAS). Although there was significant improvement in all scores in both the groups before and after intervention, on comparison between groups, the benefit of aerobic exercise in addition to PPI therapy remained significant. The role of exercise in improving gut health in addition to general health is worthy of further study.

### **miR-222 regulates cell growth, apoptosis and autophagy of interstitial cells of Cajal isolated from slow transit constipation rats by targeting c-kit**

Slow-transit constipation (STC), is the most common form of constipation, characterized by increased colonic transit time (CTT) and a poor response generally to available therapies. From a mechanistic perspective, reduction in interstitial cell of Cajal (ICCs) with autophagy and apoptosis have been reported in the colon of patients with STC [17]. Zheng et al. from Nanjing University of Chinese Medicine, Jiangsu Province, China, studied the influence of microRNA (miRNA), following on from previous work, demonstrating upregulation of miR-222 in gastrointestinal cancer. They evaluated miR-222, c-kit and stem cell factor (SCF) in STC rats compared to normal controls using qRT-PCR and western blot analysis. They found miR-222 to be significantly upregulated in STC compared with healthy control rats, and able to induce excessive autophagy and apoptosis of isolated ICCs [18]. Excessive activation of autophagy triggers self-digestion and degradation of essential cellular constituents, with resultant autophagic cell death and may be associated with impairment of gut function. Further mechanistic insights of this biology could have exciting implications for pharmacological research and therapy.

### **Prevalence and risk factors for gastroesophageal reflux disease in the Indian population: A meta-analysis and meta-regression study**

Gastroesophageal reflux disease GERD is common in the Western population and probably less so in India. Despite this, it may result in significant morbidity and impairment in quality of life, and left untreated, complications like peptic stricture, Barrett's esophagus, and esophageal adenocarcinoma [13]. Rai and colleagues from the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India report the first Indian population-based meta-analysis assessing the prevalence and risk factors of GERD [19]. Among 9 studies with over 20,000 subjects; the prevalence of GERD ranged from 5% to 28.5%.

The pooled proportion of GERD (random-effects model) was 15.573 (95% CI 11.046–20.714). They identified risk factors for GERD, namely age, high body mass index, non-vegetarian diet, tea/coffee intake, tobacco, and alcohol consumption. There was significant heterogeneity in the studies likely driven by the limited number of studies available, differential definitions for GERD used in the studies and lack of controls in some. Nonetheless, the risk factors identified will be useful to clinicians in practice and study limitations could be addressed in prospective well-controlled studies.

### **The relationship between dietary intakes and prevalence of irritable bowel syndrome in adolescent girls: A cross-sectional study**

Food related triggers are recognized sources of psychosocial morbidity in people suffering from irritable bowel syndrome (IBS) [20]. Roudi and colleagues from Mashhad University of Medical Sciences, Mashhad, Iran, report a cross-sectional study from Iran, on 988 adolescent girls studying the prevalence of IBS and its relationship to dietary intake [21]. A 168-item validated food frequency questionnaire (FFQ) of dietary intakes was administered and a diagnosis of IBS (using the Rome III criteria) was made in 158 girls. After adjusting for confounders, soluble fiber intake was noted to be protective and caffeine intake linked to exacerbation of IBS symptoms. These findings corroborate with our understanding of the multiple putative mechanisms by which food components may affect the gut and induce symptoms, such as satiety signaling, chemo-stimulation of gut receptors, neuroendocrine influences, and psychosocial factors. Dietary research is fraught with challenges, such as capturing the type and proportion of food intake, the complex interactions between food groups, varied metabolism and complexities of food handling. Recognition and avoidance of known triggers can significantly alleviate symptoms.

### **Efficacy of Polyethylene Glycol 3350 as compared to Lactulose in treatment of ROME IV criteria defined pediatric functional constipation: A randomized controlled trial in India**

Functional constipation affects between 0.7% to 29.6% children and is both challenging to treat and sub-optimally managed [22]. International societal guidelines advocate a combination of dietary, lifestyle and pharmacological measures with laxatives to treat this condition [22, 23]. Dheivamani et al. from the Institute of Child Health, Chennai and Kolkata, India report a randomized trial on 100 children with functional constipation comparing the efficacy of polyethylene glycol (PEG) 3350 and lactulose in the treatment of functional

constipation [24]. A significant increase in stool frequency was noted in the (PEG) 3350 group by week 1, a trend maintained through week 4. Correspondingly, the PEG group reported a significant reduction in painful bowel movements and straining and a statistically significant reduction in ROME IV criteria by week 4. Notably, disimpaction for fecolma and encopresis was required for the majority of children before randomization. Although limited by lack of longer-term follow-up data, it demonstrates superior efficacy of (PEG) 3350 to lactulose in the treatment of young children with functional constipation, consistent with international guidelines.

### **Can unrecognized fecal loading without infrequent bowel movements be a cause of symptoms in a subset of patients with functional bowel disorders?**

Perceptions about stool frequency in functional constipation vary [25]. Kang and colleagues from St George's Hospital, London, UK, studied the role of fecal loading as a cause of symptoms in consecutive patients with regular bowel movements attending a gastroenterology clinic for functional bowel symptoms, not including infrequent bowel movements and who did not fulfill the criteria for constipation predominant irritable bowel syndrome or functional constipation [26]. If plain abdominal radiography revealed fecal loading, patients received dietary advice and laxative treatment. Of 74 patients meeting criteria for enrolment, 26 had fecal loading on abdominal radiology with higher Leech scores than those of control patients. Three out of 20 patients (15%) who returned for review after dietary advice and laxatives were asymptomatic and 17/20 (85%) reported improvement. The study has several limitations such as a small sample size, and use and timing of radiography but questions our perceptions around functional constipation and highlights the need for an improved understanding of its pathophysiology and treatment.

### **Evaluation of esophageal motor function in patients with gastroesophageal reflux using multiple rapid swallows**

Patients with gastroesophageal reflux disease (GERD) are often referred for high-resolution esophageal manometry (HREM) to assess symptoms of dysphagia or chest pain. The clinical significance of occasional findings of ineffective esophageal motility (IEM) and fragmented peristalsis is unclear. Multiple rapid swallows (MRS), is a provocative maneuver used to demonstrate the integrity of neural and motor processes in the smooth muscle of esophagus [27]. Jain and Agrawal from Arihant Hospital and Research Centre, Indore, India report a retrospective study of 68 patients (38 normal



motility, 30 minor motility disorders) undergoing HREM at their centre [28]. Although three-fifths of the patients with normal motility had normal MRS sequences, in patients with minor motility disorders, abnormalities in the inhibition and contraction phases were noted in 50% and 80% cases, respectively. The study discusses and highlights the utility of MRS testing in GERD.

## Declarations

**Conflict of interests** JKL declares that he has no conflict of interest.

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