Indian Journal of Gastroenterology (September–October 2022) 41(5):419–423
https://doi.org/10.1007/s12664-022-01297-6

EDITORIAL

Editorial commentary on the Indian Journal of Gastroenterology—September–October 2022

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Published online: 22 September 2022

Plugged percutaneous liver biopsy using Tru-cut needle and coils: A retrospective study

Histopathological examination of liver tissue has a key role in the diagnosis, staging, and prognostic assessment of liver diseases. In patients with contraindications to percutaneous liver biopsy (PLB) such as known or suspected risk of bleeding, "plugged" PLB may be used, wherein the biopsy tract is embolized, following the percutaneous approach [1]. Rathod and colleagues from the K E M Hospital, Mumbai, India, describe their experience of plugged liver biopsy in 127 consecutive patients (aged 7–73 years) over a 2-year period [2]. Adequate samples were obtained in all cases, and none required a repeat biopsy for technical reasons. Thirteen procedures required ultrasound guidance. Reported complications in 3 cases included arterioportal fistula, pneumothorax, and mild hemoperitoneum from inadequate coiling. The authors conclude that plugged liver biopsy in well-selected cases can be safe and effective.

Dyspepsia with alarm symptoms in patients aged less than 60 years: Is upper gastrointestinal endoscopy justified in Indian scenario?

Upper gastrointestinal endoscopy (OGD) plays a pivotal role in the evaluation of upper gastrointestinal (UGI) symptoms. International consensus recommends OGD in patients presenting with "alarm" symptoms including dysphagia, suspicion of UGI bleeding, or new-onset symptoms above the age of 60 years [3]. Kumari and colleagues from the Indira Gandhi Medical College, Shimla, India, report a single-center experience of OGD in 294 consecutive patients (76.9% of patients ≤ 50 years old), between March 2019 and February 2021 [4]. Of 192 patients with an abnormal endoscopy, 146 (49.6%) had benign organic dyspepsia, while 46 (15.6%) patients were diagnosed with UGI malignancy; 40 were gastric and 6 patients had esophageal adenocarcinoma. Anemia, progressive dysphagia, gastrointestinal bleeding, and weight loss were predictors of malignancy, while there were no statistically significant differences between malignant and non-malignant dyspepsia for duration of dyspepsia and *Helicobacter* status. The authors support UGI endoscopy in patients < 60 years with alarm symptoms. A systematic review of studies in the Asian population reported an overall malignancy detection rate in dyspeptic patients of 1.3%, with a high proportion of younger patients diagnosed with cancer, and suggested that the optimal age threshold for endoscopy screening in Asia might be 35 years [5]. Larger studies from prospectively maintained databases are needed. Meanwhile, clinicians should carefully assess for presence of alarm symptoms and counsel patients regarding an OGD for an early and accurate diagnosis of the etiology of dyspepsia.

Impact of sarcopenia on post liver transplant morbidity and mortality in cirrhotic patients

Sarcopenia, defined as a reduction in muscle mass and function, may occur as a result of aging and chronic disease such as cirrhosis and (along with frailty) is a well-established predictor of poor clinical outcomes following liver transplantation (LT) [6]. Kumar and colleagues from the KIMS Hospital, Thiruvananthapuram, India report a retrospective experience of LT for cirrhosis, at their center between

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2013 and 2018 [7]. Among 74 patients (71 male), mean age 51 years, sarcopenia was observed in 20 individuals and 15 recipients died within 12 months of LT. On binary regression, sarcopenia prior to surgery was an independent predictor of mortality. It should be noted that sarcopenia is more frequent in male patients and none in this cohort had cirrhosis due to non-alcoholic steatohepatitis. Meanwhile, standardized modalities for assessment of frailty and sarcopenia are integral to baseline assessment for LT. The true impact of sarcopenia needs further, prospective, multi-center studies using standardized definitions of sarcopenia that are sex, liver disease, and race specific.

Efficacy and safety of biosimilar versus originator infliximab in patients with inflammatory bowel disease: A real-world cohort analysis

Biosimilars are highly similar to originator biologic medications, with no clinically meaningful differences in terms of safety, purity, and potency, and were introduced to reduce cost and consequently improve access of treatment [8]. The first biosimilar in inflammatory bowel disease (IBD) was approved in 2013 in the European Union and in 2016 in the USA. In this issue, Kumar and colleagues from the All India Institute of Medical Sciences, New Delhi, India, report a retrospective experience of 137 IBD patients treated with either originator or biosimilar infliximab, between 2005 and 2020 [9]. Of 137 patients, 35 received biosimilar infliximab, wherein clinical response and remission rates at weeks 14 and 52 were 84.2%, 58%, and 68.4%, 52.6% in Crohn's disease (CD), and 81.2%, 56.2%, and 68.7%, 62.5% in ulcerative colitis (UC) patients, respectively, comparable to those treated with originator infliximab, with clinical response and remission rates at weeks 14 and 52 being 79.4%, 46%, and 57.1%, 43% in CD, and 72%, 64.1%, and 66.7%, 56.4% in UC patients, respectively. A growing body of literature continues to provide reassurance that biosimilars are effective, safe, and comparable to reference biologics in biologic treatment-naïve patients and in stable patients receiving reference products who switch. Future studies should assess switch from biosimilar to reference biologic and switching between multiple biosimilars, as indeed studies with adalimumab biosimilars.

Mutational analysis of exon 8 and exon 14 of ATP7B gene in Bangladeshi children with Wilson disease

Wilson disease (WD) is a potentially treatable, inherited disorder of copper metabolism characterized by pathological copper accumulation. The underpinning mechanism is a defect in ATP7B, a copper-transporting ATPase that is mainly expressed in hepatocytes, which encodes a transmembrane copper-transporting ATPase, leading to copper overload in the liver, brain, and other organs [10]. The clinical course of WD can vary in severity but progressive liver disease is a common feature. Patients can also present with neurological disorders and psychiatric symptoms. Early diagnosis is key to a better prognosis, and advances in genetic screening play a pivotal role. Tasmeen and colleagues from the Banglabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, report a cross-sectional study of 37 Bangladeshi children with WD, testing for mutations in exons 8 and 14 of ATP7B [11]. They identified the single novel homozygous mutation pLeu.1071Val in exon 14 in every (100%) child diagnosed with WD. Additionally, the two novel heterozygous missense mutations p.K785R (2.7%) and p.S744F (2.7%) were also found in two other children in exon 8. Further studies examining genetic and epigenetic factors will advance our understanding and aid in early diagnosis of this condition, which is universally fatal if untreated.

Correlation between magnetic resonance enterography and ileo-colonoscopy for assessment of disease activity in terminal ileal Crohn's disease

Although ileo-colonoscopy remains the reference standard for mucosal assessment, cross-sectional imaging has asserted its relevance given the transmural nature of Crohn's disease (CD) for both diagnosis and assessment of response to treatment [12, 13]. Kakkar and colleagues from the Dayanand Medical College, Ludhiana, India, report a retrospective study on comparative performance of ileo-colonoscopy and magnetic resonance enterography (MRE) in 70 patients with terminal ileal CD, undergoing both investigations between 2 weeks of each other [14]. MRE scoring of the disease activity was performed using magnetic resonance index of activity (MARIA) and simplified MARIA (MARIAs), and ileo-colonoscopy was scored using the simple endoscopic score for CD (SES-CD). Sensitivities of MARIA and MARIAs scores to detect active disease were 0.76 and 0.84 respectively but there was no correlation for mild disease between endoscopy and MRE. MARIA and MARIAs were comparable for identification of active and severe disease. The authors conclude that MRE is a reliable and sensitive tool for detection of endoscopically severe, but not mild, terminal ileal CD. Conversely, readers should note that endoscopic assessments of mucosal healing do not adequately reflect transmural and perienteric changes or complications and

that cross-sectional imaging findings better predict clinically relevant clinical outcomes and progression of bowel damage than endoscopy, reflecting the complementary nature of these investigations.

A machine learning approach for non-alcoholic steatohepatitis susceptibility estimation

Liver biopsy is the gold standard for the diagnosis of non-alcoholic steatohepatitis (NASH) but is relatively invasive and associated with potential complications. Artificial intelligence has been used for assessing liver fibrosis, predicting liver decompensation, and screening eligible liver transplant recipients as well as predicting post-transplant survival and complications [15]. Preliminary data have shown potential for a machine learning (ML) algorithm in quantifying steatosis in population scale magnetic resonance imaging (MRI) data, but our understanding of the primary drivers and genetic and environmental modifiers that cause disease progression remains limited [16]. In this issue of the *Indian1 Journal of Gastroenterology*, Ghadiri and colleagues from Istanbul University Cerrahpaşa, Istanbul, Turkey report a novel ML approach developed for individual NASH susceptibility prediction using candidate single nucleotide polymorphisms [17]. Nine different ML models were constructed and trained using 80% of both the NASH patients and the healthy controls data and were then tested on 20% of both groups Among three classification algorithms: k-nearest neighbor (KNN), multi-layer perceptron (MLP), and random forest (RF), the KNN classifier with all features as input showed the highest performance with 86% *F* measure and 79% accuracy. Further studies using ML will aid in the understanding of heterogeneity of non-alcoholic fatty liver disease and the genetic and molecular drivers linking steatosis to inflammation, fibrosis, and hepatocellular carcinoma.

Asian-Pacific consensus on small intestinal bacterial overgrowth in gastrointestinal disorders: An initiative of the Indian Neurogastroenterology and Motility Association

Small intestinal bacterial overgrowth (SIBO) is a clinical disorder wherein symptoms, clinical signs, and/or laboratory abnormalities are attributed to changes in the numbers of bacteria or in the composition of the bacterial population in the small intestine [18]. SIBO may be diagnosed among individuals presenting with a variety of gastrointestinal and even non-gastrointestinal symptoms and in the causation of a diverse array of disorders. Its definition, however, remains controversial and true prevalence, accordingly, undefined. The ability to suspect and diagnose SIBO is largely dependent on the ability to appreciate context; an awareness of the disorders; and clinical scenarios associated with risk for SIBO. The Indian Neurogastroenterology and Motility Association and experts from the Asia–Pacific region convened an expert multidisciplinary panel, tasked with producing an evidence-based consensus document to guide clinicians managing SIBO [19]. The final report, published in this issue of the *Indian Journal of Gastroenterology*, is a comprehensive evidence-based document and constitutes essential reading.

Esophageal manometry findings in patients with refractory symptoms of gastroesophageal reflux disease

High-resolution manometry (HRM) is used to assess peristalsis and to detect alternative major motor disorders prior to anti-reflux surgery or when symptoms do not improve with gastroesophageal reflux (GERD) therapy [20]. Mayank Jain from the Arihant Hospital and Research Centre, Indore, India, reports a retrospective analysis of patients with GERD, referred for high-resolution episcopic microscopy (HREM) and 24-h pH recording following endoscopy between 2019 and 2021 [21]. Patients were classified into erosive reflux disease (ERD), non-erosive reflux disease (NERD), reflux hypersensitivity (RH), and functional heartburn (FH) based on test results. Among 144 patients (NERD [56, 38.9%], ERD [42, 29.2%], RH [28, 19.5%], and FH [18, 12.5%]), type 2/3 esophagogastric junction (EGJ) morphology was more common in ERD and NERD ($p < 0.001$). Additionally, esophagogastric junction contractile integral (EGJ-CI) and basal inspiratory pressures were significantly lower in these two groups ($p < 0.05$). These findings support use of EGJ-CI as a good summary metric of EGJ barrier function, although with the caveat that the metric is largely an indicator of crural diaphragm contractility.

Gastrointestinal manifestations in children with primary immune deficiencies: A case series

Primary immune deficiencies (PID) in children are a rare but serious group of genetic disorders of the immune system which can have systemic ramifications, including the gastrointestinal (GI) tract [22]. In the less severe form, they can present later in childhood or adolescence with subtle signs and symptoms, but in the most severe form, they may lead to increased susceptibility to serious infections during

infancy and even death. Sivasankaran and colleagues from the Kanchi Kamakoti Childs Trust Hospital, Chennai, India, report a case series of 5 children with GI manifestations of PID [23]. Very early age of onset (infancy), parental consanguinity, and failure to respond to hypoallergenic formula triggered the suspicion for underlying PIDs, and next-generation sequencing led to the underlying genetic diagnosis in each child.

PID can often mimic GI diseases. Children presenting with atypical GI disease and/or failure to respond to conventional therapy should be evaluated for an underlying primary immune disorder and initiated on appropriate treatment [22].

How frequent are vancomycin-resistant enterococci in patients with primary sclerosing cholangitis and ulcerative colitis treated with oral vancomycin?

Previous studies have shown that up to one-third of patients with ulcerative colitis associated with primary sclerosing cholangitis (UC-PSC) have exacerbation of their colitis after liver transplant (LT), despite intense immunosuppression and that oral vancomycin (OV) is a potentially effective therapy for the induction and maintenance of remission of UC in patients with UC-PSC, including those with longstanding disease [24]. Shah and colleagues from the Princess Alexandra Hospital, Brisbane, Australia, report a retrospective study of 7 PSC-UC patients treated with OV for at least 6 months [25]. All patients achieved complete clinical remission of the UC, with mean reduction of fecal calprotectin by 634 µg/mg (87.3%), C-reactive protein by 21.9 mg/L (74.2%), and the total MAYO score by 9.3 (93.3%), and improvements in liver enzymes, and alkaline phosphatase enzyme and total bilirubin of − 48.7 U/L and − 2.7 mg/dL respectively. It should be remembered that the total number of patients studied as well as the period of treatment in the controlled pilot studies is small for a chronic disease which may progress over a 20-year period. Moreover, the studies used reductions in ALP and Mayo Risk score as surrogate endpoints, which have not been proven to correlate with long-term survival in PSC. Its striking effectiveness in these limited studies, however, supports further investigation in randomized trials, with careful attention to its bioavailability profile in the gut.

Declarations

Conflict of interest JKL declares no competing interests.

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