Indian Journal of Gastroenterology (May–June 2023) 42(3):299–303
https://doi.org/10.1007/s12664-023-01419-8

EDITORIAL

Indian Journal of Gastroenterology—May–June 2023 — highlights

Shobna J. Bhatia[1]

Published online: 5 July 2023

Invasive strategies for fecal microbiota transplant in irritable bowel syndrome

Irritable bowel syndrome (IBS) is classified as a disorder of the gut-brain axis. One of the possible pathophysiologic theories suggests that gut dysbiosis plays an important part. Treating dysbiosis with fecal microbiota transplant (FMT) sounds logical; many studies and meta-analysis on this topic have addressed this issue. Mohan et al. from Salt Lake City, Utah, USA, in this issue of the *Journal* addressed the impact of the route of administration of the efficacy of FMT for the management of IBS [1]. Four of the five studies had used Rome-III criteria for the diagnosis of IBS and most had a mix of IBS-C, D and M patients. The results are confusing. The delivery of 30 g FMT via colonoscopy yielded best results for improvement in IBS symptoms (OR 2.09). In contrast, the network meta-analyses showed that colonoscopic delivery was inferior to duodenal delivery of 60 g FMT. The improvement in symptoms of various groups of IBS patients was not evaluated, possibly because of small numbers.

Overall, the idea of using FMT for a chronic disease like IBS appears attractive. However, further primary studies with a larger number of patients are necessary before FMT is declared as a standard of care for IBS.

Hyperleptinemia and gallstone disease: Cue to the cause?

Gallbladder stones are very common and gallstone disease (GD) is a multi-factorial disease. The old adage that GD occurs in fat, fertile, females over 40 years is probably still true. Additional risk factors include metabolic factors such as hyperinsulinemia and dyslipidemia, as also rapid weight loss and estrogen replacement therapies among others. Srivastava and Kumar from Jabalpur, India, have done a meta-analysis of eight studies that included 932 GBD cases and 556 controls to assess whether a single parameter (serum leptin) was associated with GD [2]. Of course, they found a positive association and the mean difference of leptin levels in cases and controls was 4.48 ng/mL (95% CI 1.08–8.09). A limitation of the study, as pointed out by the authors, is that the method of estimation of leptin levels was different in included studies.

So, what does this mean for physicians who manage GD? Elevated serum leptin is just one more factor associated with gallstones.

Position statement from the Indian Society of Gastroenterology, Cardiological Society of India, Indian Academy of Neurology and Vascular Society of India on gastrointestinal bleeding and endoscopic procedures in patients on antiplatelet and/or anticoagulant therapy

Antiplatelet and/or anticoagulant therapy is prescribed frequently in a variety of vascular disorders and one of the major adverse effects of these drugs is gastrointestinal (GI) bleed. The drugs may require to be discontinued primarily for stopping the bleed and to allow endoscopic therapy for the management of a bleeding lesion in the GI tract. Considering that many of the patients with vascular diseases (IHD, stroke) are the elderly and that stopping the drugs may cause worsening morbidity of the primary disease, it is imperative that specialists from various disciplines come together to make guidelines for diseases that require multidisciplinary management. Arora et al. have published the guidelines from multiple societies for the management of patients on antiplatelet drugs with GI bleed [3]. The guidelines include statements for indications to stop the incriminating drugs as well as when to resume therapy after the endoscopic procedures and endoscopic therapies that have a high risk of bleeding.

✉ Shobna J. Bhatia
shobna.bhatia@gmail.com

[1] Department of Gastroenterology, National Institute of Medical Sciences, Jaipur 302 022, India

These guidelines are comprehensive and physicians who manage patients on antiplatelet drugs with GI bleed should be aware of these to help standardize management of these high-risk patients.

Clinical profile and outcomes of pediatric scrub typhus associated with elevated hepatic transaminases

Scrub typhus is an important cause for acute febrile illness in India. Hepatic dysfunction occurs quite often in these patients and may be associated with severe disease. In a prospective study, Narayanasamy and colleagues from Puducherry, India, found that 257 of 560 (45.8%) children with scrub typhus had elevated hepatic transaminase levels at admission [4]. Patients with elevated transaminases had generalized lymphadenopathy, ascites, thrombocytopenia and hypoalbuminemia more often as compared to those without elevated enzymes. In general, these patients had more severe disease as compared to those with normal enzymes. Thus hepatic dysfunction at baseline may predict multi-organ dysfunction associated with severe scrub typhus. The strength of the study is that it is a prospective study. However, the liver enzymes were estimated only once and additional patients who developed liver dysfunction during hospital stay may have been missed.

This study has an important message in that patients with febrile illness and elevated transaminase levels are likely to have scrub typhus and also likely to develop severe disease.

Delayed pseudoaneurysms after pancreatic surgery

Pancreatic surgery, especially pancreatoduodenectomy, is a complex surgery. There is a small risk of delayed bleeding, mostly due to the rupture of pseudoaneurysms. Earlier studies have suggested that mortality due to ruptured pseudoaneurysms is almost 50% in some series. In the era of intervention radiology, the treatment of pseudoaneurysms has shifted from morbid surgery to the embolization of pseudoaneurysm. Rajendran and colleagues from New Delhi, India, analyzed the results of pancreatic surgeries at their center and found that 25 of 616 (4.1%) patients had delayed bleeding [5]. Nearly two-thirds of the bleeding patients had a pseudoaneurysm found on angiography and all, except one, could be treated with angiographic embolization. Bleeding recurred in five of the 16 patients after successful embolization, with no pseudoaneurysm found in any of these patients. Importantly, patients who had developed delayed bleeding had other complications (pancreatic fistula (72%) and bile leak (52%)). The 90-day mortality was close to 50% and the cause for death was associated sepsis, not rebleed.

An important lesson from this large series is that a multidisciplinary approach to these patients is warranted and that angiographic embolization should be the preferred method of management of bleeding from pseudoaneurysms. Complications such as pancreatic fistula and bile leak should be looked for and the associated sepsis should be aggressively treated, which is the most common cause for death in patients with delayed bleeding after pancreatic surgery.

Universal prophylactic rectal non-steroidal anti-inflammatory drugs with a policy of selective pancreatic duct stenting significantly reduce post-endoscopic retrograde cholangiopancreatography

Post-ERCP pancreatitis (PEP) is a potentially serious complication. In most cases, the pancreatitis is mild, but when severe, the disease can be associated with significant morbidity, prolonged intensive care unit (ICU) admission and even death. Risk factors associated with PEP include female gender, precut sphincterotomy, recurrent pancreatic cannulation, prolonged procedure time and the experience of the endoscopist, among others. Adequate hydration, rectal non-steroidal anti-inflammatory drugs (NSAIDs) after the procedure and pancreatic stenting are among the therapies used to prevent PEP. There is some data to show that prophylactic rectal NSAIDs may prevent PEP in high-risk individuals. The data on prophylactic treatment for all patients is still unclear. Agarwal and colleagues from AIIMS, New Delhi, India, analyzed their retrospective data collected over a two-year period, where they had given prophylactic rectal diclofenac to all patients who underwent ERCP [6]. They found that 4.4% of 769 patients developed PEP, much lower than 9.9% of 253 patients treated earlier, who had not received rectal NSAIDs (historical controls). The risk factors for PEP were similar to those reported in literature.

The limitations of the study are its retrospective nature and that the experience of the endoscopist was not taken into account. Nevertheless, this is an important study, which shows that there is a benefit of giving rectal NSAIDs 30 minutes prior to starting ERCP in all patients, irrespective of the pre-existing or procedure-related risk factors.

Bringing sarcopenia assessment in cirrhosis to the bedside

Sarcopenia is a progressive muscle wasting syndrome involving loss in skeletal muscle mass, strength and function. It is

present in more than half of the patients with cirrhosis. It is associated with the increased risk of complications and mortality in many diseases ranging from cardiorespiratory diseases to liver diseases. The best method to assess the severity of sarcopenia is cross-sectional imaging (computed tomography and magnetic resonance imaging). Muscle strength can also be assessed clinically by using simple tests such as hand grip strength (HGS) and gait speed (GS). Singh et al. from Chandigarh, India, have done an elegant study to assess whether the bedside assessment of sarcopenia in the outpatient setting was almost as good as imaging to assess sarcopenia as well as predict mortality in patients with cirrhosis [7]. They found that 55% of 116 patients had sarcopenia as defined by skeletal muscle index (SMI) at CT scan. Both HGS and GS correlated well with SMI, as well as with outcomes, including mortality.

The potential upside and clinical application of this study is that the use of simple tests can help clinicians prognosticate patients with cirrhosis, as well as plan pharmacological and nutritional interventions to control sarcopenia. This study should be of interest to clinicians, who can now use simple bedside tools, rather than imaging techniques, for the detection of sarcopenia. With increasing interest in sarcopenia across a variety of chronic diseases, such studies may be conducted across indications. In conditions where sarcopenia is expected, routine clinical assessment may include the assessment of sarcopenia using handgrip strength and gait speed.

Terlipressin nonresponsive hepatorenal syndrome: Dose escalation or dual therapy?

Hepatorenal syndrome (HRS) type I (now termed HRS-AKI [acute kidney injury]) is one of many causes for AKI in patients with chronic liver disease. It is characterized by arterial vasodilatation in the splanchnic circulation and intense renal vasoconstriction and carries a poor prognosis. The treatment of HRS is, therefore, targeted at maintaining renal perfusion while preserving systemic hemodynamic circulation. This is often a balancing act in the clinical setting. The lack of response to terlipressin in HRS presents dilemma about its management—whether to continue the failing pressure by increasing the dose or add a "top-up" (norepinephrine). In a randomized trial, Singh and colleagues from Chandigarh, India, have prospectively compared the effect of terlipressin infusion alone ($n=30$) or a combination of terlipressin and noradrenaline infusion ($n=30$) on the outcome of patients with type-I HRS [8].

They found no difference in the response rate (50% vs. 76.7%, $p=0.06$) or 30-day survival (36.7% vs. 53.3%, $p=0.13$) between the groups. Treatment in the terlipressin alone group was more expensive and associated with more frequent adverse events probably due to a larger amount of drug used (mean daily dose 4.97 ± 1.37 mg vs. 2 mg).

Looking closely at their data, this seems to be a Type-II error due to small sample size. A randomized control trial, preferably multi-center, with a larger sample size, might just show that this treatment helps to save some patients of HRS, albeit before liver transplant is available.

Bilateral metal stenting for malignant hilar blocks: Worth the effort?

Malignant biliary obstruction is a tumor-related stricture of the bile duct and usually presents with painless jaundice. Among various options to treat malignant biliary obstruction, palliative measures include endoscopic stent placement, percutaneous drain placement and surgery. In most cases, palliative biliary drainage is done to relieve the symptoms of cholestasis or to treat cholangitis.

Sundaram et al. from Mumbai, India, have analyzed their data of 43 patients with unresectable hilar obstruction who underwent bilateral stenting with biliary self-expanding metal stents (SEMS) [9]. Most patients had good Eastern Cooperative Oncology Group (ECOG) status. The most frequent cause for hilar block was carcinoma gallbladder ($n=36$ [83.7%]) and four patients had cholangitis. Technical success (bilateral stent placement) could not be obtained in two of 43 patients and were managed with percutaneous drain placement. One patient died due to pulmonary embolism. Functional success defined as serum bilirubin, value less than 3 mg/dL at four weeks, occurred in 39 of 43 patients. Median stent patency was 137 days (range 8–790) and median survival was 153 days (range 8–870 days).

The retrospective nature and lack of controls are major limitations of the study. Nevertheless, the study does show that bilateral SEMS for hilar biliary obstruction is an effective option for palliation of jaundice in these patients. Due to low numbers, authors could not evaluate effect on the quality of life. While the study does suggest that endoscopic bilateral metal stents could work in hilar strictures, one would suggest caution in routine use of this modality in centers with limited volume and expertise in advanced procedures.

IBD in extremes of age

Inflammatory bowel disease has a bimodal presentation and the disease phenotype is different in pediatric and adult-onset disease. In a prospective, observational study, Bhangale and colleagues from Mumbai, India, evaluated 266 patients (UC 135; CD 123; IBD unclassified eight) with newly diagnosed IBD, who had followed up for at least six months to assess disease profile in various age groups [10]. Most of their patients ($n=170$ [UC 98, CD 72]) were adults. Among

patients with UC, pancolitis was more common in children and extraintestinal manifestations were more common in the elderly. Among patients with CD, colonic involvement was more common in children, whereas perianal disease was less common in the elderly. Children with CD required biologics more often.

This study has shown that inflammatory bowel disease behaves differently in pediatric and elderly onset populations in certain aspects—both in disease phenotype as well as treatment requirement.

Clostridioides difficile in IBD: Not an issue or diagnostic strategy a problem?

Acute severe ulcerative colitis (ASUC) is a medical emergency and requires the initiation of treatment with systemic corticosteroids. Many of these patients have risk factors for gut infections such as defective innate immunity, recurrent nosocomial exposures, gut dysbiosis and intake of antibiotics. The two most common infections that occur in these patients are *Clostridioides difficile* (CD) and cytomegalovirus (CMV).

Mundhra and colleagues from New Delhi, India, have looked at their data on CD infections in 153 patients with ASUC. Most patients had received steroids/azathioprine previously and 10 had received biologics [11]. In addition, 26.1% of patients had prior admission within 30 days and 22.2% had a recent history of antibiotic use. Fifty-seven patients (37.3%) had qualitative CMV deoxyribonucleic acid-polymerase chain reaction (DNA-PCR) positive in mucosal biopsies. Only one patient had stool toxin assay positive for CD. Fifty-seven (37.3%) of patients had steroid failure and eight failed salvage medical therapy. Thirty patients needed colectomy—24 of them were CMV positive.

Steroid refractoriness in ASUC is usually associated with severe disease, concomitant infection and poor outcomes. This retrospective study gives an important message that despite various risk factors, CD infection is unusual, at least in northern India. On the other hand, CMV infection is the one that should be diagnosed and treated early, as this was associated with poor outcomes.

Endosonographic liver biopsy: Ready for primetime?

Despite non-invasive markers of hepatic inflammation and fibrosis being available, liver biopsy has an important place in the management of liver disease. Percutaneous biopsies have been done over decades, with their incident risks of bleeding. In patients with deranged coagulation profile, transjugular biopsies have been performed. In recent years, endoscopic ultrasound-guided liver biopsies (EUS-LB) have become available. In contrast to single piece of liver tissue available with percutaneous liver biopsies, EUS-LB has the advantage of multiple site sampling from both liver lobes, which helps in improving the histological diagnosis. In addition, the application of Doppler allows easy identification of vasculature, thereby reducing complications like bleed.

Rai et al. from Lucknow, India, have prospectively evaluated whether EUS-LB using a single pass from the right and left lobe using the slow-pull technique with a 19-gauge needle would provide adequate histological samples to reach a diagnosis and whether there was a difference in the adequacy of specimen between the left and right lobes [12]. The pre-biopsy working diagnosis was autoimmune hepatitis in 28 (56%) and non-alcoholic steatohepatitis (NASH) in 11 (22%). Median procedure time taken for the biopsy was 10 (range: 8–12) minutes and an adequate specimen for histological diagnosis was obtained in all 50 patients. Median specimen length was 58 mm and median number of complete portal tracts was 32.5. There was no difference in complete portal tracts (CPTs) and total specimen length (TSL) between left and right lobe biopsies. Bleeding from the duodenal puncture site occurred in one patient; there was no other major complication.

This prospective study demonstrates the use of EUS to obtain adequate liver tissue for histology, with good safety profile. However, the optimal technique and device needed for EUS-LB still need to be established.

Dengue hepatitis: Incidence, Spectrum and Outcome

Dengue is a febrile illness caused by infection with dengue viruses (DENV) transmitted by mosquitoes. The disease profile ranges from asymptomatic to severe hemorrhagic fever and shock. The mortality rate is high and dengue hepatitis is among the most frequent causes for death.

Prajapati et al. from, Surat, India, analyzed the data of 199 patients with dengue hepatitis from two tertiary hospitals in India [13]. Hepatitis occurred in 12% of 1664 patients and 17 patients died. The presence of shock at the time of admission was associated with death.

Given the limitations of a retrospective study, this paper highlights an important issue in patients with dengue – patients with shock and hepatitis have a grave prognosis. Early management of these complications may improve outcomes in this very morbid disease.

Identifying the cause for rodenticides-infested liver: CT scan comes to rescue

Rodenticide ingestion as a suicidal agent is common in India. Acute liver failure (ALF) due to the ingestion of yellow phosphorous, containing rodenticides, causes severe macro

and micro-vesicular steatosis and is associated with high mortality. Diagnosis is simple if the history of the rat poison ingestion is available. Unfortunately, this is not always so. In such cases, the differentiation from other causes for ALF is difficult.

Gopal and colleagues from Vellore, India, looked at their data of patients with ALF to find out whether any parameter would help differentiate patients with different causes for ALF (yellow phosphorous poisoning [YPR; $n=13$] vs. other causes for ALF [$n=11$]) [14]. They found that the clinical and biochemical parameters were almost similar in both groups. On the other hand, liver attenuation index (LAI) on computed tomography (CT) scan greater than − 18 ruled out YPR as the cause for ALF with 91% sensitivity and 85% specificity. On regression analysis, LAI was the only independent factor predicting ALF-YPR (odds ratio − 0.86 [0.76, 0.96] $p=0.008$).

The study, though retrospective, suggests that a plain CT scan done early in the course of ALF can provide a diagnosis of yellow phosphorous poisoning and hence enable the early initiation of therapy to avoid serious complications. The study has practical implications in the management of such patients and a prospective study will definitely add value and probably recommend that plain CT scan should be done in all patients with ALF.

Declarations

Conflict of interest SJB has no conflict of interest to declare in relation to this paper.

Disclaimer The author is solely responsible for the data and the contents of the paper. In no way, the Honorary Editor-in-Chief, Editorial Board Members, the Indian Society of Gastroenterology or the printer/publishers are responsible for the results/findings and content of this article.

References

1. Mohan BP, Loganathan P, Khan SR, et al. Fecal microbiota transplant delivered via invasive routes in irritable bowel syndrome: A systematic review and meta-analysis of randomized controlled trials. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01373-5.
2. Srivastava S, Kumar R. Is hyperleptinemia associated with gallstone disease? A systematic review and meta-analysis. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-022-01332-6.
3. Arora A, Kumar A, Anand AC, et al. Position statement from the Indian Society of Gastroenterology, Cardiological Society of India, Indian Academy of Neurology and Vascular Society of India on gastrointestinal bleeding and endoscopic procedures in patients on antiplatelet and/or anticoagulant therapy. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-022-01324-6.
4. Narayanasamy DK, Arun Babu T, Fredrick J, Kittu D. Clinical profile and outcomes of pediatric scrub typhus associated with elevated hepatic transaminases. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01350-y.
5. Rajendran J, Panwar R, Singh AN, et al. Management and outcomes of pseudoaneurysms presenting with late hemorrhage following pancreatic surgery: A six-year experience from a tertiary care center. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01357-5.
6. Agarwal A, Mahapatra SJ, Sethia R, et al. Universal prophylactic rectal nonsteroidal anti-inflammatory drugs with a policy of selective pancreatic duct stenting significantly reduce post-endoscopic retrograde cholangiopancreatography pancreatitis. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01354-8.
7. Singh S, Taneja S, Roy A, et al. Simple bedside tests of muscle strength and function correlate with computed tomography-skeletal muscle index for assessment of sarcopenia in cirrhosis. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01338-8.
8. Singh V, Jayachandran A, De A, Singh A, Chandel S, Sharma N. Combination of terlipressin and noradrenaline versus terlipressin in hepatorenal syndrome with early non-response to terlipressin infusion: A randomized trial. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01356-6.
9. Sundaram S, Seth V, Patil P, Patkar S, Engineer R, Shetty N, Goel M, Mehta S. Short and long outcomes of endoscopic bilateral metal stent placement for malignant hilar biliary obstruction: Tertiary care oncology centre experience. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-022-01337-1.
10. Bhangale N, Desai D, Abraham P, Gupta T, Dhoble P, Joshi A. A prospective study of inflammatory bowel disease phenotypes in extremes of age and comparison with adults. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01360-w.
11. Mundhra S, Thomas D, Jain S, et al. Low prevalence of Clostridioides difficile infection in acute severe ulcerative colitis: A retrospective cohort study from northern India. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-022-01336-2.
12. Rai P, Majeed A, Kumar P, Rajput M, Goel A, Rao RN. Endoscopic ultrasound-guided liver biopsy using a single-pass, slow-pull technique with a 19-G Franseen tip fine-needle biopsy needle: A prospective study. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01339-7.
13. Prajapati R, Mehta R, Kabrawala M, et al. Dengue hepatitis: Incidence, spectrum and outcome. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-023-01405-0.
14. Gopal P, Krishnan SK, Malleswaran S, et al. Novel radiological technique to recognize acute liver failure caused by yellow phosphorous containing rodenticides. Indian J Gastroenterol. 2023;42. https://doi.org/10.1007/s12664-022-01334-4.