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**Abbreviations used in this review:**
- BMI = body mass index
- CRP = C-reactive protein
- ESR = erythrocyte sedimentation rate
- EUS-FNA = endoscopic ultrasonography-fine needle aspiration
- GI = gastrointestinal
- IBD = inflammatory bowel disease
- IBS = irritable bowel syndrome
- OR = odds ratio
- PE = push enteroscopy
- PET-CT = positron emission tomography-computed tomography
- RCT = randomised controlled trial
- VCE = video capsule endoscopy

Welcome to issue 22 of Gastroenterology Research Review.

This issue begins with papers reporting RCT data on iron fortification for infants in developing countries, with emphasis on the adverse effects on the gut microbiome. Other research reported positive associations between levels of free testosterone and *H. pylori* eradication in men, which may contribute to the predisposition for this condition among men. EUS-FNA (endoscopic ultrasonography-fine needle aspiration), although not without its limitations, was shown to provide a superior diagnostic yield than PET-CT for accurately establishing the aetiology of isolated adenopathies, while VCE (video capsule endoscopy) provided a diagnostic advantage over PE (push enteroscopy) for obscure GI bleeding, especially for detecting small bowel lesions.

I hope you find the papers selected for this issue of interest, and I look forward to receiving comments, feedback or suggestions.

Kind Regards,
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Iron fortification adversely affects the gut microbiome, increases pathogen abundance and induces intestinal inflammation in Kenyan infants

**Authors:** Jaeggi T et al.

**Summary:** Kenyan infants aged 6 months who consumed home-fortified maize porridge daily for 4 months (*n=115*) received a micronutrient powder with or without iron supplementation with Nafeldta 2.5mg or ferrous fumarate 12.5mg in two RCTs. Baseline gut microbiota (analysed by 16S pyrosequencing) consisted of 63% *Bifidobacteriaceae* spp. and high prevalences of other pathogens, including Salmonella spp. *Clostridium difficile*, *C. perfringens* and pathogenic *Escherichia* coli. The groups receiving iron had significant increases in enterobacteria, particularly *Escherichia* and *Shigella* spp. (p<0.05), enterobacteria/bifidobacteria ratio (p=0.02) and *Clostridium* spp. (p=0.03) on pyrosequencing, with most effects also confirmed on targeted real-time PCR (polymerase chain reaction). Iron supplements also had significant increases in faecal calprotectin levels (p=0.002), but a nonsignificantly greater proportion of those receiving 12.5mg required treatment for diarrhoea (27.3% vs. 8.3% (p=0.092)). No serious study-related adverse events were reported among the participants. An accompanying commentary highlighted and discussed increases in infection-related mortality and morbidity due to diarrhoea in these trials and several other similar trials investigating the effects of dietary fortification with iron and other micronutrients on children’s health, mostly in rural areas of developing countries.

Comment: Iron deficiency is estimated to affect more than 2 billion people worldwide and presents a major global health problem, particularly in developing countries. Apart from causing anaemia, iron deficiency can cause growth and mental retardation in children. Iron fortification programmes therefore seem sensible and are place in worldwide. However, two studies in children raise concerns about the safety of iron fortification by associating supplementation with increased morbidity due to diarrhoea or mortality through malaria and bacterial infections, the cause for it unknown. Jaeggi et al. studied the gut microbiome in two double-blind RCTs in 6-month-old Kenyan infants receiving 2.5mg versus 12.5mg iron versus no iron supplementation. Interestingly, iron supplementation increased the enterobacteria in the foetal microbiome as compared with bifidobacteria, and particularly pathogenic bacteria such as *Escherichia*, *Shigella* and *Clostridium* spp. resulting in an increase from 8.3% to 27.3% of infants requiring treatment for diarrhoea, although this did not reach significance. This showed for the first time that iron fortification changes the gut microbiome resulting in an increase in pathogenic bacteria. This provides a possible explanation for the negative outcomes of the iron supplementation trials in terms of morbidity and mortality. Nevertheless, these trials need to be interpreted with caution and in geographic context, and further study is required to make appropriate recommendations.

**Reference:** Gut 2015;64(5):731–42

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**Helicobacter pylori** second-line rescue therapy with levofloxacin- and bismuth-containing quadruple therapy, after failure of standard triple or non-bismuth quadruple treatments

**Authors:** Gisbert JP et al.

**Summary:** Patients with *Helicobacter pylori* infection who had failed a standard triple regimen (*n=131*) or a non-bismuth quadruple regimen (sequential *n=52* or concomitant *n=37*) received a 14-day regimen of esomeprazole 40mg twice daily, amoxicillin 1g twice daily, levofloxacin 500mg once daily and bismuth 240mg twice daily in this prospective study; 96% of participants received the regimen correctly. The respective per-protocol and intention-to-treat *H. pylori* eradication rates (assessed by 13C-urea breath test) were 91.1% and 90%, and did not differ according to prior failed treatment or country of origin.

**Comment:** Chronic gastritis, peptic ulcer disease and gastric cancer are mainly caused by *H. pylori* infection. While treatment with proton-pump inhibitors improves the gastritis and ulcer healing, actual eradication remains the main goal of therapy and requires the combination of a proton-pump inhibitor with at least two antibiotics such as amoxicillin and clarithromycin. However, as with other bacterial infections worldwide, growing resistance is increasing the risk of treatment failure, raising the demand for rescue therapy. The current study investigated 200 patients consecutively recruited for quadruple therapy with levofloxacin/bismuth/amoxicillin/esomeprazole as rescue therapy after failed triple (clarithromycin/amoxicillin/esomeprazole) and/or quadruple therapy (clarithromycin/amoxicillin/esomeprazole/metronidazole). Eradication rates were high in this difficult-to-treat group, and were >90% with the new regimen. As expected, adverse effects were noted by 46% of all treated patients, with nausea (17%) and diarrhoea (16%) the most common. This study underlines the importance for appropriate confirmation of eradication after first-line therapy with clarithromycin/amoxicillin/esomeprazole to assure successful therapy. It also highlights the growing problem of resistance and the importance of solving the difficulty accessing drugs such as levofloxacin for this indication in the future.

**Reference:** Aliment Pharmacol Ther 2015;41(8):768–75

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Excretion of urinary histamine and N-tele methylhistamine in patients with gastrointestinal food allergy compared to non-allergic controls during an unrestricted diet and a hypoallergenic diet

Authors: Raithel M et al.

Summary: These researchers analysed urinary excretion parameters in a retrospective cohort of 56 patients in whom subsequent food challenge tests confirmed food allergy; allergy urine samples were collected for analysis during a 12-hour period of a 2-day unrestricted diet with staple foods and also a 2-day hypoallergenic potato-rice diet. Compared with a healthy control group, the patients with GI food allergies had significantly higher histamine levels with the unrestricted diet (1.42 vs. 0.87 μg/mmol creatinine × m^2 [p<0.001]) and a "marginal" difference seen with the potato-rice diet (1.30 vs. 1.05 μg/mmol creatinine × m^2 [p=0.02]), and N-methylhistamine levels were significantly elevated with both the unrestricted and potato-rice diets (p<0.001 for both). Switching from unrestricted to hypoallergenic food was associated with significant reductions in urinary histamine excretion (p<0.04) and clinical symptom score (p<0.02).

Comment: The differential diagnosis for abdominal pain and GI symptoms after food intake is broad and can be difficult to differentiate. Particularly, food allergies remain challenging to prove. The current study went to great lengths to make a specific diagnosis of GI-suspected food allergy in 56 patients, compared with a control group without symptoms or carbohydrate malabsorption, and subjected them to urine testing for histamine and methylhistamine. Both markers were significantly higher in the allergy group versus the control group, irrespective of whether the groups had been on an unrestricted or restricted/hypoallergenic diet. Methylhistamine testing had sensitivity of 62.5%, but specificity of 86.4%, and levels were elevated in both IgE-positive and -negative patients. However, urine histamine secretion is not specific to food allergy and may occur in multiple other conditions such as mastocytosis or IBD. Thus, this test should only be employed after more serious conditions have been appropriately excluded. Nevertheless, urine testing may present a useful adjunct for distinguishing patients with GI-mediated food allergy from IBS, etc.

Natural history of bleeding risk in colonic diverticulosis patients

Authors: Nikura R et al.

Summary: This research explored the incidence of bleeding and its associated risk factors in a cohort of 1514 patients with coloscopy-confirmed asymptomatic diverticular bleeding followed for a median of 46 months. Thirty-five patients had bleeding events at a median of 56 months. The respective cumulative, 12-60- and 120-month incidences of diverticular bleeding were 0.21%, 2.2% and 9.5%, and the overall bleeding incidence rate was 0.46 per 1000 patient-years. Significant risk factors for bleeding were age ≥70 years and bilateral diverticulosis.

Comment: Diverticulosis of the colon is a common condition with increasing incidence. Colonic bleeding is a common complication of this condition, often requiring hospitalisation and blood transfusion. The current study investigated the natural history of this condition more closely in a large cohort of 1514 patients recruited between 2001 and 2013 and followed for a median of 46 months. The study was retrospective using a coloscopy follow-up database of a large metropolitan hospital in Tokyo. Patients undergoing colonoscopy for active GI bleeding at diagnosis were excluded. Diverticulosis was right sided in 55%, left sided in 24% and bilateral in 21%. The cumulative incidence of a diverticular bleeding episode was 0.21% at 12 months, 2.2% at 60 months and 9.5% at 120 months. This translated into a risk of bleeding of 0.46 per 1000 patient-years. Risk factors for diverticular bleeding were age >70 years (adjusted hazard ratio 3.7) and bilateral diverticulosis (adjusted hazard ratio 2.4). Previous studies have mostly addressed the rebleeding risk of diverticular bleeding, estimated at 20% at 12 months in Asian and 3.8% in Western countries, and thus much higher than in this study with an asymptomatic cohort. The results are therefore reassuring. They also highlight the need to employ a certain degree of caution given the incidence of other conditions causing bleeding in this study such as rectal lesions, polyps and cancers, and in alcoholic and infectious colitis. Furthermore, phenotype of diverticular disease differs between Asian, i.e. right-sided and bilateral, and Western countries, predominantly left-sided. Finally, this study did not collect data on concomitant medications, herbal remedies, diet and symptoms that could influence the incidence of bleeding, and thus the findings need to be interpreted with caution.

Association between circulating levels of sex steroid hormones and Barrett’s oesophagus in men

Authors: Cook MB et al.

Summary: The relationships between 13 circulating sex steroid hormones and Barrett’s oesophagus in men were explored by comparing blood samples from 174 men with Barrett’s oesophagus with those from 213 control men without Barrett’s oesophagus. Men in the highest quartiles for free testosterone and free dihydrotestosterone levels had significantly increased likelihoods of Barrett’s oesophagus (respective ORs 5.36 [95% CI 2.21–13.03] and 4.25 [1.87–9.69]), whereas an inverse relationship was seen between estrone sulfate level and Barrett’s oesophagus risk (p=0.02 for trend); none of the other hormones evaluated were associated with Barrett’s oesophagus risk.

Comment: Adenocarcinoma of the oesophagus is a consequence of recurrent erosive gastro-oesophageal reflux disease and subsequent Barrett’s oesophagus. A well-established risk factor is BMI, but similarly to reflux, its contribution seems to be similar between genders and does not account for the significantly increased risks of Barrett’s oesophagus and oesophageal adenocarcinoma in males. Given the association between male gender and increased inflammation in general and the fact that oesophageal epithelium may express receptors for sex hormones, this paper investigated a possible association between sex hormone levels and the incidence of Barrett’s oesophagus in males undergoing endoscopy for a variety of reasons. The study was performed as a case-control study by comparing those with histology-proven Barrett’s oesophagus (n=174) and those without (n=213). Testosterone and dihydrotestosterone levels were positively associated with Barrett’s oesophagus, whereas estrone sulfate showed a negative association. These associations were significant in a multiple regression analysis that also included age, race, smoking and alcohol history, BMI and symptom scores. This study therefore supports a role of male sex hormones in the predisposition of males to Barrett’s oesophagus over females. However, the mechanism is not entirely clear, although there are suggestions that testosterone and dihydrotestosterone may influence the degree of inflammation, wound healing and lower oesophageal sphincter tone.

Budesonide foam induces remission in patients with mild to moderate ulcerative proctitis and ulcerative proctosigmoiditis

Authors: Sandborn WJ et al.

Summary: Patients with mild-to-moderate ulcerative proctitis or ulcerative proctosigmoiditis (n=546) were randomised to receive budesonide foam 2 mg/25mL twice daily for 2 weeks followed by once daily for 4 weeks or placebo in two identical trials. Compared with placebo, budesonide foam was associated with significantly greater rates of remission, resolution of rectal bleeding and endoscopic improvement at 6 months in both. Most adverse events occurred at similar rates between the groups, although more events related to changes in cortisol levels were seen in the budesonide foam group.

Comment: Distal disease, i.e. proctitis, proctosigmoiditis and left-sided colitis, represents about 70% of patients with ulcerative colitis. Symptoms such as diarrhoea and urgency, tenesmus and bleeding are often significant despite the relatively short segment of bowel involved. Topical therapy with 5-ASA agents or corticosteroids is the mainstay of therapy and is appealing given their limited systemic side effects as compared with oral or intravenous therapy. Due to its high first-pass metabolism of ~30%, systemic adverse effects are very limited with budesonide as compared with other corticosteroids. The current study presents the combined results of two identically designed, randomised, double-blind, placebo-controlled trials with more than 500 patients with mild-to-moderate ulcerative proctitis or proctosigmoiditis treated with budesonide foam or placebo. Remission, as defined as endoscopy subscore of <1, rectal bleeding subscore of 0 and improvement/no change from Mayo stool frequency score, was achieved with budesonide in 41% as compared with 24% with placebo when the studies were combined, with a significantly greater frequency of patients with improved endoscopy scores and bleeding scores. While the frequency of severe adverse events was similar between groups, the majority of adverse events were mild to moderate and most commonly related to decreased blood cortisol levels. It is important to note that mesalazine is still the most effective first-line therapy for this condition, and steroids are considered second line. Indeed, the difference between budesonide and placebo was only 42% vs. 32% for patients also treated with mesalazine, but 40% vs. 14% in patients without mesalazine therapy. The role of budesonide in the therapeutic algorithm and especially in comparison with systemic steroids still has to be further refined, and the importance of patient education regarding appropriate use of topical steroids should not be underestimated.


Reference: Gastroenterology Research Review

Independent commentary by Associate Professor Golo Ahlenstiel, Gastroenterologist and Hepatologist at Westmead Hospital, Sydney. After completing his medical and doctoral degrees at the University of Bonn, Germany, Golo Ahlenstiel received research fellowship awards from the National Institutes of Health (NIH, USA) and the German Research Foundation (DFG, Germany) to work in the Rehermann laboratory at the NIH on the immunopathogenesis of viral hepatitis. Apart from his clinical duties, he also leads a Liver Immunology group at Westmead Millennium Institute.
**COLAZIDE® MINIMUM PRODUCT INFORMATION**  (750 mg balsalazide sodium capsules).

**INDICATIONS:** Treatment of mild-to-moderate active ulcerative colitis and maintenance of remission in patients who are intolerant to sulfasalazine. 

**CONTRAINDICATIONS:** Hypersensitivity to mesalazine (including metabolites), salicylates or any components of Colazide®, severe hepatic impairment; moderate-to-severe renal impairment; last weeks of pregnancy; patients with tendency to bleeding and those on concomitant anticoagulants; active peptic ulcer. 

**PRECAUTIONS:** Use with caution in patients with asthma, mild-to-moderate hepatic impairment, mild renal impairment, pregnancy (category C), lactation, children <18 years. During treatment blood counts, BUN/creatinine and urine analysis should be performed. Other: See Product Information 

**INTERACTIONS:** No formal drug interactions have been conducted with balsalazide. Other: see Product Information 

**ADVERSE EFFECTS:** Common: Headache, GI symptoms (e.g. abdominal pain, diarrhoea, nausea, vomiting); Other see Product Information. 

**DOSAGE AND ADMINISTRATION:** Colazide should be swallowed whole with food. Treatment of active disease - 3 capsules orally 3 times/day until remission or max 12 weeks. Maintenance treatment - 2 capsules orally twice daily, adjust according to response (additional benefit shown with 8 capsules daily). Based on TGA approved Product Information 09 June 2010. 


**PBS Information:** Authority required (STREAMLINED). Ulcerative colitis where hypersensitivity to sulfonamides exists. Ulcerative colitis where intolerance to sulfasalazine exists. 

**Note:** Not for the treatment of Crohn’s disease.
Endoscopic ultrasonography-fine needle aspiration versus PET-CT in undiagnosed mediastinal and upper abdominal lymphadenopathy

Authors: Redondo-Cerezo E et al.

Summary: In this comparative clinical study, the accuracies of PET-CT and EUS-FNA were compared in 54 patients with lymphadenopathy confirmed on conventional CT, with nodes located in the subcarinal space (33.3%), porta hepatitis (31.5%), upper mediastinum (15%), peripancreatic (7.4%) and other locations (12.8%). The most common cytologically based diagnoses were bronchiovascular (42%), epidermoid carcinoma (8.4%), lymphoma (8.4%) and ductal adenocarcinoma of pancreatic origin (6.3%), and 67% of patients were positive on PET. The respective sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy value for EUS-FNA were 91.3%, 100%, 100%, 92.5% and 95.6%, and for PET-CT were 75%, 25%, 50% and 50%, respectively.

Comment: Accurate staging of lymph node spread is essential for accurate cancer staging. Currently, CT staging is recommended as a first step in newly diagnosed or suspected neoplasms despite its poor sensitivity for diagnosing smaller lymph nodes and differentiating malignant spread from reactive nodes. PET is often considered the best next test, given that it is noninvasive, despite its false-positive rate of >20%. EUS allows FNA to make a cytodiagnosis and thus has been proposed to have higher diagnostic yield. The current study compared PET-CT with EUS-FNA in 54 patients with lymphadenopathy on CT and unknown primary malignancy. Adequate cytology was obtained in 48/54 patients (89%) by EUS-FNA as compared with PET-CT, which was positive in 67%. Cytology showed benign/reactive lymph node in 42%, epidermoid carcinoma (8.4%), lymphoma (8.4%) and ductal adenocarcinoma of pancreatic origin (6.3%). The respective sensitivity, specificity and positive and negative predictive values for EUS-FNA were high at 91%, 100%, 100% and 93% compared with PET-CT with values of 75%, 25%, 50% and 50%. This supports the high diagnostic yield of EUS-FNA. Notably, this study was small and did not observe any major complications from EUS-FNA, even though EUS-FNA remains an invasive procedure with a bleeding risk of around 1%. Secondly, given that EUS-FNA usually requires sedation, it is not without anaesthetic risk. Finally, the quality of EUS-FNA is operator dependent and not readily available everywhere.


Randomized controlled trial comparing outcomes of video capsule endoscopy with push enteroscopy in obscure gastrointestinal bleeding

Authors: Segarajasingam DS et al.

Summary: These researchers randomized patients with obscure GI bleeding and negative oesophagogastroduodenoscopies and colonoscopies to VCE or PE, and followed them for 12 months; 82.3% of participants had overt obscure GI bleeding. Compared with PE, VCE was associated with a significantly greater diagnostic yield (72.5% vs. 48.7% [p<0.05]), particularly in the distal small bowel (58% vs. 13% [p<0.01]), and significantly more identified lesions that were rated possible or certain causes of bleeding (79.3% vs. 35.0% [p<0.05]). Ongoing acute and chronic bleeding rates during follow-up did not differ significantly between the VCE and PE groups (40.0% vs. 38.5% and 32.5% vs. 45.6%, respectively), nor did health resource utilisation. The rate of crossover due to ongoing bleeding was significantly lower in the VCE group (22.5% vs. 48.7% [p<0.05]).

Comment: In GI bleeding, panendoscopy and colonoscopy provide a diagnosis in up to 95% of patients. The remaining 5% are labeled as obscure GI bleeding and result in a substantial cost to healthcare systems through further investigations, blood transfusions and repeated hospital admissions. The approach to investigating obscure GI bleeding remains subject to discussion, although VCE has been considered an appropriate test. Recently however, PE compared favourably with VCE in terms of diagnostic yield but not in terms of clinical outcomes. The current study presents an interesting alternative using randomised controlled trial to VCE (n=40) vs. PE (n=39). The diagnostic yield was higher for VCE in this study at 72.5% as compared with 48.7% for PE, especially for the distal small bowel (58% vs. 13%). There was no difference between groups in terms of subsequent acute or chronic bleeding episodes. However, the study was small and thus the implications for clinical outcomes remain limited. Secondly, in this cohort 37% of patients had gastric, duodenal or colonic pathology highlighting the need for high quality studies in the context of obscure GI bleeding before escalation to VCE or PE. Finally, the limited extent of PE as compared with VCE and 40% of lesions being found in the jejunum suggests that VCE may be considered as first line after panendoscopy and colonoscopy.


Risk factors on the development of new-onset gastroesophageal reflux symptoms

Authors: Hallan A et al.

Summary: Using data from respondents to the population-based prospective cohort HUNT study surveys, risk factors for new-onset gastro-esophageal reflux symptoms were identified. Compared with respondents reporting no gastro-oesophageal reflux symptoms at baseline or follow-up (n=14,416), those with new-onset gastro-oesophageal reflux symptoms (no symptoms at baseline but severe symptoms at follow-up; n=510) were more likely to be older (OR 1.01 per year [95% CI 1.00–1.02], have a higher BMI regardless of baseline value (1.30 per unit increase [1.25–1.35]) and be a current or past smoker (1.37 [1.07–1.76] and 1.29 [1.00–1.67], respectively), and were less likely to be male (0.81 [0.66–0.98] or have a higher education (0.69 [0.56–0.86]). The likelihood of new-onset gastro-esophageal reflux symptoms was particularly increased in patients whose BMI increased by >3.5 kg/m² upon quitting smoking (OR 2.03 [95% CI 1.31–3.16]).

Comment: The HUNT study is comprised of three consecutive surveys (1984–1986, 1995–1997 and 2006–2009) and involves the Nord-Trondelag County in Norway. Its 135,000 residents are considered an appropriate representation of the Norwegian population as a whole. Hallan et al. used data from these surveys to understand risk factors for new onsets gastro-oesophageal reflux symptoms. Over 29,000 subjects responded to the survey with 510 participants reporting new onset of gastro-oesophageal reflux symptoms as compared with 14,416 describing no symptoms. Multivariate regression identified positive associations of gastro-oesophageal reflux symptoms with age, BMI, history of smoking and negative associations with male gender and higher education. Interestingly, smoking cessation was associated with new onset of gastro-oesophageal reflux symptoms in those who gained weight. The results, while not necessarily unexpected, are interesting, particularly in terms of the association with gender. Further analysis suggests that the association with gender and gastro-oesophageal reflux symptoms is at least to some degree due to the higher weight gain in female participants. The strength of this study is that it is population based, but therein also lies the weakness, i.e. the study describes the symptoms of gastro-oesophageal reflux but no investigations were done to prove actual reflux disease such as pH measurements or endoscopy. However, it clearly outlines the need to address these risk factors in symptomatic patients.

Reference: Am J Gastroenterol 2015;110(3):393–400 Abstract

A meta-analysis of the utility of C-reactive protein, erythrocyte sedimentation rate, fecal calprotectin, and fecal lactoferrin to exclude inflammatory bowel disease in adults with IBS

Authors: Menees SB et al.

Summary: This systematic review and meta-analysis of journal articles/abstracts reporting on biomarkers for distinguishing between IBS, IBD and neither included four with CRP data that met inclusion criteria, four with ESR data, eight with calprotectin data and two with lactoferrin data. None of these biomarkers were able to reliably distinguish between IBS and healthy controls, CRP and ESR. However, ESR and calprotectin levels were significantly lower in patients with IBS and IBD than IBS and IBD patients. Adequate cytology was obtained in 48/54 patients (89%) by EUS-FNA. The accuracy of CRP and ESR and calprotectin levels in predicting IBD was found to be >20%. EUS allows FNA to make a cytological diagnosis and PET is often considered the best next test, given that it is noninvasive, despite its significant overlap with IBS in terms of symptoms. The current meta-analysis aimed to compare the utility of CRP, ESR and faecal calprotectin or lactoferrin to discriminate between IBS and IBD. Ultimately, 12 studies with 1059 IBD and 595 IBS patients were included. The analysis supported CRP and faecal calprotectin to allow population diagnosis of IBD (<1% probability), whereas ESR and lactoferrin level providing little clinical utility.

Comment: IBS is a common disorder with significant symptoms such as abdominal pain, and altered bowel habits remain a diagnosis of exclusion. Thus, it creates significant healthcare costs due to investigations required to exclude other organic causes, especially IBD, which has significant overlap with IBS in terms of symptoms. The current meta-analysis aimed to compare the utility of CRP, ESR and faecal calprotectin or lactoferrin to discriminate between IBS and IBD. Ultimately, 12 studies with 1059 IBD and 595 IBS patients were included. The analysis supported CRP and faecal calprotectin to allow population diagnosis of IBD (<1% probability), whereas ESR and faecal lactoferrin did not perform to the same standard. This highlights that by excluding active inflammation, IBS remains a diagnosis of exclusion. Also, given that these markers may be low even in IBD, these tests should be considered an adjunct rather than the only diagnostic test. However, they may prove useful to reassure patients and primary healthcare providers after appropriate investigations and avoid ongoing expensive investigations.


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