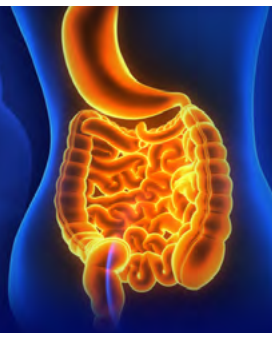
IBD Practice Review™



Making Education Easy

Issue 10 - 2023

In this issue:

Abbreviations used in this issue:

AGA = American Gastroenterological Association; **AGITG ASM** = Australasian Gastro-Intestinal Trials Group Annual Scientific Meeting; **AI** = artificial intelligence; **ASGE** = American Society for Gastrointestinal Endoscopy; **BSG** = British Society of Gastroenterology; **CD** = Crohn's disease; **CeA** = coeliac autoimmunity; **CeD** = coeliac disease; **EASL** = European Association for the Study of the Liver; **EIMs** = extraintestinal manifestations; **GESA** = Gastroenterological Society of Australia; **GI** = gastrointestinal; **IBD** = inflammatory bowel disease; **ISCs** = intestinal stem cells; **NZSG** = New Zealand Society of Gastroenterology; **OSA** = obstructive sleep apnoea; **PBS** = Pharmaceutical Benefits Scheme; **PHRI** = PICaSSO Histologic Remission Index; **TA** = transit amplifying; **UC** = ulcerative colitis.

Welcome to the 10th issue of Inflammatory Bowel Disease Practice Review.

This Review covers news and issues relevant to clinical practice in inflammatory bowel disease. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. Finally, on the back cover you will find our COVID-19 resources for Gastroenterologists, and a summary of upcoming local and international educational opportunities including workshops, webinars, and conferences.

We hope you enjoy this Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

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Clinical Practice

Association between IBD, coeliac disease, and coeliac autoimmunity

Given the limited population-based data available, a recent nationwide study aimed to explore the associations between inflammatory bowel disease (IBD), coeliac disease (CeD), and coeliac autoimmunity (CeA). The study utilised health administrative data from all four health maintenance organisations in Israel, covering 98% of the population. The researchers focused on examining the prevalence of CeD in children and adults with IBD compared to non-IBD matched controls. CeD was defined using three specific International Classification of Disease-9 codes, while CeA was identified through positivity for tissue transglutaminase antibodies.

Among the 34,375 patients with IBD included in the study (with 56% having Crohn's disease [CD] and 44% having ulcerative colitis [UC]), 319 individuals (0.93%) were found to have CeD. This was significantly higher compared to the prevalence of CeD in non-IBD controls, which stood at 294 individuals (0.31%; $p<0.001$). Moreover, CeA was identified in 575 patients with IBD (1.67%) versus only 158 controls (0.17%; $p<0.001$). The prevalence of CeD was found to be higher in paediatric-onset IBD cases (1.66%) compared to adult-onset IBD cases (0.79%; $p<0.001$). Additionally, within the IBD cohort, patients with CD exhibited a higher prevalence of CeD (1.19%) compared to UC patients (0.56%; $p<0.001$). Notably, the diagnosis of CeD often preceded the diagnosis of IBD in most cases (76%), indicating that CeD may serve as an early marker for subsequent development of IBD. Furthermore, patients with both IBD and CeD experienced shorter times to treatment escalation compared with those who had IBD alone ($p=0.017$).

These findings highlight the higher prevalence of CeD and CeA in patients with IBD, particularly in paediatric-onset cases and those with CD. Detecting CeD before the onset of IBD can provide valuable insights for early intervention strategies. Additionally, the presence of CeD appears to be associated with more intensified treatment for IBD.

Overall, the findings contribute to our understanding of the connections between IBD, CeD, and CeA. This study underscores the importance of considering these associations when managing patients with IBD, especially in terms of early diagnosis and treatment escalation.

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Impact of vedolizumab on extraintestinal manifestations in IBD

The EMOTIVE study aimed to investigate the impact of vedolizumab on extraintestinal manifestations (EIMs) in patients with IBD. This retrospective study involved 99 adults with moderately to severely active IBD and active EIMs at the start of vedolizumab treatment, followed up for at least 6 months. The primary goal was to assess the resolution of all EIMs within 6 months of starting vedolizumab.

The most common EIMs observed in the study cohort were arthralgia (joint pain) affecting 69.7% of patients, followed by peripheral spondylarthritis (inflammation of peripheral joints) and axial spondylarthritis (inflammation of the spine) in 21.2% and 10.1% of patients, respectively. Within 6 and 12 months of initiating vedolizumab, 19.2% and 25.3% of patients, respectively, reported the complete resolution of all EIMs. Furthermore, a combined improvement (resolution and partial response) was seen in 36.5% and 49.5% of all EIMs at these respective time points. The persistence of vedolizumab treatment at 12 months was 82.8%. Adverse events were reported in 18.2% of patients, with arthralgia being the most frequently reported side effect, affecting 4.0% of the participants.

These findings demonstrate that vedolizumab is effective in managing EIMs in patients with IBD. Approximately one-fourth of patients experienced the resolution of all EIMs, and nearly half showed improvement within 12 months of starting vedolizumab. Moreover, vedolizumab exhibited a good safety profile, with a high persistence rate at 12 months. This real-world study provides valuable insights into the efficacy and safety of vedolizumab for managing EIMs in patients with IBD.

https://tinyurl.com/4npunxua

Paediatric IBD risk linked to antibiotics, western diet, and higher family income

The global incidence of paediatric IBD is increasing, with approximately 1 in 4 cases now diagnosed before the age of 21 years. Parents need to be aware of this condition and its modifiable risk factors, as paediatric IBD can impact a child's growth and puberty.

A recent meta-analysis of 36 observational studies involving around 6.4 million children was presented at Digestive Disease Week® 2023 conference, which took place between May 6–9, 2023 in Chicago, USA. Findings demonstrated that any exposure to antibiotics before the age of 5 years was associated with a threefold increased risk of paediatric IBD. Furthermore, exposure to four or more courses of antibiotics correlated with a 3.5 times higher risk. Lower socioeconomic status appeared to be a protective factor, associated with a 65% reduced risk of childhood IBD. Other protective factors included greater vegetable consumption, having two or more siblings, and childhood exposure to pets. Further, early exposure to second-hand smoke was identified as a risk factor, doubling the risk of IBD in children. A Western diet, high in sugars and ultra-processed foods while low in vegetables, also increases the risk of paediatric IBD. These factors can impact gut microbiota, particularly in children. A novel finding from the study indicated that non-Caucasian children living in high-income countries face a threefold increased risk of IBD. The researcher plans to explore the influence of migration in future work.

Given these findings, it is suggested that families with young children should prioritise a diet rich in vegetables and minimally processed whole foods, use antibiotics cautiously in early childhood, consider pet adoption, prevent second-hand smoke exposure, and avoid excessive concerns about hygiene. Breastfeeding and a healthy diet pattern for children, especially for those with a family history of IBD or a history of eczema/rhinitis, can help minimise the compounding effects of a Western diet on genetic risk. In non-Caucasian children from high-income countries, promoting breastfeeding and a healthy, minimally processed weaning foods and diet pattern may help reduce the risk of developing IBD.

https://tinyurl.com/msz5ndae

Simple novel screening tool for obstructive sleep apnoea in IBD

Given that IBD has been associated with an increased risk of obstructive sleep apnoea (OSA), researchers investigated the associations of OSA, sleepiness, and various factors related to IBD, with the aim of developing a screening tool for OSA in this patient population.

A total of 670 adults with IBD responded to a comprehensive online survey, which incorporated assessments of OSA risk, IBD activity, IBD-related disability, anxiety, and depression. The median age and disease duration of participants were 41 and 11.9 years, respectively. Many patients (57%) were diagnosed with CD (57%). Notably, 22.6% of the cohort demonstrated a moderate to high risk of OSA.

A multivariate regression model revealed several factors associated with moderate to high risk of OSA, including increasing age, obesity, smoking, and abdominal pain sub-score. Similarly, the multivariate model for the combined outcome of moderate to high risk of OSA and at least mild daytime sleepiness included abdominal pain, age, smoking, obesity, and clinically significant depression. Based on these results, a simple screening score was developed, incorporating age, obesity, IBD activity, and smoking status. A score above 2 exhibited a sensitivity of 89% and a specificity of 56% for identifying moderate to high risk of OSA and it can be effectively utilised for screening in clinical practice. Over one-fifth of the IBD cohort met significantly high-risk criteria for OSA, warranting referral for a diagnostic sleep study. Abdominal pain emerged as a noteworthy risk factor, along with traditional factors such as smoking, increasing age, and obesity.

Early screening and intervention can play a crucial role in managing these conditions effectively and enhancing the overall wellbeing of individuals with IBD. Health care professionals should consider screening patients with IBD for OSA by implementing this novel screening tool that utilises parameters typically available in the IBD clinic.

https://tinyurl.com/bde5habv

AI-enabled histological prediction of remission or activity and clinical outcomes in UC

Although microscopic inflammation in UC holds significant prognostic value, its assessment has been challenging due to interobserver variability. A recent publication outlined a new artificial intelligence (AI) computer-aided diagnosis system, which has been developed and validated to overcome these limitations.

The study involved a total of 535 digitalised biopsies from 273 patients. The biopsies were graded using the PICaSSO Histologic Remission Index (PHRI), Robarts Histological Index, and Nancy Histological Index. A convolutional neural network classifier was trained to differentiate between remission and activity using a subset of 118 biopsies. The model was then calibrated on 42 biopsies and tested on 375 biopsies. Additionally, the model was evaluated for its ability to predict endoscopic assessment and occurrence of flares at 12 months. The system's output was compared with human assessment to determine diagnostic performance.

The AI model demonstrated impressive sensitivity and specificity in distinguishing histological activity from remission. The system achieved sensitivities of 89%, 94%, and 89%, and specificities of 85%, 76%, and 79% for the PHRI, Robarts Histological Index, and Nancy Histological Index, respectively. Moreover, the model accurately predicted endoscopic remission/activity with 79% and 82% accuracy for the UC endoscopic index of severity and Paddington International virtual ChromoendoScopy ScOre, respectively. Hazard ratios for disease flare-up between histological activity and remission groups were 3.56 for pathologist-assessed PHRI and 4.64 for AI-assessed PHRI. These findings were further validated in an external cohort of 154 biopsies from 58 patients, confirming the reliability of the AI model.

The development of this AI model offers significant benefits in expediting, standardising, and enhancing histologic assessment in clinical practice and trials. By leveraging AI technology, health care professionals can accurately distinguish histologic remission from activity in UC biopsies, enabling early prognostic prediction, streamlining clinical decision-making, and facilitating appropriate intervention strategies.

https://tinyurl.com/235w32kr

Excess dietary sugar alters colonocyte metabolism and impairs the early proliferative response to damage

In a recently published study, researchers investigated the impact of excess dietary sugar on the function of intestinal stem cells (ISCs) and transit amplifying (TA) cells in the colonic epithelium. Using 3-dimensional colonoids and a mouse model of colon damage, they found that high sugar conditions directly hindered the development of colonoids and reduced the expression of genes associated with proliferation and stem cell function.

High-glucose conditions resulted in the accumulation of pyruvate, a glycolytic metabolite, in colonoids, leading to decreased ATP levels and impaired glycolytic fuel metabolism. However, treatment with dichloroacetic acid, which redirected pyruvate into the tricarboxylic acid cycle, restored colonoid growth, adenosine triphosphate levels, and gene expression related to proliferation and stem cell function.

In mice fed a high sugar diet and subjected to colon damage, irreparable damage occurred independently of the colonic microbiota and its metabolites. Metabolic analysis revealed increased glycolytic potential but impaired oxidative phosphorylation and fuel metabolism in the colonic epithelium of high-sucrose-fed mice. Furthermore, high-sucrose-fed mice with colon damage showed impaired proliferative potential of ISCs and a reduced number of TA direct daughter cells. These findings suggest that excess dietary sucrose can directly influence the metabolism of intestinal crypt cells and inhibit regenerative proliferation of ISCs and TA cells.

The study highlights the potential impact of short-term, high-sugar diets on intestinal health. Although these findings remain to be confirmed in humans, the study suggests the importance of considering dietary interventions that support the treatment of acute intestinal injury, such as in patients experiencing an acute flare of UC.

https://tinyurl.com/yvrez5sy

Regulatory News

New and amended PBS listings for UC

New and amended Pharmaceutical Benefits Scheme (PBS) listings were implemented on May 01, 2023, for moderate to severe UC. These include ustekinumab (Stelara®; injection 90 mg in 1 mL pre-filled syringe, solution concentrate for IV infusion 130 mg in 26 mL), ozanimod (Zeposia®; 920 µg 28 capsules, initiation pack containing 230 µg 4 capsules and 460 µg 3 capsules), and upadacitinib (Rinvoq®; 15 mg, 30 mg, and 45 mg tablets).

https://tinyurl.com/2s3n6996

Budget 2023-24: Sixty-day dispensing of PBS medicines

The recent Federal Budget announced by the Australian government aims to improve affordability and access to vital medications, providing substantial relief to millions of Australians. Starting from September 1, 2023, eligible patients with stable, chronic health conditions, such as CD and UC, will be able to obtain a two-month supply of their prescribed medicine. These modifications in the PBS align with the recommendation made by Pharmaceutical Benefits Advisory Committee in 2018, which initially proposed extending the script refill from one month to two for over 140 medications. The recent decision builds upon that recommendation and expands it to more than 320 medicines, offering significant benefits to patients managing chronic health conditions.

Patients can expect to save up to $180 per year per medicine (for general patients) and up to $43.80 per year per medicine (for concession card holders). These savings are in addition to the reduction in the PBS co-payment for general scripts, which was implemented on January 1, 2023. Over a span of four years, this change is expected to save patients approximately $1.6 billion in out-of-pocket costs. Patients will not only benefit from reduced medication costs but will also experience savings by reducing frequent visits to pharmacies and doctors.

The implementation of this change will occur in three stages, with approximately 100 medicines involved in each stage. The first stage commences on September 1, 2023, followed by the next stage on March 1, 2024, and the final stage starting from September 1, 2024.

https://tinyurl.com/2d44p5k2

References: 1. XELJANZ (tofacitinib citrate) Approved Product Information. **2.** Sandborn WJ, *et al. New Eng J Med* 2017;376:1723–36. **3.** Taxonera C, *et al. Inflamm Bowel Dis* 2022;28(1):32–40. **4.** Sandborn WJ, *et al. J Crohns Colitis* 2022. doi: 10.1093/ecco-jcc/jjac141. **5.** Sandborn WJ, *et al. Aliment Pharmacol Ther* 2022;55(4): 464–478. **6.** Hanauer S, *et al. Clin Gastroenterol Hepatol* 2019;17:139–147.

News in Brief

Updated guideline on use of probiotics and prebiotics

The World Gastroenterology Organisation and the International Scientific Association for Probiotics and Prebiotics have jointly published an updated guideline on the clinical applications of probiotics and prebiotics. The guideline provides evidence-based recommendations for the use of probiotics and prebiotics in various gastrointestinal conditions, including IBD, helping health care providers choose appropriate interventions to match patient needs.

https://tinyurl.com/294vd2my

Optimising maternal and neonatal outcomes through remote monitoring IBD during pregnancy

A recent study demonstrated the feasibility of remote monitoring using a home point-of-care faecal calprotectin test (IBDoc) and a self-reported clinical disease activity program (IBD Dashboard) in pregnant patients with IBD. Most patients completed the monitoring at all time points and preferred the home kit over lab-based testing. Discordance was found between clinical and objective disease activity measures, suggesting that a combination of both may improve disease activity prediction. Although tight control with remote monitoring shows promise, further work is required to thoroughly assess its impact on the care and management of pregnant individuals with IBD.

https://tinyurl.com/43kzsvnv

Elevated risk of cervical cancer in elderly women with incident UC

A recent study investigated the association between UC and cervical cancer in South Korean women using national health insurance claims data. The incidence of cervical cancer was higher in patients with UC patients compared to the control group, particularly among elderly patients (≥60 years) with newly diagnosed UC. Regular cervical cancer screening is recommended for this population.

https://tinyurl.com/mseemtsy

Profiling the human intestinal environment under physiological conditions

A new ingestible device allows for non-invasive collection of multiple samples from different regions of the human intestinal tract during digestion. Analysis of samples from healthy individuals revealed significant differences in bacteria, phages, host proteins, and metabolites between the intestines and stool. Overall, this device has the potential to provide non-invasive profiling of the gut microbiome, proteome, and metabolome, revealing how gut microorganisms influence different physiological states and contribute to the development of various disease conditions.

https://tinyurl.com/ydef85hy

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American Gastroenterological Association

American College of Gastroenterology

European Crohn's and Colitis Organisation

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Please click on the links below for upcoming local and international cardiology meetings, workshops, and CPD.

NZSG

GESA

AGITG ASM, Christchurch, NZ, 13-16 Nov 2023

World Gastroenterology Organisation – meetings and events

COMS – conferences and meetings on gastroenterology

Research Review Publications

Gastroenterology Research Review with Dr Andrew Buckle and Associate Professor Jonathan Segal.

IBD Research Review with Associate Professor Britt Christensen, Dr Emily Wright, and Dr Rimma Goldberg

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