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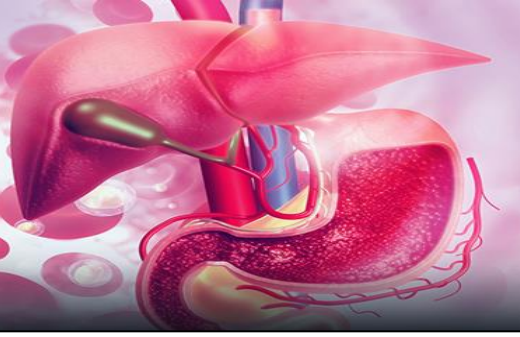

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Dear Doctor,

Greetings from Micro Labs limited. We are happy to bring you "ENTERON" which contains latest and interesting news in the field of Gastroenterology.

Inside This Issue:

Should you require any specific article or medical information, please feel free to contact us at medicalservices@microlabs.in

Looking forward to your valuable feedback

Best Regards,

Medical Team, Micro Labs Ltd

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Association of enteropathogen detection with diarrhoea by age and high versus low child mortality settings: A systematic review and meta-analysis

Introduction

The development of vaccines against enteropathogens has been identified as a public health priority to reduce the diarrhoeal disease burden. The success of such a strategy will depend on correctly identifying, and then developing vaccines against, the enteropathogens that contribute most to diarrhoeal disease mortality. A central challenge in accurately estimating burden is determining the proportion of diarrhoeal disease attributable to a particular enteropathogen. Presence of an enteropathogen in stool does not necessarily indicate the cause of diarrhoea, because enteropathogens can often be detected in the stool of healthy, asymptomatic individuals. An approach that has been adopted for ascribing cause is calculation of the odds ratio (OR) comparing the prevalence of a pathogen in stool of diarrhoeal patients versus asymptomatic controls; this gives an indication of the strength of association of the pathogen and the syndrome of diarrhoea. The ORs from individual studies have been used to parameterise attribution models that estimate the burden of disease for specific pathogens. The Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) uses a model that apportions diarrhoeal mortality based on a pathogen-specific population attributable fraction. This attributable fraction is a function of the OR quantifying the relationship between pathogen detection and the odds of having diarrhoea. However, because the studies incorporated into the GBD estimates do not always have controls, the ORs used in the calculations are derived from the Global Enteric Multicenter Study (GEMS), a study among children younger than 5 years in seven low-income and middle-income countries.

This application requires a critical assumption that the ORs from GEMS are generalizable across age groups, settings, and the range of disease outcomes for which GBD produces burden estimates. Limiting ORs to those produced by a single study—even one as rigorously conducted as GEMS—might result in incorrect assumptions about diarrhoeal disease cause, leading to inaccurate attribution of pathogen-specific burden of disease estimates, risking misguided vaccine investment and public health intervention efforts. In 2018, the Product Development

for Vaccines Advisory Committee recommended WHO establish the Burden of Enteric Disease Working Group to explore differences in modelling approaches and recent enteric disease burden estimates.

Methods:

A systematic review to identify case-control and cohort studies published from Jan 1, 1990, to July 9, 2019, which examined at least one enteropathogen of interest and the outcome diarrhoea. The analytical dataset included data extracted from published articles and supplemented with data from the Global Enteric Multicenter Study and the Malnutrition and Enteric Disease study. Random effects meta-analysis models were fit for each enteropathogen, stratified by age group and child mortality level, and adjusted for pathogen detection method and study design to produce summary ORs describing the association between pathogen detection in stool and diarrhoea.

Results:

1964 records were screened and 130 studies (over 88 079 cases or diarrhoea samples and 135 755 controls or non-diarrhoea samples) were available for analysis. Heterogeneity (I^2) in unadjusted models was substantial, ranging from 27·6% to 86·6% across pathogens.

Unadjusted and adjusted random effects meta-analysis model results by pathogen

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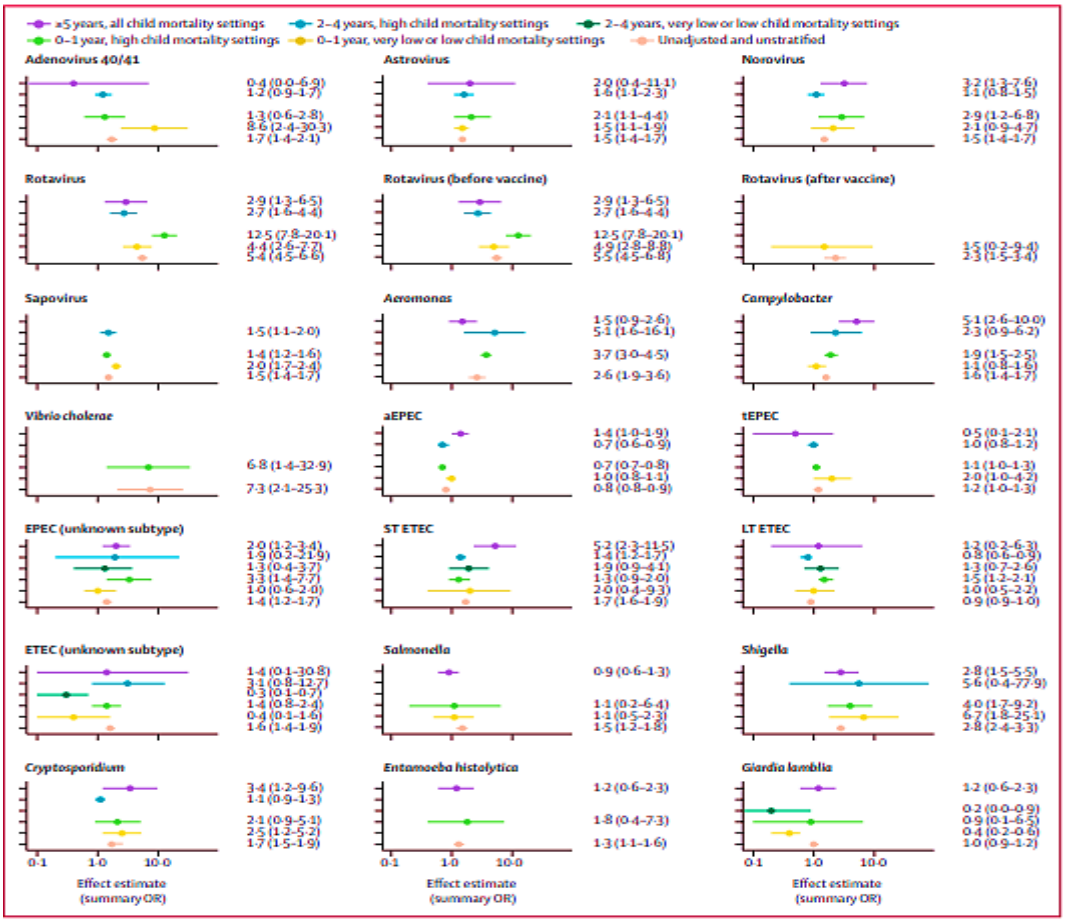

In stratified and adjusted models, summary ORs varied by age group and setting, ranging from 0·4 (95% CI 0·2–0·6) for Giardia lamblia to 54·1 (95% CI 7·4–393·5) for Vibrio cholera.

Conclusion

Incorporating effect estimates from diverse data sources into diarrhoeal disease cause and burden of disease models is needed to produce more representative estimates.

Source: Baker JM, et al. Association of enteropathogen detection with diarrhoea by age and high versus low child mortality settings: a systematic review and meta-analysis. Lancet Glob Health 2021; 9: e1402–10

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IgG4-related disease as a rare cause of gastric outlet obstruction: a case report and literature review

Background

IgG4-related disease (IgG4-RD) is a systemic inflammatory disorder characterized by abundant infiltration of IgG4-positive plasma cells in the affected organs. The liver, biliary system and pancreas are the most commonly affected organs. The most common form of undiagnosed IgG4-RD leading to a Whipple resection is type 1 autoimmune pancreatitis, which may present as a mass lesion mimicking pancreatic ductal carcinoma clinically. IgG4-RD involvement of the digestive tract is very rare. To date, only a few cases of isolated gastric/duodenal IgG4-RD have been reported, none of which resulted in luminal obstruction. Because IgG4-RD can mimic various disorders, correlation between clinical, pathological and radiological findings is often required to establish the diagnosis. In terms of treatment, immunosuppression remains the cornerstone of management, especially in symptomatic patients, with surgery reserved for highly fibrotic lesions unresponsive to medical therapy.

Case presentation

A 59 year old female with a past medical history of Guillain-Barré syndrome and previous gastric ulcer on multiple medications including naproxen 500 mg and omeprazole 20 mg daily presented with longstanding abdominal pain and progressive postprandial nausea, vomiting and weight loss over 6 months' period. CT showed mural thickening of the proximal duodenum.

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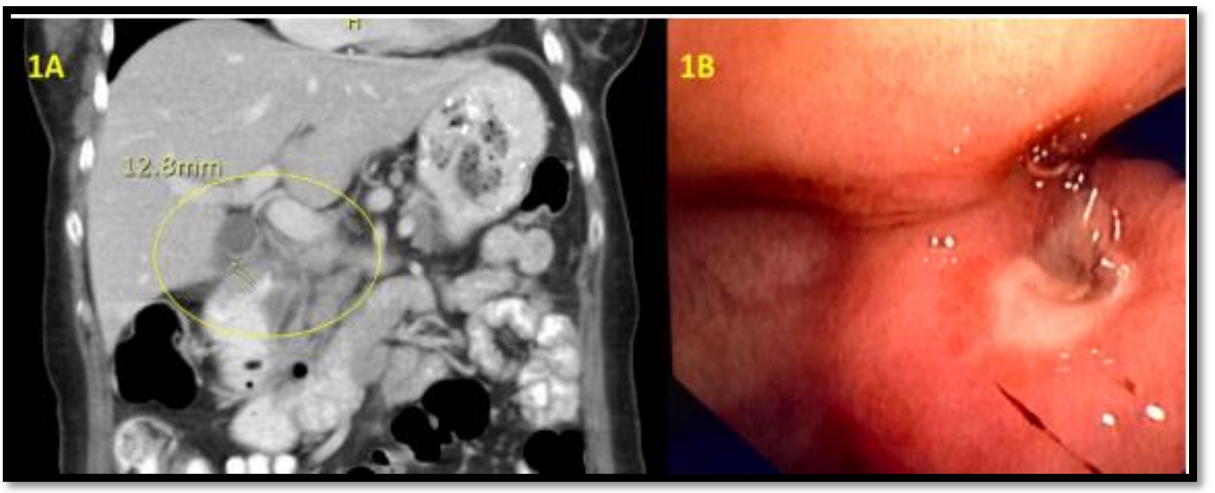
Preoperative CT showed mural thickening of the proximal duodenum



The patient received gastroscopy on multiple occasions, the most recent gastroscopy showed a clean based antral ulcer extending into the duodenum with severe obstructing duodenal stricture that impeded the ability to pass an adult size gastroscope. Biopsy of the duodenal stricture showed acute on chronic duodenitis with gastric biopsies negative for helicobacter pylori infection. Initially, peptic ulcer disease was thought to be the etiology. However, malignancy could not be ruled out, and surgical management with Whipple's procedure was therefore pursued. Gross examination of the resected specimen revealed a large ulcerated mass (2.5×1.2×1.0 cm) involving stomach and duodenal wall.

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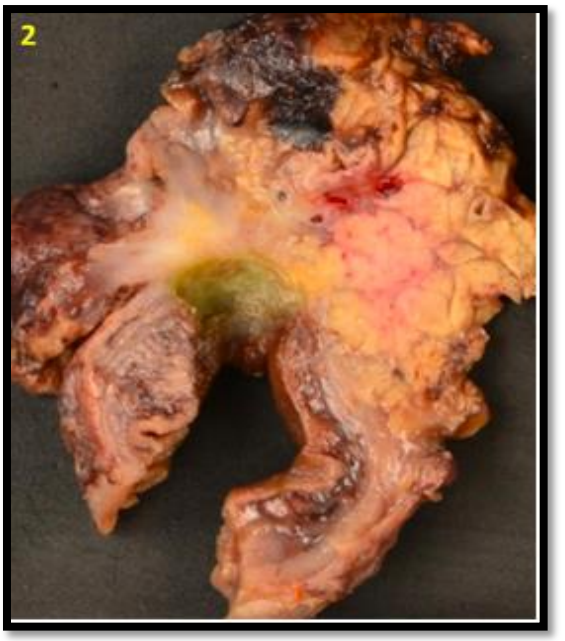
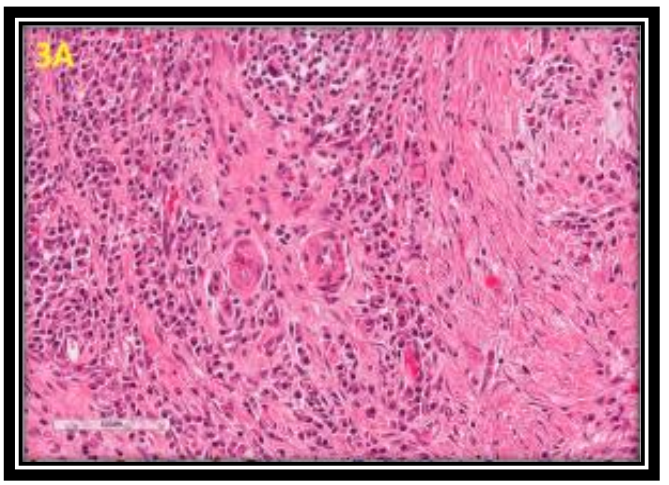
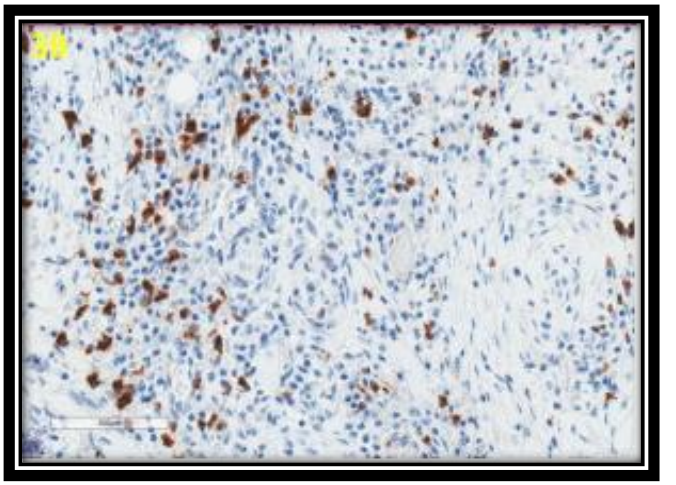
Gross examination of the resected Whipple specimen revealed a large ulcerated mass involving stomach and duodenal wall

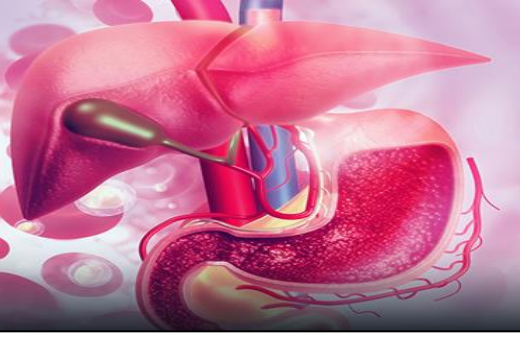


Microscopically, sections showed a duodenal ulcer and associated underlying extensive sclerosing fbrosis and lymphoplasmacytic infammation involving the duodenal wall and extending into the adjacent pancreas.

Extensive sclerosing fibrosis and lymphoplasmacytic inflammation







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There was no malignancy or dysplasia present. IgG4 stain demonstrates up to 50 IgG4 positive cells per high power field. Postoperatively, the patient developed an anastomotic leak that was managed conservatively with antibiotics and drainage resulting in significant symptomatic improvement. MRCP did not show any pancreatic or biliary abnormalities. A few weeks later, she represented with abdominal pain, nausea and vomiting, with trivially elevated serum IgG4 at 0.965 g/L (0.039–0.864 g/L). CT scan revealed inflammatory changes at the anastomosis site with severe duodenal thickening. Therefore, upper endoscopy was repeated; which showed very subtle perianastomotic erosions and erythema, and a patent small bowel with non-diagnostic random biopsies. These changes likely represented recurrent IgG4-RD. To induce remission, prednisone was started (1 mg/kg, then 40 mg), with symptom resolution within two weeks, and marked improvement of the perianastomotic changes on follow up imaging. Subsequently, she was started on mycophenolate mofetil 500 mg with a slow prednisone taper, with no recurrence at 3 months. Retrospectively, the patient's pre-operative duodenal biopsy was reviewed and IgG4 stain was performed. In addition to the chronic and active duodenitis reported initially, there was ulceration with submucosal fibrosis and inflammation. IgG4 positive cell counts were 27/ HPF.

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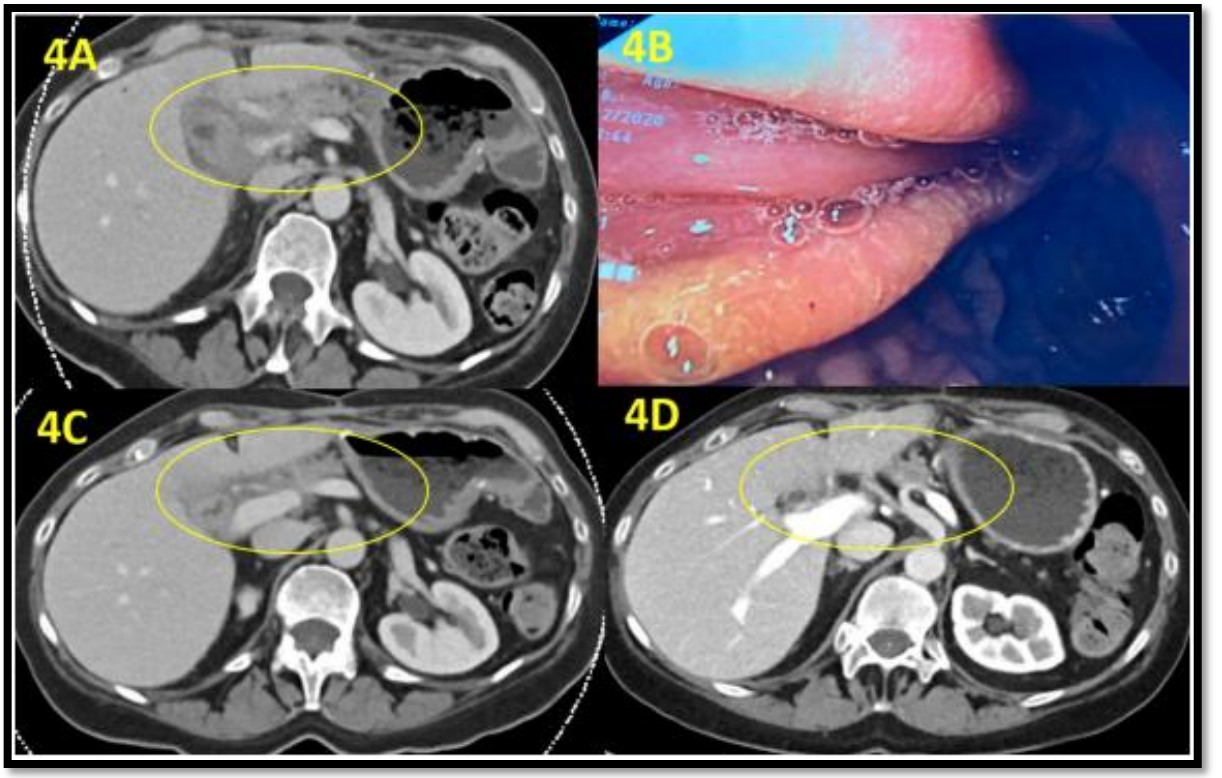
Postoperatively, CT scan revealed infammatory changes at the anastomosis site with severe duodenal thickening, representing recurrent IgG4-RD



Conclusions:

The only reported case with gastric outlet obstruction secondary to gastroduodenal IgG4- related disease. The diagnosis should be considered in the differential diagnosis of unexplained duodenal stricture, gastric outlet obstruction or gastrointestinal ulceration. IgG4-related disease usually responds to steroids but long term response rates to steroid-sparing agents, especially in the subset of patients with luminal IgG4-related disease remains to be determined.

Source: Chen et al. IgG4-related disease as a rare cause of gastric outlet obstruction: a case report and literature review. BMC Gastroenterol (2021) 21:349.

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Increased incidence of inflammatory bowel disease on etanercept in juvenile idiopathic arthritis regardless of concomitant methotrexate use

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most frequent chronic rheumatic disease in childhood with a reported prevalence varying from 16-150 per 100,000 children. As per International League of Associations for Rheumatology (ILAR) criteria, 7 mutually exclusive categories of JIA with distinct clinical features can be identified. Treatment of JIA is mainly targeted towards reducing disease activity and commonly used drugs are nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, conventional synthetic disease-modifying anti-rheumatic drugs (cs-DMARDs) and biologic DMARDs. A rare comorbidity in JIA is represented by inflammatory bowel disease (IBD), a chronic inflammatory condition of the gastrointestinal tract which comprises ulcerative colitis, Crohn's disease and indeterminate colitis. Entheropathic arthritis may also present as an extraintestinal manifestation prior to gastrointestinal symptoms in IBD. Reported prevalence of IBD in Western countries varies up to 200 per 100.000 children. It is known that IBD has a significant negative impact on quality of life besides complicating the therapeutic approach to JIA. Due to sparse data, there is currently limited knowledge about the characteristics of JIA patients who develop IBD and risk factors for its development.

Aim: To describe characteristics of JIA patients who develop IBD in comparison to those who did not, determine predictors for the development of IBD and establish a possible association between drug therapy and IBD.

Methods: JIA patients who developed IBD were identified from the international Pharma child register. Characteristics were compared between IBD and non-IBD patients and predictors of IBD were determined using multivariable logistic regression analysis. Incidence rates of IBD events on different disease-modifying anti-rheumatic drugs (DMARDs) were calculated, differences between therapies were expressed as relative risks (RR).

Results: Out of 8,942 patients, 48 (0.05%) developed IBD. These were more often male (47.9% versus 32.0%) and HLA-B27 positive (38.2% versus 21.0%) and older at JIA onset (median 8.94 versus 5.33 years) than patients without IBD development.

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Risk factors for IBD on multivariable logistic regression analysis

Variable	OR	95% CI
Female	0.70	0.33 – 1.48
Family history of autoimmune disease(s)[1]	2.27	1.12 – 4.54*
Age at JIA onset	1.05	0.96 – 1.15
Enthesitis-related JIA	3.68	1.41 – 9.40*
HLA-B27 positive	0.81	0.33 – 2.02

They also had more often a family history of autoimmune disease (42.6% versus 24.4%) and enthesitis - related arthritis (ERA) (39.6% versus 10.8%). The strongest predictors of IBD on multivariable analysis were ERA (OR: 3.68, 95% CI: 1.41 – 9.40) and a family history of autoimmune disease (OR: 2.27, 95% CI: 1.12 – 4.54).

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Incidence rates of IBD events with available onset date on drug therapy

	All patients (n = 8,921)			ERA patients (n = 967)		
Drug therapy[1]	**% (n) of IBD events (n = 27)[2]**	**Incidence rate[3] (95% CI)**	**RR (95% CI)**	**% (n) of IBD events (n = 9)[4]**	**Incidence rate[3] (95% CI)**	**RR (95% CI)**
Synthetic DMARDs						
MTX mono	11.1% (3)	0.02 (0.00 – 0.06)	Reference	22.2% (2)	0.22 (0.03 – 0.79)	Reference
Sulfasalazine	3.7% (1)	0.07 (0.00 – 0.41)	3.68 (0.38 – 35.40)	11.1% (1)	0.15 (0.00 – 0.83)	0.68 (0.06 – 7.51)
Leflunomide	3.7% (1)	0.14 (0.00 - 0.78)	6.96 (0.72 – 66.87)	0.0% (0)	-	-
Biological DMARDs						
ETN mono	25.9% (7)	0.15 (0.06 – 0.32)	7.69 (1.99 – 29.74)*	33.3% (3)	0.67 (0.14 – 1.97)	3.07 (0.51 – 18.37)
ETN + MTX	22.2% (6)	0.11 (0.04 – 0.25)	5.70 (1.42 – 22.77)*	11.1% (1)	0.27 (0.01 – 1.51)	1.24 (0.11 – 13.66)
Infliximab	7.4% (2)	0.15 (0.02 – 0.55)	7.61 (1.27 – 45.57)*	11.1% (1)	0.53 (0.01 – 2.98)	2.44 (0.22 – 26.89)
Adalimumab	3.7% (1)	0.03 (0.00 – 0.16)	1.45 (0.15 – 13.89)	0.0% (0)	-	-

Compared to methotrexate monotherapy, the incidence of IBD on etanercept monotherapy (RR: 7.69, 95% CI: 1.99 – 29.74), etanercept with methotrexate (RR: 5.70, 95% CI: 1.42 – 22.77) and infliximab (RR: 7.61, 95% CI: 1.27 – 45.57) therapy was significantly higher. Incidence on adalimumab was not significantly different (RR: 1.45, 95% CI: 0.15 – 13.89).

Conclusion: IBD in JIA was associated with ERA and a family history of autoimmune disease. An increased IBD incidence was observed for etanercept therapy regardless of concomitant methotrexate use.

Source: Panaviene V, et al. Paediatric Rheumatology International Trials Organisation (PRINTO). Increased incidence of inflammatory bowel disease on etanercept in juvenile idiopathic arthritis regardless of concomitant methotrexate use. Rheumatology (Oxford). 2021 Sep 11:keab678.

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