**Paediatric inflammatory bowel disease- improving early diagnosis**

*Editorial on: Diagnostic delay in Canadian children with inflammatory bowel disease is more common in Crohn’s disease and associated with decreased height*

James J Ashton1,2, Anthony Harnden3, R Mark Beattie1

1. Department of Paediatric Gastroenterology, Southampton Children’s Hospital, Southampton, UK
2. Department of Human Genetics and Genomics, University of Southampton, Southampton, UK
3. Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford

Correspondence to-

Professor R Mark Beattie

Department of Paediatric Gastroenterology,

Southampton Children’s Hospital,

University Hospitals Southampton

Tremona Road

Southampton

SO16 6YD

UK

Mark.beattie@uhs.nhs.uk

The authors declared no conflicts of interest

**Word count 1166**

For many conditions delayed diagnosis results in worse outcomes, increased mortality and amplified disease burden. In children an emphasis on rapid, accurate diagnosis in leukaemia, lymphoma and solid tumours has been associated with an increasing survival rate and reduced morbidity over the last 25 years. The challenge is to extend early diagnosis to chronic conditions in children where early intervention will improve long term outcomes. Similarly in adult patients, rapid access clinics for specific conditions are now routine, enabling quick referral to the specialist care service to make the precise diagnosis and start the correct treatment.

In their paper *Riccuito et al* report diagnostic delay and subsequent impact on outcome in Canadian children with inflammatory bowel disease (IBD)[1].

IBD, consisting of Crohn’s disease, ulcerative colitis and IBD unclassified, is a chronic, heterogeneous, relapsing and remitting condition primarily as a consequence of inflammation within the bowel lumen. The early and effective treatment is crucial to control symptoms, minimise impact on nutrition and growth and enable the child to function well (e.g. attend school). Over the last 20 years there has been a steady increase in the incidence of PIBD, with a consequent increase in children presenting to primary, secondary and tertiary care [2]. Paediatric gastroenterologists have been concerned for over 25 years that diagnostic delay is common. This delay is clearly multifactorial and to determine how best to effect change would require an analysis of all aspects of the patient pathway.

*Riccuito et al* gathered data on 111 patients over a 2 year period. The median time from symptom onset to diagnosis was 4.5 months (IQR 2.1-8.8) for IBD; 6.8 months (IQR 2.9-12.5) for Crohn’s disease[1]. The diagnostic process for PIBD in the Canadian healthcare system is similar to the United Kingdom, with patients requiring referral to a specialist paediatric gastroenterologist for a diagnostic endoscopy. The authors analysed the time interval between symptoms and diagnosis through the relative contribution of different components of the wait (symptoms to referral to a paediatric gastroenterologist, referral to consultation, consultation to diagnostic endoscopy). The findings indicate that the greatest time was from onset of symptoms to referral to specialist services (89 days, IQR 48-250), with the interval between referral to specialist services and diagnosis making up a minority of the time (15 days, IQR 7-45)[1]. Perhaps the most concerning finding was that 20% of patients were waiting over a year from symptoms to diagnosis[1]. The results need cautious interpretation. It is not surprising that once the referral to a paediatric gastroenterologist has been made there is a prompt diagnosis as the very reason that these patients have been referred is due to symptoms (and basic investigations) indicating that IBD is a possible, if not probable diagnosis. What is not reported in this study however is the median duration between onset of symptoms and children presenting to their primary care physician. It is possible that many children will hide their symptoms for weeks or months due to embarrassment or anxiety and this is likely to contribute to a delay in presentation to primary care. A problem facing those that work in primary care is that abdominal pain and non-specific gastrointestinal symptoms are common presentations and IBD relatively rare. An awareness of ‘red flags’ for IBD in children (see table 1) can be helpful in deciding which children require referral to specialist care.

The most common symptoms of IBD are diarrhoea, abdominal pain, blood in stools and weight loss[3]. There are an additional group of patients who present with less typical features such as isolated perianal disease, isolated growth failure or extra-intestinal manifestations (such as arthopathy etc.)[3]. *Riccuito et al* analysed features associated with a delay in diagnosis. In univariate analysis diarrhoea (OR 0.29), blood per rectum (OR 0.33), bloody diarrhoea (OR 0.25) and weight loss (OR 0.38) were all significantly associated with decreased risk of a diagnostic delay, reflecting the most common symptoms seen in practice[1]. The authors did not find any association between age, gender, socio-economic background or, interestingly, a family history of IBD. Previous work has pointed to younger age being a risk factor for a longer delay in diagnosis but this was not observed in this study[3]. Height impairment was significantly more common in those with delayed diagnosis (height-for-age z-score -0.5) vs non-delayed diagnosis (height-for-age z-score 0.1) and this deficit persisted to 1 year follow-up. These observations demonstrate a measurable and negative impact on the children with a diagnostic delay, although confounding factors (such as disease severity) must be accounted for [1].

The data from *Riccuito et al* highlights the crucial role a primary care physician has in assessing children with gut symptoms and selecting those to refer on for further assessment or investigation. However there is no ‘fast track’ referral process even when red flags are present (table 1). Faecal Calprotectin may be helpful and now has an established place in stratifying the need for diagnostic endoscopy in symptomatic patients and in the ongoing monitoring of IBD[4].

Faecal calprotectin is a protein produced by inflammatory cells within the gastrointestinal tract, with a very high sensitivity for detection of PIBD, 0.92 (95% CI 0.84 to 0.96)[5]. It is raised in intestinal inflammation but also in gastrointestinal infection and coeliac disease. Calprotectin is stable for up to one week and is widely available in primary and secondary care. The major downsides are the relatively poor specificity in children, 0.76 (95% CI 0.62 to 0.86), uncertainty regarding the upper limit of normal (cut-off value for referral) and the high cost per sample[5]. Meta-analysis of available data has promoted faecal calprotectin as a screening tool for IBD. The lack of specificity can be largely discounted when calprotectin levels are very high[4]. Whilst *Riccuito et al* do not discuss faecal calprotectin, the key message from the authors of trying to minimise delay in non-specialised services suggest a role for a rapid screening tool. Implementation would potentially enable fast-track referral to a paediatric gastroenterologist and a quicker diagnosis. A major challenge of implementation of such a system would be the cut-off value for faecal calprotectin. Table 2 shows that specificity and sensitivity are altered significantly by varying the ‘normal’ cut-off value for faecal calprotectin. The likelihood of having a diagnosis of IBD with a faecal calprotectin of greater than 50 is only 62% whereas values above 800 indicate that 93% of patients will have a diagnosis of IBD[4]. A consensus value needs to be reached a trigger for a fast-track referral.

Significant delay in diagnosis for children with IBD, and subsequent impact on growth is unacceptable. Whilst the authors report the longest time delay appears to lie in prior to referral to specialist services there is undoubtedly a need to improve education and awareness, enable better communication between primary and specialist care and to develop a fast-track, direct, referral system for children at high risk. As incidence of PIBD increases the challenge to all those involved in the care of these children is to provide a rapid, precise diagnosis enabling effective, prompt and holistic treatment.

Table 1

Summary of red flag symptoms, signs and investigations for PIBD[3].

|  |  |
| --- | --- |
| **Symptoms** | * Loose stools (diarrhoea) for > 14 days without another cause (such as recent travel)
* Bloody diarrhoea or blood per rectum
* Weight loss (Crohn’s disease only)
* Abdominal pain >14 days without another cause (consider functional abdominal pain)
 |
| **Signs** | * Perianal disease (fistulae, fissures and skin tags)
* Frequent severe mouth ulcers (Crohn’s disease only)
* Extra-intestinal manifestations (arthopathy, uveitis, erythema nodosum)
 |
| **Investigations** | * Negative stool microscopy and culture
* High inflammatory markers (CRP + ESR)
* Low albumin
* Deranged liver function
* High platelet count
* Low haemoglobin (especially in ulcerative colitis)
* Positive family history of IBD (of any type)
 |

Table 2

Measures of diagnostic accuracy for increasing concentration of faecal calprotectin in children with suspected inflammatory bowel disease. Data adapted from Henderson et al[4].

|  |  |  |
| --- | --- | --- |
| **Faecal calprotectin cut-off (µg/g)** | **Sensitivity**  | **Specificity** |
| **>50** | 0.98  | 0.44  |
| **>100** | 0.97  | 0.59  |
| **>200** | 0.93  | 0.74  |
| **>800** | 0.73  | 0.95  |

References

1 Ricciuto A, Fish JR, Tomalty DE, *et al.* Diagnostic delay in Canadian children with inflammatory bowel disease is more common in Crohn’s disease and associated with decreased height. *Arch Dis Child* 2017;:archdischild-2017-313060. doi:10.1136/archdischild-2017-313060

2 Ashton JJ, Wiskin AE, Ennis S, *et al.* Rising incidence of paediatric inflammatory bowel disease (PIBD) in Wessex, Southern England. *Arch Dis Child* 2014;**99**:659–64. doi:10.1136/archdischild-2013-305419

3 Ashton JJ, Ennis S, Beattie RM. Early-onset paediatric inflammatory bowel disease. *Lancet Child Adolesc Heal* 2017;**1**:147–58. doi:10.1016/S2352-4642(17)30017-2

4 Henderson P, Anderson NH, Wilson DC. The diagnostic accuracy of fecal calprotectin during the investigation of suspected pediatric inflammatory bowel disease: a systematic review and meta-analysis. *Am J Gastroenterol* 2014;**109**:637–45. doi:10.1038/ajg.2013.131

5 van Rheenen PF, Van de Vijver E, Fidler V. Faecal calprotectin for screening of patients with suspected inflammatory bowel disease: diagnostic meta-analysis. *BMJ* 2010;**341**:c3369. doi:10.1136/bmj.c3369