ORIGINAL ARTICLE

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Evolution of diagnostic delay in pediatric inflammatory bowel disease and the Impact of the COVID-19 pandemic

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ABSTRACT – Background – Pediatric inflammatory bowel disease (IBD) is increasingly prevalent, but diagnosis can still be challenging. Diagnostic delay is particularly deleterious in this age group. **Objective** – This study explores the evolution of diagnostic delay in pediatric IBD and the influence of the COVID-19 pandemic. **Methods** – Retrospective study including all pediatric IBD patients diagnosed during 2014, 2019 and 2020 in a tertiary hospital. Diagnostic delay, time to first medical visit, time to pediatric gastroenterologist (PG) visit and time to diagnosis were calculated and compared within a gap of five years (2019 and 2014) and with the year of onset of the pandemic (2020 and 2019). **Results** – A total of 93 participants were included (2014: 32, 2019: 30, 2020: 31). No significant differences were observed in diagnostic delay, time to first medical visit in Crohn's disease (CD), time to PG visit and time to diagnosis when comparing 2019-2014 and 2020–2019. Time to first visit in ulcerative colitis (UC) and Undetermined-IBD increased in 2019 (P=0.03), with new decrease in 2020 (P=0.04). Diagnostic delay was longer in DC compared to UC plus Undetermined-IBD. **Conclusion** – Diagnostic delay is still an important matter in pediatric IBD, with no significant change over the last years. The time to the first PG visit and the time for diagnosis seem to have the greatest impact on diagnostic delay. Thus, strategies to enhance recognition of IBD symptoms among first-line physicians and to improve communication, facilitating referral, are of utmost importance. Despite the restraints in the health care system caused by the pandemic, time to diagnosis in pediatric IBD was not impaired during 2020 in our center.

Keywords – Inflammatory bowel disease; diagnostic delay; COVID-19; pediatric.

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INTRODUCTION

Pediatric inflammatory bowel disease (IBD) is increasingly prevalent worldwide, reaching an incidence in Europe of up to 9–10 per 100 000 population for Crohn's disease (CD) and slightly lower incidences for ulcerative colitis (UC)[1,2].

The diagnosis of IBD continues to be challenging. Not only can IBD manifest with a multitude of intestinal and extraintestinal symptoms, that can present insidiously or in a fulminant way, but also there is no gold-standard technique for diagnosis. A high index of clinical suspicion and the correct conjugation and interpretation of complementary tests is vital for accurate and prompt diagnosis[3].

Diagnostic delay in pediatric IBD is particularly important, as it leads to increased risk of complications, loss of opportunity to recover optimal growth, and a negative impact on overall psychosocial and physical development[4].

To identify the causes behind diagnostic delay that can be subject to modification strategies, Martín-de-Carpi et al. defined three-time intervals till diagnosis. The first interval is the time from the first symptom to the first medical visit, which is essentially dependent on the recognition of symptoms and search for medical help by the patient and caregivers. The second interval follows the time from the first medical visit to the first Pediatric Gastroenterologist (PG) appointment, which can be compromised by a lack of clinical suspicion and attribution of symptoms to more frequent disorders, such as infectious diseases. The last interval is the time from the first PG visit to the diagnosis, dictated mainly by the availability of resources[5].

Several studies have been published until the moment describing diagnostic delay in adult and pediatric IBD, but none has focused on its evolution over time. The present study aims to explore the evolution of the diagnostic delay in pediatric IBD in a tertiary center and to understand if it was influenced by the COVID-19 pandemic.

METHODS

This was a retrospective study conducted in a tertiary hospital in Porto, Portugal. All pediatric patients diagnosed with IBD in our center during 2014, 2019 and 2020 were included. Diagnosis of IBD was made according to the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Revised Porto Criteria[3].

The following variables regarding demographic and clinical characteristics were collected from medical records: age at diagnosis, gender, family history of IBD, date of first IBD-related symptoms, date of first medical visit for IBD-related symptoms, date of first PG visit, date of diagnosis, symptoms at diagnosis, complementary investigation performed before PG visit, disease extent at diagnosis and results from the complementary investigation at presentation in our center.

Diagnostic delay (time from first IBD symptom to IBD diagnosis) and the different time intervals as described by Martín-de-Carpi et al.[5]- time to first medical visit (from first IBD symptom to first medical visit), time to PG visit (from first medical visit to first PG visit) and time to diagnosis (from first PG visit to IBD diagnosis) - were calculated and are expressed as median plus interquartile ranges.

To understand the evolution of diagnostic delay in our center, the different timings were compared within a gap of five years (2019 and 2014). In addition, a comparison between the years 2020 and 2019 was performed, the former marked by the COVID-19 pandemic, which began in Portugal in March 2020, to understand the impact of the pandemic on diagnostic delay.

Although our PG unit remained open and kept the same human resources throughout 2020, multiple restrictions had to be implemented as advised by the Portuguese Directorate-General for Health (DGS) and ESPGHAN. Also, some hospital facilities had to be restructured to accommodate the needs imposed by the pandemic. As a result, our endoscopic procedure room was temporarily moved, and the time dedicated to procedures was reduced from twice to once a week. Elective upper endoscopies and colonoscopies were suspended between mid-March and April. After that, they were resumed, but it was still mandatory to have a negative PCR for SARS-CoV-2 or a valid recovery certificate. Urgent and emergent procedures were performed the entire time without delays. At all times, health professionals wear the

recommended personal protective equipment. The telemedicine system was implemented from mid-March until the end of April. First consultations with patients referred by the emergency department or primary care services continued to take place according to their priority through telemedicine. From May on, face-to-face appointments were resumed slowly as many patients and their families were still afraid of coming to the hospital and would rather have telephonic appointments. At this point, all patients with worrisome symptoms had face-to-face consultations. Contact with our team through email or phone was facilitated to clarify doubts from our IBD patients and their families.

Statistical analysis was performed using SPSS Statistics v.23.0 (SPSS Inc, Chicago, IL, USA) and a level of significance of $P<0.05$ was assumed. Normality tests were performed and, since time intervals had a non-Gaussian distribution, the non-parametric test of Mann-Whitney U was used.

The study was approved by the Ethical Committee of our institution. All information is anonymous and confidential.

RESULTS

While the number of consultations and endoscopic procedures did not change significantly between 2014 and 2019, in 2020, there was an important reduction, with nearly half of upper endoscopies and colonoscopies being performed (TABLE 1).

TABLE 1. Outpatient's flow and endoscopic diagnostic procedures performed in our Pediatric Gastroenterology Unit during 2014, 2019 and 2020.

Year	2014	2019	2020
Outpatient's flow			
First consultations	653	752	628
Subsequent consultations	3018	3116	2837
Endoscopic procedures			
Upper endoscopy	425	444	222
Colonoscopy	62	77	43
Capsule endoscopy	9	19	13

A total of 93 participants with IBD were included in our study, 32 diagnosed in 2014, 30 diagnosed in 2019, and 31 diagnosed in 2020. Demographic characteristics, symptoms at presentation and investigation prior to PG visit are summarized in TABLE 2. Disease extension and results from complementary tests at diagnosis are presented in TABLE 3.

Samples across 2014, 2019, and 2020 were similar concerning the main symptoms at presentation in CD, which were abdominal pain, diarrhea, and involuntary weight loss (TABLE 2). In the case of UC and Undetermined-IBD, bloody stools were the main complaint, present in 100% of the patients in 2020. Diarrhea was the second most frequent symptom in 2014 and 2020, while in 2019 abdominal pain was more frequent.

Blood tests were the most common diagnostic tool performed before PG referral (TABLE 2). Of note, fecal calprotectin requests had a more than twofold increase in 2019 compared with 2014, accompanied by a decrease in stool bacteriology and parasitology requests. In 2020, it was observed a slight reduction in all complementary tests requested, except for stool bacteriology and parasitology.

CD remained the most prevalent form of IBD over the years, often with ileocolic involvement and inflammatory behavior (TABLE 3). UC and Undetermined-IBD had mainly left side or extensive involvement.

Results from the complementary investigation at disease presentation showed consistent elevation of the fecal calprotectin, which reached 100% in 2020, and the inflammatory markers (C-reactive protein and erythrocyte sedimentation rate). Also, anemia was frequently present.

No significant difference was observed in diagnostic delay, time to PG visit, time to first medical visit in CD, and time to diagnosis over the 5 years and in the first year of the pandemic (TABLE 4 and 5). Time to first visit in UC and Undetermined-IBD increased in 2019 ($P=0.03$), followed by a decrease in 2020 ($P=0.04$). Diagnostic delay was longer in DC compared to UC plus undetermined-IBD (FIGURE 1).

DISCUSSION

Diagnostic delay remains a concern in pediatric IBD, despite growing experience in its approach and increasing availability of diagnostic techniques over the last decades.

TABLE 2. Demographic characteristics, symptoms at presentation and complementary investigation prior to PG referral of IBD pediatric patients diagnosed in our center during 2014, 2019 and 2020.

Year of diagnosis	2014 (n=32)	2019 (n=30)	2020 (n=31)
Age at diagnosis (median and range, years)	14 (3–17)	15 (0–18)	15 (1–17)
Positive family history of IBD	21.9%	23.3%	16.1%
Symptoms at diagnosis			
Crohn's disease	71.9% (n=23)	66.7% (n=20)	54.8% (n=17)
Abdominal pain	73.9%	80.0%	82.4%
Diarrhea	65.2%	65.0%	70.6%
Bloody stools	39.1%	30.0%	35.3%
Involuntary weight loss	91.3%	70.0%	70.6%
Constitutional symptoms (anorexia, asthenia, fever)	47.8%	45.0%	70.6%
Growth failure and/or pubertal delay	6.3%	6.7%	–
Recurrent oral aphthous ulcers	8.7%	5.0%	29.4%
Perianal manifestations	43.5%	25.0%	23.5%
Other manifestations (ocular, articular, dermatologic)	30.4%	15.0%	23.5%
Ulcerative colitis plus undetermined-IBD	28.1% (n=9)	33.3% (n=10)	45.2% (n=14)
Abdominal pain	55.6%	70.0%	71.4%
Diarrhea	66.7%	40.0%	92.9%
Bloody stools	88.9%	90.0%	100.0%
Involuntary weight loss	44.4%	30.0%	28.6%
Constitutional symptoms (anorexia, asthenia, fever)	11.1%	60.0%	35.7%
Recurrent oral aphthous ulcers	11.1%	10.0%	–
Other manifestations (articular, dermatologic)	11.1%	10.0%	7.1%
Complementary investigation prior to PG visit			
Blood tests	68.8%	86.7%	74.2%
Abdominal ultrasound	31.3%	50.0%	25.8%
Stool bacteriology and/or parasitology	34.4%	13.3%	38.7%
Fecal calprotectin	18.8%	46.7%	29.0%
Other	37.5%	46.7%	35.5%

IBD: inflammatory bowel disease; PG: pediatric gastroenterologist.

TABLE 3. IBD extension and complementary investigation at presentation of IBD pediatric patients diagnosed in our center during 2014, 2019 and 2020.

Year of diagnosis	2014 (n=32)	2019 (n=30)	2020 (n=31)
Disease extension			
Crohn's disease	71.9% (n=23)	66.7% (n=20)	54.8% (n=17)
Ileum only (L1)	21.7%	35.0%	35.3%
Colon only (L2)	13.0%	15.0%	11.8%
Ileocolic (L3)	65.2%	50.0%	52.9%
Concomitant upper gastrointestinal disease (L4)	47.8%	25.0%	35.3%
Inflammatory (B1)	82.7%	100.0%	100.0%
Stricturing (B2)	13.0%	–	–
Penetrating (B3)	4.3%	–	–
Ulcerative colitis plus undetermined-IBD	28.1% (n=9)	33.3% (n=10)	45.2% (n= 14)
Proctitis (E1)	33.3%	10.0%	7.1%
Left-sided disease (E2)	22.2%	50.0%	50.0%
Extensive disease (E3)	44.4%	40.0%	42.9%
Complementary investigation at presentation			
Anemia	22/30	20/3	16/30
Thrombocytosis	16/30	6/30	12/29
C-reactive protein and/or erythrocyte sedimentation rate elevation	24/30	23/30	26/30
Fecal calprotectin elevation	20/25	28/29	30/30
Positive anti–Saccharomyces cerevisiae antibody	7/17	5/22	8/26
Positive anti-neutrophil cytoplasmic antibody	2/18	2/23	5/26

IBD: inflammatory bowel disease; PG: pediatric gastroenterologist.

TABLE 4. Comparison of time intervals to the diagnosis of IBD pediatric patients diagnosed in our center during 2014 and 2019.

Year of diagnosis	2014 (n=32)	2019 (n=30)	*P*-value
Crohn's disease			
Diagnostic delay (months)	4 (3–9)	3 (2–7)	0.55
Time to first medical visit (days)	22 (0–86)	25 (11–90)	0.76
Time to PG visit (days)	57 (23–123)	55 (7–156)	0.94
Time to diagnosis (days)	10 (4–20)	7 (2–23)	0.94
Ulcerative colitis plus undetermined-IBD			
Diagnostic delay (months)	1 (0–2)	3 (1–4)	0.07
Time to first medical visit (days)	5 (3–32)	31 (18–61)	0.03
Time to PG visit (days)	8 (3–32)	22 (1–48)	0.66
Time to diagnosis (days)	2 (0–10)	3 (0–36)	0.72

IBD: inflammatory bowel disease; PG: pediatric gastroenterologist.

TABLE 5. Comparison of time intervals to the diagnosis of IBD pediatric patients diagnosed in our center during 2019 and 2010.

Year of diagnosis	2019 (n=30)	2020 (n=31)	*P*-value
Crohn's Disease			
Diagnostic delay (months)	3 (2–7)	3 (2–6)	0.48
Time to first medical visit (days)	25 (11–90)	16 (5–67)	0.39
Time to PG visit (days)	55 (7–156)	57 (21–97)	0.91
Time to diagnosis (days)	7 (2–23)	13 (3–32)	0.52
Ulcerative colitis plus undetermined-IBD			
Diagnostic delay (months)	3 (1–4)	1 (0–2)	0.14
Time to first medical visit (days)	31 (18–61)	12 (5–33)	0.04
Time to PG visit (days)	22 (1–48)	16 (7–31)	0.98
Time to diagnosis (days)	3 (0–36)	2 (0–12)	0.75

IBD: inflammatory bowel disease; PG: pediatric gastroenterologist.

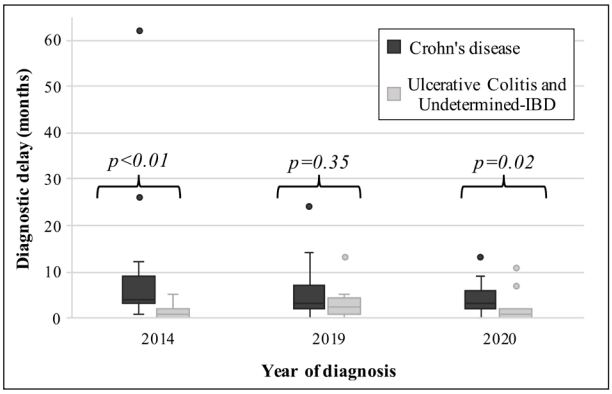

FIGURE 1. Comparison of diagnostic delay for Crohn's Disease and Ulcerative Colitis plus Undetermined-IBD in 2014, 2019 and 2020.

As shown in this study, there was no significant difference in diagnostic delay over a 5-year span. This is explained by a lack of improvement in the time intervals for diagnosis, which remained stable for the majority. The time for the first medical visit was the only time interval that seemed to fluctuate, however, with no impact in diagnostic delay, indicating that the latter might be mostly determined by the time to the first PG visit and the time for diagnosis.

The time for the first PG visit is often the longest interval. Therefore, it should be one of the main targets for strategies to reduce diagnostic delay. It is dependent on clinical suspicion and PG referral. Thus, enhancing recognition of IBD symptoms among primary care physicians and general pediatricians is fundamental, not only in the case of severe disease with alarming signs but also in cases of insidious disease.

IBD can present merely with mild clinical activity or have a significant overlap with symptoms seen in infectious diseases and functional disorders, such as irritable bowel syndrome[6,7]. It would be useful to create guidelines with decision algorithms to differentiate IBD and these more common disorders. Factors such as the absence of epidemiological context, signs of chronicity (as anemia), allied to the typical age of IBD presentation should incite further investigation. Moreover, our results showed that bloody stools are a chief complaint in UC and undetermined-IBD, present in all patients in 2020, so we believe it should always motivate additio-

nal investigation, except in the presence of severe constipation if a benign anal fissure is identified.

Improving the communication between the PG and the first-line physicians facilitating referral can also be a means to shorten the time for the first PG visit.

Fecal calprotectin can be an excellent screening tool for IBD[8], as supported by our results where all patients had an elevation of fecal calprotectin at presentation in 2020. Though requests prior to PG referral increased in 2019 compared to 2014, it was still requested in less than half of patients. An effort should be made to increase the availability of fecal calprotectin outside the hospital setting so it can aid the decision of referral in the absence of alarm signs.

Of note, the median time in our study from the first symptom to IBD diagnosis from 2014 to 2020 was 3–4 months in CD and 1–3 months in UC plus undetermined-IBD, a diagnostic delay that is already lower compared to studies published concerning, at least in part, the same period[9-11]. The longer diagnostic delay in CD compared to UC observed in our study is in agreement with the literature and can somewhat be explained by the clinical manifestations of CD that are much more variable than those of UC[6,7,9,11,12].

Due to the COVID-19 pandemic, 2020 was marked by restrictions that ultimately affected PG units. ESPGHAN recommended postponing elective procedures (upper gastrointestinal endoscopy and ileocolonoscopy)[13]. Urgent endoscopic diagnostic testing was advised to be kept at a minimum[13].

Remarkably, there was no significant increase in diagnostic delay in our study in 2020 compared to 2019, implying that there was no impairment in the quality of care provided, despite the great reduction in the number of endoscopic procedures performed during this period. Besides, the number of diagnoses per year was kept stable in spite of the constraints caused by the pandemic. This can be explained by a reduction that affected mainly elective procedures where the intent was disease monitoring, perhaps allied to a better triage of the patients with suspected IBD in need of endoscopy.

Solutions created during the pandemic and some resulting changes to working practices can likely be assimilated to our advantage in the future. For example, telemedicine can be an attractive practice in stable patients as long as email/telephone support is facilitated for patients in need. In the UK, self-monitoring of disease activity was encouraged, with home fecal calprotectin testing kits being available for selected patients, empowering patients and reducing hospital visits[14]. Moreover, judicious selection of patients needing endoscopy can reduce the time a patient with a strong suspicion of IBD is waiting for a diagnostic procedure.

Our study has some limitations. First, it includes a limited number of participants. However, they represent the total number of inaugural diagnoses in the respective years of a tertiary hospital in the second largest city of the country. Secondly, it would have been useful to extend the time span and compare the diagnostic delay with a year before 2014, but that was not possible due to the lack of available registries. Lastly, the retrospective nature of the study in some cases may have hinderer the accurate definition of the first IBD manifestations since it was difficult to understand if symptoms occurring long before the diagnosis might have been the initial complaint of IBD or were utterly unrelated to IBD.

In conclusion, diagnostic delay is still an important matter in pediatric IBD, with no significant change over the last years. Practical strategies must be defined in order to speed up the approach, facilitating recognition and referral. Though the COVID-19 pandemic was responsible for many restraints in the health care system, the time from the first symptom to diagnosis in pediatric CD, UC and Undetermined-IBD was not impaired during 2020 in our center. Solutions created during the pandemic can be an ally for the future and help improve the follow-up of IBD patients.

Authors' contribution

Manuel AR, Magalhães T, Granado MC, had a critical role in the conception and design of the study, acquiring, analyzing, and interpreting data, drafting the manuscript, and giving the final approval of the version to be published. Espinheira MC and Trindade E had a critical role in the conception and design of the study, revising the manuscript, and in the final approval of the version to be published.

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Manuel AR, Magalhães T, Granado MC, Espinheira MC, Trindade E. Evolução do atraso diagnóstico na doença inflamatória intestinal em idade pediátrica e o impacto da pandemia COVID-19. Arq Gastroenterol. 2023;60(1):91-7.

RESUMO – Contexto – Apesar da prevalência crescente da doença inflamatória intestinal (DII) em idade pediátrica, o seu diagnóstico pode ser desafiante. Um atraso no diagnóstico é particularmente deletério nesta faixa etária. **Objetivo** – Este estudo investiga a evolução do atraso diagnóstico na DII pediátrica e o impacto da pandemia COVID-19 no mesmo. **Métodos** – Estudo retrospetivo que incluiu todos os doentes em idade pediátrica diagnosticados com DII durante 2014, 2019 e 2020 num hospital terciário. O atraso diagnóstico, o tempo para a primeira visita médica, o tempo para a primeira visita ao gastroenterologista pediátrico (GP) e o tempo para o diagnóstico foram calculados e comparados num intervalo de cinco anos (2019 e 2014) e com o ano marcado pelo surgimento da pandemia COVID-19 (2020 e 2019). **Resultados** – Foram incluídos 93 participantes (2014: 32, 2019: 30, 2020: 31). Não se observou diferença significativa no atraso diagnóstico, no tempo para a primeira visita médica na doença de Crohn (DC), no tempo para a primeira visita ao GP e no tempo para o diagnóstico após comparação entre 2019-2014 e 2020-2019. Na colite ulcerosa e colite indeterminada, o tempo para a primeira visita médica aumentou em 2019 (P=0,03), com nova diminuição em 2020 (P=0,04). O atraso diagnóstico foi superior na DC comparativamente com a colite ulcerosa e colite indeterminada. **Conclusão** – O atraso diagnóstico na DII pediátrica continua a ser um tema importante, que não sofreu alteração significativa ao longo dos últimos anos. O tempo para a primeira visita ao GP e o tempo para o diagnóstico parecem ter maior impacto no atraso diagnóstico, pelo que são necessárias estratégias para aumentar o reconhecimento dos sintomas da DII entre os médicos de primeira linha, bem como melhorar a comunicação e a referenciação. Apesar das restrições causadas pela pandemia no sistema de saúde, o tempo para o diagnóstico na DII pediátrica não foi comprometido no nosso centro em 2020.

Palavras-Chave – Doença inflamatória intestinal; atraso diagnóstico; pandemia COVID-19; pediatria.

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