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Risk Factors and Impact of Diagnostic Delay in Patients with Inflammatory Bowel Disease in Bangladesh

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Abstract: Background and Aims: A delay in the diagnosis of inflammatory bowel disease (IBD) is a risk of developing complications and surgery. This study was done to evaluate the factors and impact of diagnostic delay on IBD patients in Bangladesh. Methods: This cross-sectional study was carried out in the Department of Gastroenterology of a tertiary care center in Bangladesh. Diagnostic delay was defined as the period from symptom onset to diagnosis of IBD. Results: Of the total 112 IBD patients 50 (44.6%) had Crohn's disease CD and 62 (55.4%) had ulcerative colitis (UC). Males (67.9%) were predominant in the study. The median diagnostic delay was longer for patients with CD compared with patients with UC (median 24 versus 12 months; P-value 0.025). Rectal bleeding as presenting feature and male gender were negatively and positively associated with the longer diagnostic delay of IBD respectively (P-value <0.05). Of the patients with CD 14 (28%) had a history of IBD-related surgery and 7 (14%) had a history of perianal fistula. The presence of intestinal strictures, surgery, and perianal fistula at the time of diagnosis was significantly associated with long diagnostic delay for CD. Conclusion: Absence of rectal bleeding as presenting symptoms and also the male gender were the significant factors related to the longer diagnostic delay of IBD in our study. Long diagnostic delay is associated with an increased rate of complications in IBD, especially in CD.

Keywords: Diagnostic Delay, Inflammatory Bowel Disease (IBD), Crohn's Disease (CD), Ulcerative Colitis (UC), Referral Delay

1. Introduction

Inflammatory bowel diseases (IBD), namely Crohn's disease (CD) and ulcerative colitis (UC) are a group of chronic idiopathic disorder with the relapsing and remitting course. The highest incidence and prevalence are in Western populations. However, recent studies from Asian and developing countries indicate an increasing incidence of time trends [1]. The outcome of IBD cases mostly depends on early diagnosis and timely intervention. Early initiation of immunosuppressive and/or biological agents has been reported to be associated with better outcomes [2-4]. Delay in diagnosis is associated with delayed therapy which causes continued disease activity, prolonged suffering, and complications requiring early surgery [5, 6]. The diagnosis of IBD is challenging and usually delayed due to a broad variety of presenting symptoms, which are nonspecific and misleading for gastrointestinal infections or functional disorders [7, 8]. A diagnostic delay of several months to years is common in IBD, especially in CD [9-17]. Factors associated with diagnostic delay are incompletely understood and many have conflicting results, such as young age at diagnosis, active smoking, socioeconomic factors, and ileal location [9-17]. No published data regarding the diagnostic delay in Bangladeshi IBD patients have been reported so far. Therefore, this study aimed to evaluate the diagnostic delay and its associated factors, and the impact of it on IBD patients at a tertiary care center in Bangladesh.

2. Methods

2.1. Study Population and Data Collection

It is a cross-sectional study at a tertiary care center in Bangladesh. Patients were recruited between September 2018 and September 2019. Adult IBD patients (≥18 years of age) with an established diagnosis based on clinical, endoscopic, histological, and radiological criteria according to the European Crohn's and Colitis Organization (ECCO) guidelines [18, 19] attending dedicated IBD clinic of Gastroenterology were asked to participate in the study. The data were collected prospectively using a predesigned questionnaire, which included items concerning demographic characteristics (age, gender, educational level, household income, residential area, and smoking habits, diagnostic delay and referral delay to the specialist) and IBD-related data (e.g. Disease types, Predominant presenting complaints, complications).

2.2. Definitions

Total diagnostic delay was defined as the time from the onset of symptoms related to IBD to the final diagnosis by gastroenterologists.

2.3. Statistical Analysis

The data were analyzed by using Statistical Package for Social Studies (SPSS 25; IBM Corp., New York, NY, USA). Nonparametric data were expressed as median±interquartile range (IQR) and categorical data were expressed as frequency and percentages. Spearman Rho correlation coefficient was used to see the correlation. Risk factors and the rate of complications were assessed with long (>75th percentile) diagnostic delays. A P value <0.05 was considered statistically significant.

2.4. IRB Approval

We conducted this study in compliance with the principles of the Declaration of Helsinki. The study's protocol was reviewed and approved by the Institutional Review Board of the University. Written informed consent was obtained.

3. Results

The characteristics of the study population are summarized in Table 1. A total of 112 IBD patients were enrolled from a dedicated IBD clinic. Of the patients 50 (44.6%) had CD and 62 (55.4%) had UC. The mean age was 35.43±11.87 years. Males (67.9%) were predominant in both patients with CD (78%) and UC (59.7%). Of the patients with CD 14 (28%) had a history of IBD-related surgery and 7 (14%) had a history of perianal fistula. More patients with CD were smokers than with UC (18% vs. 4.8%). Most of the patients had secondary and higher secondary level education. The majority had a household income of up to 120$ per month, nearly half of the patients lived in rural areas. Only 7 (6.3%) of IBD patients directly consulted to a gastroenterologist and 65 (58%) of IBD patients were referred to a gastroenterologist by other physicians after a median referral delay of 12 months (IQR 5.5-24 months). The referral delay was positively correlated with diagnostic delay (correlation coefficient, r=0.87).

Table 1. Characteristics of study population (n=112).

Characteristic		Disease type		Total IBD (n=112)	P-value
		CD (n=50)	UC (n=62)		
Age in years (Mean±SD)		35.08±12.78	35.71±11.18	35.43±11.87	0.782
Gender					
	Male	39 (78.0)	37 (59.7)	76 (67.9)	0.044
	Female	11 (22.0)	25 (40.3)	36 (32.1)	
Residence					
	Rural	20 (40.0)	33 (53.2)	53 (47.3)	
	Urban	13 (26.0)	13 (21.0)	26 (23.2)	0.376
	Semi-urban	17 (34.0)	16 (25.8)	33 (29.5)	
Educational level					
	Primary and below	12 (24.0)	16 (25.8)	28 (25.0)	
	Secondary and higher secondary	24 (48.0)	35 (56.5)	59 (52.7)	0.424
	Graduate and above	14 (28.0)	11 (17.7)	25 (22.3)	
Family history of IBD		2 (4.0)	8 (12.9)	10 (8.9)	0.181
Monthly family income					
	< 120$	33 (66.0)	27 (44.3)	60 (54.1)	
	120 – 350$	12 (24.0)	27 (44.3)	39 (35.1)	0.059
	> 350$	5 (10.0)	7 (11.5)	12 (10.8)	
Smoking status					
	Smoker	9 (18.0)	3 (4.8)	12 (10.7)	
	Former smoker	6 (12.0)	8 (12.9)	14 (12.5)	0.081
	Non smoker	35 (70.0)	51 (82.3)	86 (76.8)	
History of NSAID use		20 (40.0)	10 (16.1)	30 (26.8)	0.006
History of Anti tubercular therapy		23 (46.0)	0 (0.0)	23 (20.5)	<0.0001
Diagnostic Delay in months (Median±IQR)		24 (9.8-48)	12 (6-24)	18 (7-36)	0.025
Predominant presenting complaints					
	Diarrhoea	27 (37.0)	46 (63.0)	73 (100.0)	0.026

Characteristic		Disease type		Total IBD (n=112)	P-value
		CD (n=50)	UC (n=62)		
	Rectal bleeding	14 (21.9)	50 (78.1)	64 (100.0)	<0.0001
	Abdominal pain	43 (55.1)	35 (43.2)	78 (100.0)	0.001
Complications					
	Surgery	14 (70.0)	6 (30.0)	20 (100.0)	0.012
	Stenosis	10 (90.9)	1 (9.1)	11 (100.0)	0.002
	Perianal fistula	7 (87.5)	1 (12.5)	8 (100.0)	0.021
First attended physician					
	GI specialist	4 (8.0)	3 (4.8)	7 (6.3)	
	Non-GI physician	31 (62.0)	33 (53.2)	64 (57.1)	0.388
	Non registered practitioner	15 (30.0)	26 (41.9)	41 (36.6)	
Referred to GI specialist before diagnosis		27 (54.0)	38 (61.3)	65 (58.0)	0.437
Referral delay to GI specialist (months, Median±IQR)		12 (5.8-24)	12 (5-24)	12 (5.5-24)	0.641

Values are presented as mean±SD, Median±IQR, number (%). IBD, Inflammatory Bowel Disease; CD, Crohn's Disease; UC, Ulcerative Colitis; IQR, Inter Quartile Range.

Table 2. *Factors associated with a long diagnostic delay in overall study population (n=112).*

Factors		Long diagnostic delay		P-value
		Yes (n=31)	No (n=81)	
Age group (years)				
	18 – 30	10 (32.3)	38 (46.9)	0.209
	31 – 45	13 (41.9)	32 (39.5)	
	≥ 46	8 (25.8)	11 (13.6)	
Gender				
	Male	26 (83.9)	50 (61.7)	0.025
	Female	5 (16.1)	31 (38.3)	
Residence				
	Rural	13 (41.9)	40 (49.4)	0.480
	Urban and Semi-urban	18 (58.1)	41 (50.6)	
Educational level				
	Below secondary	6 (19.4))	22 (27.2)	0.393
	Secondary and above	25 (80.6)	59 (72.8)	
Family history of IBD		3 (9.7)	7 (8.6)	1.000
Monthly family income				
	< 120$	17 (54.8)	43 (53.1)	0.868
	> 120$	14 (45.2)	38 (46.9)	
Smoking status				
	Smoker	10 (32.3)	16 (19.8)	0.161
	Non smoker	21 (67.7)	65 (80.2)	
History of NSAID use		10 (32.3)	20 (24.7)	0.418
History of Anti tubercular therapy		7 (22.6)	16 (19.8)	0.740
Predominant presenting complaints				
	Diarrhoea	20 (64.5)	53 (65.4)	0.927
	Rectal bleeding	6 (19.4)	58 (71.6)	<0.0001
	Abdominal pain	22 (71.0)	56 (69.1)	0.850

Values are presented as number (%). Long diagnostic delay for IBD ≥36 months (3rd quartile of diagnostic intervals).

Table 3. *Crohn's disease-related complications in the study population according to the diagnostic delay (n=50).*

Complications (CD)	Long diagnostic delay		P-value
	Yes (n=13)	No (n=37)	
Surgery	9 (64.3)	5 (35.7)	<0.0001
Stenosis	6 (54.5)	5 (45.5)	0.023
Perianal fistula	6 (85.7)	1 (14.3)	0.001

Values are presented as number (%). Long diagnostic delay for Crohn's disease ≥48 months (3rd quartile of diagnostic intervals).

3.1. Diagnostic Delay

The median diagnostic delay for the total IBD patients was 18 months (Inter Quartile Range, IQR 7–36 months). The median diagnostic delay in patients with CD was 24 months (IQR 9.75–48 months) and in patients with UC 12 months (IQR 6–24 months) (p< 0.025). According to the division standard of the Swiss inflammatory bowel disease study [9], the diagnostic interval was defined as the diagnostic delay. Long diagnostic delay was more than 36 months and 48 months for total IBD patients and patients with CD respectively in our study (third quartile of diagnostic intervals).

3.2. Factors Influencing Diagnostic Delay

All IBD patients were stratified into 2 groups based on a long diagnostic delay of 36 months. Among examined factors, predominant presenting symptom with rectal bleeding was associated with a shorter diagnostic delay (p-value <0.0001). By contrast, male patients had a longer time to diagnosis compared with the female (p-value 0.025). Other factors like age, living area, level of education, household income, smoking status, NSAIDs use, history of getting anti-tubercular medication, family history of IBD did not seem to be associated with diagnostic delay (Table 2).

3.3. Complications Associated with Long Diagnostic Delay in CD

IBD-related complications by the time of diagnosis among patients with CD were stratified by third quartiles of time to diagnosis and are summarized in Table 3. The presence of intestinal strictures, surgery, and perianal fistula at the time of diagnosis was significantly associated with long diagnostic delay for CD.

4. Discussion

Identifying risk factors of diagnostic delay is a demanding issue in case of chronic disabling and progressive conditions. Only a few studies have reported the issue of diagnostic delay. The length of diagnostic delay and its associated factors, and the impact of it on IBD patients vary widely. To our knowledge, this is the first study on diagnostic delay in patients with IBD in Bangladeshi. We found that the diagnostic delay was significantly longer in CD than in UC which is a similar finding with the other studies [9-17]. The median diagnostic delay was 24 months for CD and 18 months for UC. Our study population had a longer diagnostic delay than the diagnostic delay found in other studies. This finding might be due to the majority of our IBD patients were first attended to general practitioners and non-registered local practitioners, and they were referred to a specialist after a median referral delay of 12 months. The initial presenting features seem to be the main drivers for diagnostic delay. For example, rectal bleeding is an alarming symptom that causes awareness of both patients and physicians to investigate and usually leads to early diagnosis. This is probably the main reason for the earlier diagnosis in UC and also in CD with presenting features of rectal bleeding. In this study, rectal bleeding was the chief presenting complaint in 78.1% of patients with UC, which may explain the earlier diagnosis of UC. Patients with CD presented with rectal bleeding were also diagnosed earlier and had fewer complications at diagnosis [5]. In this study male patients with IBD were more commonly associated with long diagnostic delay compared to females, (34.2% vs. 13.9%). This observation might be due to the predominance of male patients in this study. Studies have reported that CD progresses to stricturing and/or penetrating disease over time [20, 21]. We found that CD patients with a long diagnostic delay were associated with an increased rate of complications at diagnosis which is consistent with other studies [5, 10-15, 17]. The relationship of complications at diagnosis with a long diagnostic delay indicates earlier diagnosis might have an impact on disease outcomes. In this study, there was also considerable physician-related delay, especially among general practitioners and non-registered practitioners, in detecting the nature of the disease and also referring to the GI specialist for evaluation. This emphasizes the necessity of development of awareness about the disease among physicians, especially primary health care providers [22].

This is the first study evaluating the diagnostic delay of IBD in Bangladeshi patients. Nevertheless, limitations exist in this study: due to the small number of patients recruited from a single center, our results may not completely reflect the actual risk factors and impacts of diagnostic delay.

5. Conclusion

Diagnostic delay is associated with an increased rate of complications in IBD. The observations from this study can provide support for efforts to reduce delaying of diagnosis in patients with IBD. We also need to arouse the concern of the general people and primary health care providers about avoiding such delays, which can contribute to a worse prognosis. The prognostic importance of diagnostic delay should be emphasized and appropriate measures should be implemented to reduce this delay.

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