IBD Diagnosis Delay and Its Predictors in Jordan: A Retrospective Study

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ABSTRACT

AIM - Delayed diagnosis of inflammatory bowel disease (IBD) may lead to increased treatment costs and surgical risks. This study aims to describe the extent of IBD diagnosis delay in Jordan.

METHODS - Our study included 110 IBD patients, utilizing interviews and medical records from Jordan University Hospital. Data covered sociodemographic characteristics, health history, time from symptom onset to diagnosis, time from the first consultation to diagnosis, number of physicians consulted before diagnosis, and IBD-related surgical history.

RESULTS - The median time from symptom onset to IBD diagnosis was 9 months. Median diagnosis times for Crohn's disease (CD) and ulcerative colitis (UC) were 11 and 9 months, respectively. Regression analysis revealed that longer diagnosis delays were associated with higher paternal education levels. Lower maternal education levels (high school or less) and a household income between 1200 and 2000 Jordanian dinars correlated with consulting more physicians before diagnosis.

CONCLUSIONS - Early aggressive treatment is essential for IBD, as delayed diagnosis negatively impacts patient outcomes. Further research is needed to identify factors contributing to diagnosis delay. Our findings suggest that parental education and income levels influence diagnosis delays, highlighting the importance of targeted awareness campaigns for specific population groups and general practitioners to mitigate delays.

KEYWORDS - Inflammatory bowel disease, diagnosis delay, Crohn's disease, ulcerative colitis.

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List of Abbreviations:
BMI: Body mass index.
CD: Crohn's disease.
IBD: Inflammatory bowel disease.
JUH: Jordan University Hospital.
OR: Odds ratio.
TNF-α: tumor necrosis factor-alpha.
UC: Ulcerative colitis.

INTRODUCTION

Inflammatory bowel diseases (IBDs) are a group of chronic, lifelong, relapsing, and remitting gastrointestinal diseases (1). These diseases are mainly characterized by bouts of abdominal pain, diarrhea, blood from the rectum, and weight loss (2). IBD predisposes affected patients to complications, including intestinal obstruction, perianal fistula, and gastrointestinal oncogenesis (3). These complications, substantial social burden, and economic costs necessitate advancing safer and more effective diagnostic and therapeutic approaches.

Additionally, awareness-raising programs through governmental and non-governmental organizations pushed for the development of educational programs, recognizing May 19 as World IBD Day (4). These programs were necessary to address people's poor awareness of IBD symptoms, often mistaken for irritable bowel syndrome (IBS), leading to diagnosis delays (5, 6). Zaharie et al. reported a median diagnosis delay of 5 months in 478 patients with Crohn's disease (CD) and 1 month in 682 patients with ulcerative colitis (UC) in Romania, all of which correlated with increased frequency of bowel stenoses and need for IBD-related surgeries (5). In line, diagnosis delay, defined as the time interval between the first symptom onset and IBD diagnosis in which the 76th to 100th percentiles of patients were diagnosed, increased intestinal surgery risk by 2.54 and 6.81 in CD and UC patients, respectively (7). Longer diagnosis delays were reported in the United States, where the median time to diagnose was 9.5 months and 3.1 months for CD and UC patients, respectively (8). A very recent meta-analysis of 101 studies and 112,194 patients with IBD found that diagnosis delay increased the odds of stricturing disease, penetrating disease, and intestinal surgery in CD, and was associated with a 413% higher risk of colectomy in UC patients (9).

According to previous studies, ileal disease, perianal discomfort, and active smoking were independent risk factors for a long diagnosis delay in CD patients (5-7). In UC, ages > 40 experienced a reduced likelihood of diagnosis delay (8).

These delays are probably higher among Jordanian and other developing countries, mainly due to self-medication, low socioeconomic conditions, and misdiagnosis as IBS. Accordingly, this study aims to describe the extent of the IBD diagnosis delay in Jordan along with its predicting factors and investigate the impact of IBD diagnosis delay on IBD-related surgeries.

MATERIALS AND METHODS

STUDY DESIGN

This is a retrospective study comprising 110 IBD patients; among them, 70 were diagnosed with CD and 40 with UC. Data was collected through an interview-based questionnaire referring to Jordan University Hospital (JUH) medical records between October and December 2021. All cases and controls provided written consent. The collected data included the patients' sociodemographic characteristics (age, sex, education, nationality, and household income), diagnosis (CD or UC), health characteristics such as body mass index (BMI) class, smoking status, and family history of IBD or other autoimmune diseases. Furthermore, we also collected data regarding the duration from symptoms initiation to diagnosis establishment, duration from first consultation to diagnosis establishment, and the number of physicians consulted to reach the diagnosis, as well as their IBD-related surgical history, including strictureplasty, bowel resection, and surgery for abscesses and fistulas. The inclusion criteria for the study were a diagnosis of one of the IBDs, while the exclusion criteria included critically ill patients and patients with undetermined IBD phenotypes.

STATISTICAL ANALYSIS

Data were recorded in an Excel spreadsheet and imported into R and RStudio for descriptive and inferential analysis (10, 11). Tidyverse package functions were used for descriptive statistics and data wrangling, and plots were generated with the ggplot2 and ggpubr packages (12-14). Moreover, functions from the rstatix package were used for inferential statistical analysis, including the shapiro_test function to assess the normality of diagnosis delay parameters and the wilcox_test, wilcox_effsize, kruskal_test, and kruskal_effsize functions for assessing the association of variables with diagnosis delay parameters(15). Surgical indications such as tumors, perforations, and megacolon were excluded from the analysis due to the small sample size. Furthermore, logit transformation was performed on these parameters before multiple linear regression using the lm function to reduce the impact of non-normality. The multiple linear regression results were converted to APA tables using the apa.reg. table function from the apaTable package(16). A significance level of 0.05 was used.

RESULTS

SOCIODEMOGRAPHIC CHARACTERISTICS OF IBD PATIENTS AND THEIR

EFFECT ON DIAGNOSIS DELAY

The participants had a mean age of 44.04 ± 14.99 years, and 62.73% were males. Regarding education level, 49.09% attained a high school education or less, while 42.73% had a bachelor's degree. The only significant association was between paternal education and the number of consulted physicians (p = 0.005, η2 = 0.081). For more details, refer to Table 1.

The median duration from symptom to diagnosis was 9 months (IQR = 20 months), while the median duration from consultation to diagnosis was 3 months (IQR = 11 months). The median number of consulted physicians was 3 (IQR = 3). There were no significant differences between CD and UC patients in these parameters (p > 0.05). See Figure 1.

Figure 1. Diagnosis delay parameters in Crohn's and ulcerative colitis patients. The figure shows the median of the three diagnosis parameters in CD and UC patients. Figures 1A and 1B show median months from symptom-to-diagnosis and consultation-to-diagnosis, respectively. Whereas Figure 1C shows the median number of consulted physicians. Insignificant differences were observed in these three categories between CD and UC patients.
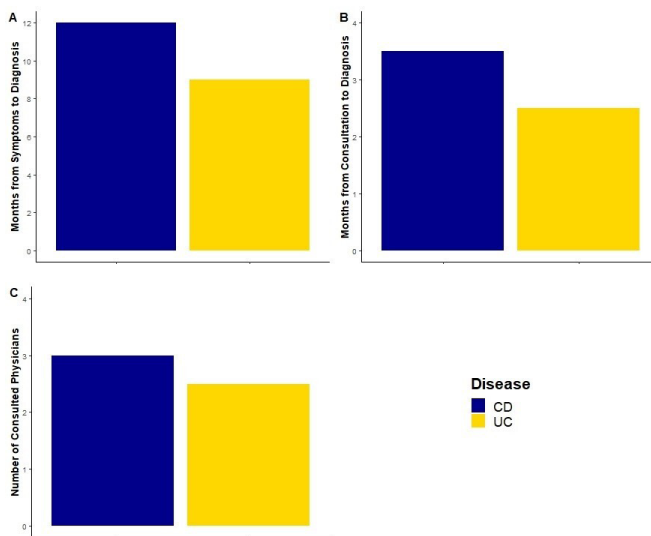
MEDICAL CHARACTERISTICS OF IBD PATIENTS AND THEIR EFFECT ON DIAGNOSIS DELAY

Approximately one-third of CD patients were active smokers, while only 15% of UC patients reported active smoking. The average BMI for all patients was 25.33 ± 5.26, and no significant correlation was found between BMI and diagnosis delay parameters in either the correlation test or Kruskal-Wallis analysis of BMI classes (p > 0.05). Moreover, a family history of IBD or other autoimmune conditions did not have a statistically significant effect on diagnosis parameters. Further information is provided in Table 2.

THE EFFECT OF DIAGNOSIS DELAY ON PATIENTS' IBD-RELATED SURGERY PROFILE

Of the total 110 IBD patients in the study, 50.91% had undergone IBD-related surgery. The indications for surgery varied, with 30.91%, 15.45%, and 7.27% of patients having undergone surgery for intestinal obstruction, fistula, and abscess, respectively. As presented in Table 3, no significant association was found between the number of IBD-related surgeries and surgical indications with median months from symptom to diagnosis, first consultation to diagnosis, and the number of consulted physicians (p > 0.05).

LINEAR REGRESSION ANALYSIS IDENTIFIES INDEPENDENT PREDICTORS OF DIAGNOSIS DELAY

Following logit transformations to reduce the impact of non-normality, a multiple linear regression model was conducted, which identified several predictors. Paternal higher education significantly predicted longer months from symptom to diagnosis and first consultation to diagnosis (β = 1.67, p = 0.03 and β = 2.59, p = 0.002, respectively). In addition, maternal education that was high school or less and income level between 1200 and 2000 JODs were also significant predictors of the number of consulting physicians (β = 0.77, p = 0.027 and β = 0.87, p = 0.041, respectively). Supplementary Tables (1, 2, and 3).

DISCUSSION

Early diagnosis of autoimmune diseases such as inflammatory bowel disease (IBD) reduces morbidity, disability, and mortality(17, 18). Increasing evidence supports a top-down approach instead of the conventional step-up therapy approach, in which a 'window of opportunity' where early effective therapies, such as biological therapy, can significantly reduce IBD progression. Clinical evidence supports the superior outcomes of anti-tumor necrosis factor-alpha (anti-TNFs) therapy in patients with shorter disease duration, such as infliximab, adalimumab, and certolizumab. For instance, a study reported that CD patients who received the medication within the first 2 years of diagnosis had a 15% improvement in remission rates compared to patients who received the treatment 5 years after diagnosis(19). Moreover, a meta-analysis of 2501 patients from eleven studies demonstrated a statistically significant reduction in surgical risk and disease progression, improved early remission, and clinical response in patients with CD receiving anti-TNF-α within 3 years of diagnosis(20).

Nguyen et al. showed a correlation between diagnosis delay and surgical risk and a median delay of 9.5 and 3.1 months for CD and UC patients in a US cohort(8). Our findings, surprisingly, did not reveal an association with surgical risk but showed an overall median of 9 months and longer delays in both CD and UC patients (11 and 9 months, respectively). This may be related to geographical variation as the disease phenotype probably is less aggressive in Middle Eastern countries. These results also exceed the 6- and 3-month median delays in CD and UC diagnosis in Austria and South Korea(7, 21). Additionally, our results surpass these in a recent meta-analysis that showed a pooled weighted median of 7 and 4.6 months for CD and UC, respectively, along with 4.13-folds and 2.24-fold higher risk for colectomy and intestinal surgery in CD and UC patients, respectively(9).

Identifying predictors of diagnosis delay is of paramount importance and may help in the development of awareness-raising programs. Our study identified higher paternal education as an independent predictor of months from symptom to diagnosis and first consultation to diagnosis. However, our results showed that older age and personal high educational level did not correlate with diagnosis delay, which is inconsistent with a multicenter Austrian study(21). Previous research has explored paternal education's influence on adolescents' health-seeking behavior. Zhao and colleagues found that teenagers with lower-educated parents were equally or more likely to seek health information online compared to those with higher-educated parents(22). Additionally, studies on post-World War II Germans revealed that maternal education, but not paternal education, correlated with reduced rates of smoking and overweight among adolescents(23). However, there is a gap in the literature concerning the relationship between parental education and the health-seeking behavior of adult children. This gap presents a challenge to the interpretation of our findings.

Our study also showed that lower maternal educational levels, reaching only high school or less, predicted more physician visits and consultations before reaching a final diagnosis. This might be explained by better health-seeking behavior observed in mothers of higher educational levels, which could influence the offspring's future health-seeking behavior(24). This is in agreement with a study by DeVoe and colleagues that reported better children's access to healthcare when parents had higher education(25). In developing countries such as Jordan, patients tend to visit local private clinics of general practitioners (GPs) to avoid the costly specialist consultation, remote transportation, and the inconveniences of public healthcare services, such as shortage of trained healthcare professionals, population overgrowth, and the increasing burden of chronic diseases(26-28). In that sense, exploring the knowledge and attitude of GPs toward IBD becomes of paramount importance given that 3 and 2.5 months of the delay in CD and UC patients occurred after the first physician visit. While this study provides valuable insights, several limitations must be considered. Firstly, the sample size was small, and the study had a retrospective design, which may have introduced recall bias. Additionally, the study primarily focused on sociodemographic factors and did not examine clinical factors such as disease presentation and phenotype. Therefore, future research should aim to address these limitations by using a larger sample size and including more comprehensive clinical data.

Furthermore, current and future research could be used to develop targeted awareness-raising campaigns. By examining more specific population groups and involving general practitioners in the campaigns, it may be possible to better address the challenges these groups face in seeking appropriate medical care.

AUTHOR CONTRIBUTIONS

AR: Conceptualization, formal analysis, methodology, project administration, visualization, writing – original draft preparation. NS: Conceptualization, formal analysis, methodology, project administration, visualization, writing – original draft preparation. AA, OIH, OF, and SH: Data curation and writing – original draft preparation. NA, MR, and YR: Project administration, supervision, and writing – review and editing. All authors read and approved the submitted version.

INFORMED CONSENT

ETHICAL APPROVAL

SUPPLEMENTAL MATERIALS

Table 1. Sociodemographic characteristics of IBD patients and their effect on diagnosis delay

Variable	Total	CD	UC	Symptom-to-diagnosis (Months)		First consultation-to-diagnosis (Months)		Number of Consulted Physicians	
	n (%)	n (%)	n (%)	Median (IQR)	p-value (effect size)	Median (IQR)	p-value (effect size)	Median (IQR)	p-value (effect size)
Age (mean ± sd)	44.04 ±14.99	40.57±15.06	50.1±12.94	NA	0.821 (Spearman's ρ = -0.022)	NA	0.898 (Spearman's ρ = -0.012)	NA	0.071 (Spearman's ρ = -0.173)
Sex Male	69 (62.73)	43 (61.43)	26 (65.00)	7 (18)	.06 (Cohen's d = 0.18)	2 (11)	0.621 (Cohen's d = 0.047)	3 (3)	0.877 (Cohen's d = 0.015)
Female	41 (37.27)	27 (38.57)	14 (35.00)	12 (18)		4 (11)		2 (3)	
Education High school or less	54 (49.09)	35 (50.00)	19 (47.50)	9 (10)	0.228 ($\eta2$ = .009)	3 (11)	0.368 ($\eta2$ =-0.00001)	3 (3)	0.796 ($\eta2$ =-0.014)
Bachelor	47 (42.73)	30 (42.86)	17 (42.50)	9 (23)		2 (9.5)		2 (2.5)	
High education	9 (8.18)	5 (7.14)	4 (10.00)	24 (54)		18 (23)		3 (1)	
Paternal Education High school or less	81 (73.64)	49 (70.00)	32 (80.0)	9 (14)	0.335 ($\eta2$ = .002)	2 (8)	0.053 ($\eta2$ = .036)	2 (3)	0.005 ($\eta2$ = 0.081)
Bachelor	22 (20.00)	14 (20.00)	8 (20.0)	11 (20)		3 (17)		3 (2.75)	
High education	7 (6.36)	7 (10.00)	0 (0.0)	36 (73)		32 (74)		5 (5)	
Maternal Education High school or less	94 (85.45)	57 (81.43)	37 (92.50)	9 (20)	0.335 ($\eta2$ = .002)	3 (11)	0.918 ($\eta2$ = -0.017)	3 (3)	0.287 ($\eta2$ =0.005)
Bachelor	15 (13.64)	12 (17.14)	3 (7.50)	12 (20)		2 (11)		2 (1.5)	
High education	1 (0.91)	1 (1.43)	0 (0.00)	4 (0)		4 (0)		10 (0)	

Income	Total n (%)	CD n (%)	UC n (%)	Symptom-to-diagnosis Median (IQR)	p-value (effect size)	First consultation-to-diagnosis Median (IQR)	p-value (effect size)	Number of Consulted Physicians Median (IQR)	p-value (effect size)
0-400 JODs	33 (30.00)	23 (32.86)	10 (25.00)	11 (21)	0.588 (η2 = -.011)	3 (11)	0.226 (η2 = 0.016)	3 (2)	0.067 (η2 = 0.045)
401-800 JODs	45 (40.91)	28 (40.00)	17 (42.5)	10 (19)		3 (11)		3 (3)	
801-1200 JODs	20 (18.18)	9 (12.86)	11 (27.5)	6.5 (11)		1.75 (2.25)		2 (1.25)	
1200-200 JODs	6 (5.45)	5 (7.14)	1 (2.5)	18 (18)		15 (16.5)		7.5 (10.25)	
>2000 JODs	6 (5.45)	5 (7.14)	1 (2.5)	4 (12)		3.5 (7.75)		2.5 (4)	

Table 2. Health characteristics of IBD patients and their impact on diagnosis delay

Variable	Total	CD	UC	Symptom-to-diagnosis (Months)		First consultation-to-diagnosis (Months)		Number of Consulted Physicians	
	n (%)	n (%)	n (%)	Median (IQR)	p-value (effect size)	Median (IQR)	p-value (effect size)	Median (IQR)	p-value (effect size)
BMI	25.33±5.26	25.17±5.99	25.62±3.68	NA	0.954 (Spearman's ρ = 0.006)	NA	0.606 (Spearman's ρ = 0.05)	NA	0.285 (Spearman's ρ = -0.103)
Smoking Status Not a smoker	59 (53.64)	37 (52.86)	22 (55.00)	10 (19.5)	0.573 (η2 = -.008)	4 (11)	0.569 (η2 = -.008)	3 (2)	0.796 (η2 = -0.014)
Previous smoker	22 (20.00)	10 (14.29)	12 (30.00)	7.5 (31.75)		2 (26.25)		2 (3)	
Current smoker	29 (26.36)	23 (32.86)	6 (15.00)	6 (10)		2 (11)		2 (4)	
Smoking Method Cigarettes	42 (38.18)	26 (37.14)	16 (40.00)	6.5 (20.75)	0.405 (Cohen's d = 0.08)	2 (11)	0.078 (Cohen's d = 0.169)	2 (3)	0.516 (Cohen's d = 0.062)
E-cigarettes	3 (2.73)	3 (4.29)	0 (0.00)	12 (52)	0.514 (Cohen's d = 0.063)	4 (53.5)	0.578 (Cohen's d = 0.054)	2 (2)	0.729 (Cohen's d = 0.034)
Hookah	14 (12.73)	11 (15.71)	3 (7.50)	8 (29)	0.822 (Cohen's d = 0.022)	4 (26)	0.587 (Cohen's d = 0.052)	2 (2)	0.303 (Cohen's d = 0.099)

Variable	Total n (%)	CD n (%)	UC n (%)	Symptom-to-diagnosis (Months) Median (IQR)	p-value (effect size)	First consultation-to-diagnosis (Months) Median (IQR)	p-value (effect size)	Number of Consulted Physicians Median (IQR)	p-value (effect size)
Family History of IBD	25 (22.73)	13 (18.57)	12 (30.00)	12 (16)	0.349 (Cohen's d = 0.093)	4 (11)	0.669 (Cohen's d =0.12)	3 (3)	0.398 (Cohen's d = 0.127)
Family History of Autoimmune Diseases	33 (30.00)	16 (22.86)	17 (42.5)	9 (42)	0.517 (Cohen's d = 0.062)	2 (3)	0.093 (Cohen's d = 0.161)	2 (2)	0.149 (Cohen's d =0.138)

Table 3. The impact of diagnosis delay on patients' IBD-related surgery profile

Variable		Total n (%)	CD n (%)	UC n (%)	Symptom-to-diagnosis (Months) Median (IQR)	p-value (effect size)	First consultation-to-diagnosis (Months) Median (IQR)	p-value (effect size)	Number of Consulted Physicians Median (IQR)	p-value (effect size)
IBD Surgeries		56 (50.91%)			NA	0.707 (Spearman's $\rho = 0.04$)	NA	0.386 (Spearman's $\rho = -0.092$)	NA	0.578 (Spearman's $\rho = -0.059$)
Indication	Obstruction	34 (30.91)	26 (37.14)	8 (20.00)	8.5 (9.5)	0.476 (Cohen's d = 0.068)	4 (10)	0.894 (Cohen's d = 0.013)	3 (2)	0.425 (Cohen's d= -0.003)
	Abscess	8 (7.27)	5 (7.14)	3 (10.00)	8.5 (11.5)	0.84 (Cohen's d = 0.02)	1 (3)	0.228 (Cohen's d = 0.115)	2 (2)	0.36 (Cohen's d = -0.001)
	Fistula	17 (15.45)	10 (14.29)	7 (17.50)	12 (22)	0.154 (Cohen's d = 0.136)	4 (10)	0.181 (Cohen's d = 0.128)	2 (1)	0.98 (Cohen's d =-0.009)

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