Inflammatory Bowel Disease in a Central Rural Area, Riyadh Province Al-Kharj of Saudi Arabia: Epidemiology, Clinical Characteristics, Natural Course of Disease and Current Clinical Practice

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1. Abstract

1.1. Background and Aim

The epidemiology, clinical characteristics, natural course, and treatment of Inflammatory Bowel Disease (IBD) in the gastroenterology centres of Al Kharj, Riyadh Province, are still largely unknown. Therefore, a survey was conducted to describe IBD features to correlate the findings with published data from the rest of the country and to elucidate future monitoring and treatment patterns.

This cross-sectional, prospective, and retrospective study was conducted to assess the prevalence and characteristics, disease course, and therapeutic options for IBD in adult Saudi patients from January 2020 to June 2022. All endoscopy reports, patient files, colonic biopsy reviews, and registry data formed the cohort. In addition, patients who were diagnosed with IBD for the first time since 2015 and were followed up for a period of seven years were included. During the follow-ups, disease severity and hospital admission, treatment response, surgery/therapy, and especially those who developed cancer due to chronic inflammation were evaluated.

A cohort of 221 adult Saudi IBD cases was gathered, including 108 with Ulcerative Colitis (UC) and 113 with Crohn's Disease (CD). The mean age at diagnosis of IBD was 28 years (range, 18–37 years), with a male predominance (53%). The incidence rate of UC was 1.68 per 100,000 persons per year and for CD was 0.96 per 100,000 persons per year.

A broad-based epidemiological study was conducted on IBD epidemiology, patterns, outcomes, and therapies. The incidence of IBD has gradually increased in Al-Kharj and there is a need for specialised IBD units for these patients.

2. Introduction

Chronic Inflammatory Bowel Disease (IBD) includes Crohn's Disease (CD) and Ulcerative Colitis (UC), with accompanying intestinal disease and extraintestinal manifestations in almost all systems.

The aetiology of such diseases is unknown, although multiple environmental, genetic, and immunoregulatory factors appear to be involved. The natural course of IBD is related to increased morbidity and periodic remission of inflammation, followed by exacerbations that affect quality of life [1]. Furthermore, the incidence of IBD varies in different regions in the world [2-7]. The incidence of IBD has steadily increased worldwide over the last few years, with a high prevalence in most developed countries, even in regions where IBD is considered infrequent.

In Saudi Arabia, the IBD pattern has also been described in terms of prevalence, natural course of the disease, and therapeutic strategies, despite the limited number of publications [8-20]. In 1982, IBD was almost absent in Saudi Arabia [11]. Between 1976 and 1994, the King Faisal Specialist Hospital and Research Center (KFSHRC) in Riyadh reported 101 Saudi patients treated for IBD [12]. Another prospective hospital-based study by El Mouzan et al reported an increase in the incidence of IBD in Saudi children from 0.5/10000 to 5.0/10000 between 1993 and 2002 [13]. The increasing incidence of IBD in the paediatric population will transition to adult IBD care. Another study also assessed the state of IBD transition of care in the country based on a survey of paediatric and adult gastroenterologists, emphasising the need for a nationwide IBD transition program [14]. In 2004, a study from King Khalid University Hospital in Riyadh reported 77 patients with CD with an increase in IBD incidence over a period of 20 years. Over the last 10 years, they reported an incidence of IBD of 0.32/10000 and 1.66/10000 with an annual incidence of 0.94/10000 over the past 20 years [15]. In conclusion, similar to other countries, the steady increase in IBD frequency reflects the importance of early recognition and accurate diagnosis.

Therapeutic regimens have changed rapidly in patients with UC and CD. The therapeutic regimens for UC and CD depend on the disease activity and extent. The current regimens for IBD are aminosalicylates, immunomodulators such as corticosteroids, thiopurine metabolites, and methotrexate, and many biological mediators such as the antitumour necrosis factor infliximab, adalimumab, golimumab, certolizumab pegol, vedolizumab, ustekinumab, and Janus kinase inhibitors, such as tofacitinib, approved only for UC [21, 22]. Serum levels of these drugs are usually reactively monitored in cases of loss of response or proactively monitored regardless of the disease state. Other indices for follow-up imaging include ultrasound, MRI, calprotectin and C-Reactive Protein (CRP), endoscopy, and histology according to the recent European Crohn's and Colitis Organisation (ECCO) guidelines for diagnostic assessment [23], monitoring of known IBD [24], and medical and/or surgical treatment [24, 25]. Apart from medical treatment, surgery is inevitable because disease progression occurs over the years although there are reported declined rates of surgery in the era of biological therapy [26, 27]. Surgery is recommended for medically refractory UC, complications of CD such as intra-abdominal abscesses, medically intractable fistula, fibrotic strictures with obstructive symptoms, toxic megacolon, intractable disease with impaired quality of life, severe adverse events from medical treatment, and cancer [26, 27].

In a recent meta-analysis in Arab countries [28], a limited number of studies in Saudi Arabia on IBD epidemiology, patterns, outcomes, and therapies and the small sample size of these studies and potential confounders may have either overestimated or underestimated the incidence of IBD. These reports cannot be generalized throughout the country. In addition, genetic, environmental, and cultural differences may play a role in the IBD pattern of Saudi patients, which may differ from the Western countries from which most of the information clarifying the importance of our study was obtained. In this systematic review [28], the incidence of IBD has been reported to increase exponentially, with the highest incidence of IBD appearing to be in Kuwait and Saudi Arabia. They also reported that in most Arab countries, the pooled estimates revealed the incidence of UC and CD as 2.33 and 1.46 per 100,000 persons per year, respectively. Between 1990 and 2000, a study in Saudi Arabia also reported an increasing incidence of IBD [29].

Al-Ghamdi et al. (2014) carried out a retrospective study gathering data on confirmed CD cases from a tertiary centre in Riyadh for a period of 20 years between 1983 and 2004 [15]. The incidence of CD increased from 0.32 per 100,000 individuals per year between 1983 and 1993 to 1.66 per 100,000 individuals per year between 1994 and 2004. The total mean annual incidence was 0.94 per 100,000 individuals per year during this period.

This high incidence rate in Saudi Arabia can be explained by the increased lifestyle changes of the country toward lifestyles seen in Western countries [16, 18, 20] and many other factors, such as consanguinity [28].

First-time diagnosis mostly occurs in young people, with male preponderance in the Arab world [28, 29] compared to studies in Japan [30], Korea [31], and other Asian countries [32] that have shown a similar incidence in men and women. The treatment response in Saudi appears to be similar to that in Western countries [29].

Hossain et al. (1991) reported IBD cases 91 without disease location, 55 with mild and 36 moderate [17]. Khan et al. (1996) reported in the Al-Medinah region, during a period of six years, ulcerative colitis cases with proctitis 22.5% (n = 18), proctosigmoiditis 30% (n = 24), and left-sided colitis 27.5% (n = 22) [19].

Regarding IBD in the Middle East as a whole, in the limited number of studies that have been conducted, Palestine and Iran reported lower incidence than that in Europe, while a higher incidence has been reported in different Iranian studies as well as in Lebanon and Turkey [33]. The study remarked about the increasing incidence of disease in migrant populations, with postulations being put forward on whether this increment is due to pure lifestyle changes or if there is even an infective origin. One study predicted the incidence of IBD in the Middle East by 2035 and extrapolated a 2.3-fold increase [34]. In Middle Eastern populations, the most common extra-intestinal

manifestation is arthritis [35].

The incidence of IBD has increased worldwide, which is mainly attributed to higher meat consumption, especially higher protein intake, in modern lifestyles [36]. In fact, in Europe, it has been recently associated with a high economic burden, costing around €3500 for CD and €2000 for UC per patient per year [37], as biologic mediators and immunomodulators are expensive. This poses challenges to many developing countries who cannot afford these drugs, as IBD is transitioning to an expanding global health problem [38].

The aims of this cross-sectional, prospective, and retrospective study were to review the characteristics of Saudi patients with IBD from 2015 to 2022 (seven years), who were diagnosed for the first time with IBD and who were referred to the gastroenterology centres of Al Kharj, to study the epidemiological and demographic features, natural courses such as extent and pattern of diseases, and therapeutic options revealing the course of the two diseases in terms of medications and surgery.

3. Methods

3.1. Study Design

A cross-sectional, prospective, and retrospective study was conducted to collect data on the epidemiological characteristics of IBD, disease course, and therapeutic options in Kharj, Saudi Arabia. Three hospitals were involved in Al Kharj: (1) Prince Sattam bin Abdulaziz University Hospital, (2) Al Kharj Military Hospital, King Khaled Hospital, and (3) Prince Sultan Center for Health Care from January 2020 to June 2022. All newly diagnosed cases of IBD, as confirmed by clinical, laboratory, endoscopic, and histological findings, were included in our cohort, and data were collected and analysed according to the ECCO guidelines [22]. All endoscopy reports, patient files, and colonic biopsies were reviewed and registry data were obtained. In addition, patients diagnosed with IBD for the first time and referred to Al Kharj hospitals starting in 2015 were followed-up over the last seven years. During follow-up, patients with severe disease and hospital admission for surgery or medical treatment, and those who developed cancer due to chronic inflammation were recorded.

Ethical approval was obtained from the Standing Committee of Bioethics Research (SCBR) Bioethical and Research Committee of Prince Sattam bin Abdulaziz University, Deanship of Scientific Research No SCBR-05-2022.

3.2 Patients

The inclusion criteria were Saudi nationality, being above 18 years of age, and being diagnosed with IBD. Exclusion criteria included patients with any other inflammatory or autoimmune disease other than IBD without a confirmed diagnosis, according to the ECCO guidelines [22], being of any nationality other than Saudi Arabian, and being aged less than 18 years.

3.3 Data Extraction

Two independent gastroenterologists extracted the data and another gastroenterologist resolved any discrepancies. The extracted data included several pieces of information: (1) baseline and epidemiological characteristics of the affected patients enrolled in the study, (2) prevalence and pattern of IBD, (3) monitoring of patients, (4) the natural course of IBD, and (5) therapeutic strategies.

3.4 Data Analysis

We used a commercially available version of Statistical Package of Social Science (SPSS version 22 for Windows; SPSS Inc, Chicago, IL). Continuous data were presented as mean and Standard Deviation (SD) and were compared using a Student's t-test or a nonparametric test. Categorical variables were presented in frequency and percentage and were analyzed using the χ2 or Fisher's exact tests. A 2-tailed P<0.05 was considered to be statistically significant. For categorical values, raw numbers and percentages were calculated. The cumulative frequency of IBD over the years and variables, such as clinical features, medical treatment, and surgical rates for UC and CD, were assessed.

4. Results

During the period from 2015 to 2022, a cohort of 221 adult Saudi IBD cases was gathered, including 108 with UC and 113 with CD. The mean age at diagnosis of IBD was 28 years, range from18 to 37 years, with a slight male predominance (53%, 116 out of 221). The sex and age distributions of patients with CD and UC are shown in Tables 1 and 2, respectively. There was no significant difference in IBD based on sex (p > 0.005). Compared with patients with UC, patients with CD presented significantly at a younger age (p = 0.001). The peak presentation of total 221 IBD cases was in the age group 30-30 years 113 (51%), compared to other age groups 18-29 years 98 (40%) and 40-49 years 19 (9%), (p=0.02).

The referral rate was 59% (n = 131) for patients with IBD symptoms to Al Kharj gastroenterology centres from other medical specialties, mostly family doctors, for further investigation.

The incidence rate of UC was 1.68 (95% confidence interval [CI] 1.6–4.4) per 100,000 persons per year, and for CD, it was 0.96 (95% [CI] 1.43–2.89) per 100,000 persons per year.

The most common sites of colon involvement in UC were pancolitis (33%) and left-sided colitis (22%). Concerning disease severity and extent, ulcerative proctitis accounted for 6.9%–27.3% of the cases, while pancolitis accounted for 10%–45% of the cases. Histological subtypes and endoscopic findings of IBD are shown in Table 3.

UC and CD were mainly diagnosed at a younger age and three–four years needed for diagnosis from the time of the first symptom, as shown in Table 4, which emphasises the need for quicker medical diagnosis, detection, referral, and treatment.

The risk factors and treatment in our cohort are summarised in Table 5. Most IBD patients (81%) had no previous history of smoking but had a significant proportion of positive family history of IBD. In the present study, the consanguinity rate was 26%.

The patients were followed for a mean duration of five years. During the follow-up period, younger patients were mostly diagnosed with IBD for the first time and showed a good treatment response (85%) to aminosalicylates and/or corticosteroids/immunomodulators with low use of biological mediators (9%).

Only 51 patients (23%) required at least one hospital admission. Surgery was needed in 13% (15 out of 113) of patients with CD when compared with 5% (5 out of 108) of patients with UC (p= 0.001) and 1% with colorectal cancer. In total, 18% (40) of patients were

lost during follow-up in Riyadh IBD centres or during surgical management of gastrointestinal complications.

The clinical symptomatic manifestations of our patients are shown in Table 6. The findings indicate a higher prevalence of haematochezia in UC, while the severe systemic inflammatory manifestations of CD, such as abscesses, perianal fistulas, and generalised weight loss, are statistically significant higher.

The distribution of extraintestinal symptoms of both UC and CD in our study is given in Table 7.

Table 1: Gender distribution of IBD patients

Gender	UC (n=108)	CD (n=113)	IBD (n=221)
Males - n (%)	56 (52%)	60 (53%)	116 (53%)
Female - n (%)	52 (48%)	53 (47%)	105 (47%)

(UC: ulcerative colitis; CD: Crohn's disease; IBD: Inflammatory Bowel Disease)

Table 2: Age at presentation and distribution of patients with IBD

	UC	CD	IBD
Mean age of diagnosis	29.4	26	28
Standard deviation	11.2	9.6	11.1
Age bracket	No of patients with UC (%)	No of patients with CD (%)	No of patients with IBD (%)
18–29	(39) 42	(41) 47	(40) 89
30–39	(54) 58	(49) 55	(51) 113
40–49	(7) 8	(10) 11	(9) 19
50–59	-	-	-
Total	49 (108)	(51) 113	221

(UC: ulcerative colitis; CD: Crohn's disease; IBD: Inflammatory Bowel Disease)

Table 3: Histological subtypes and Endoscopic Findings of Inflammatory Bowel Diseases

Histological Subtype	Numbers	%
UC	108	49
CD	113	51
Intermediate colitis	0	0
Total	221	100
Endoscopic Findings of UC - location		
Pancolitis	36	33
Extensive Disease	13	12
Left-sided colitis	24	22
Proctosigmoiditis	19	18
Proctitis	16	15
Total	108	100
Endoscopic Findings of CD - location		
Ileocolic	46	41
Colonic colitis	19	17
Small intestine-terminal ileus	36	31
Upper GI tract	12	11
Total	113	100
Behaviour of CD		
Inflammatory	51	45

perianal disease	24	21
penetrating	11	10
-simple fsimple	-7	-64
- complicated fistula	-4	-36
Stricturing	27	24
Total	113	100
Disease severity CDAI		
150> remission	75	67
mild 150–219	22	19
moderate 220–450	9	8
severe > 450	7	6
overall	113	100
UC disease severity		
mild	47	44
moderate	50	46
severe	11	10
overall	108	100

(UC: ulcerative colitis; CD: Crohn's disease; GI: gastrointestinal; CDAI: Crohn's disease activity index)

Table 4: Mean timelines of diagnosis for UC and CD

	UC	CD	p value
Age of onset of the first symptom, years (SD in months)	(9.1) 26	(6.3) 23	p=0.002
Mean age (SD) of diagnosis	(11.2) 29.4	(9.6) 26	p=0.001
Mean time up to diagnosis in months	47	51	P=0.72

Table 5: Risk factors and treatment modes for UC, CD and IBD

Risk Factors	UC no, (%)	CD no, (%)	IBD no, (%)	p value UC Vs CD
Family history	26 (24)	21 (19)	57 (26)	p>0.05
Smoking	23 (21)	19 (17)	42 (19)	p>0.05
Treatment	UC	CD	IBD	
5-ASA	102 (95)	103 (91)	205 (93)	p>0.05
Steroids	33 (31)	12 (11)	45 (21)	p= 0.02
Immunomodulators	72 (67)	52 (59)	124 (56)	p=0.03
Biological Factors				
-Infliximab/adalimumab or biosimilar	8 (7)	9 (8)	19 (9)	p>0.05
-Ustekinumab	-	-		
-Vedolizumab	2 (2)	-		
Hospitalization	31 (29)	20 (18)	51(23)	p=0.001

(no: number of patients and percentage of cohort % in brackets)

Table 6: Clinical Features of IBD

Symptoms	CD No of patients and %	UC No of patients and %	p value
Abdominal pain	96 (85)	85 (79)	0.02
Diarrhoea	110 (97)	140 (103)	0.1
Haematochezia	52 (46)	105 (97)	0.001
Abscess	20 (18)	22 (2)	0.0002
Perianal fistula	21 (19)	32 (3)	0.0001
Weight loss	34 (30)	19 (18)	0.001

Table 7: Distribution pf extra-intestinal manifestations of ulcerative colitis and Crohn's disease (UC and CD, respectively)

	UC no, (%)	CD no, (%)	P value
Eye	3 (2.7)	6 (5.5)	p= 0.01
Skin	10 (9)	19 (17)	>0.05
Stomatitis	1 (0.9)	1 (0.9)	>0.05
Musculoskeletal	14 (13)	21 (19)	>0.05
Joint pain	6 (5.5)	9 (8)	>0.05
Bone manufestation	28 (26)	15 (17)	>0.05
Liver Primary Sclerosing Cholangitis	1 (0.9)	1 (0.9)	>0.05
Venous thrombosis	3 (2.7)	2 (1.8)	>0.05
Erythema nodosum	2 (1.8)	8 (7)	p= 0.001
Pyoderma gangrenosum	1 (0.92)	1 (0.9)	>0.05

(no: number of patients and percentage of cohort % in brackets)

5. Discussion

In our current study, the incidence rate of UC was 1.68 (95% confidence interval [CI], 1.6–4.4) per 100,000 persons per year, and for CD, it was 0.96 (95% CI, 1.43–2.89) per 100,000 persons per year. A lower incidence of IBD during the period to 2015-2022 was found in our study, which included a 7-year follow-up study compared to other Arab countries, with larger variation among different countries [28]. In Saudi Arabia, a similar incidence rate of IBD as found in our study was reported in Riyadh (1.66/105 over the last 10 years for CD in 2004) [15]. A higher incidence rate has been reported in Europe. In 2017, UC incidence rates ranged from 0.97 to 57.9 per 100,000 and 8.8 to 23.14 per 100,000 in North America, which were similar, although still higher than the incidence rates reported in Arab studies that showed values at 2.33 (95% confidence interval [CI] of 1.2–3.4) per 100,000 persons per year for UC and 1.46 (95% CI of 1.03–1.89) per 100,000 persons per year for CD [28].

Regarding the natural course of IBD patients, our cohort study indicated that the mean age at diagnosis was 28 years, with an age range from 18 to 37 years, and male predominance (53%, 117 out of 221).

Similar to our study, a majority of UC cases in young people (17–40 years) with a male predominance were also shown in another study [6]. The age and sex correlations were similar to those in the study conducted in Riyadh [20]. In our study, the patients were followed up for a mean duration of five years. During during follow-up, only one (out of five) of our patients required at least one hospital admission, one patient with UC developed cancer, and none died. Surgery was needed in 13% (15 out of 113) of patients with CD compared to 5% (5 out of 108) of patients with UC (p= 0.001), and one patient developed colorectal cancer. However, in another study in Saudi Arabia [20], 206 patients (66%) required hospital admission and nine patients (2.9%) with UC progressed to colon cancer. Six patients died during the follow-up. 53% (n = 104) of patients with CD underwent surgery as part of their treatment, whereas only 20% (n = 23) of UC patients underwent colectomy. Higher rates and worse outcomes were reported in this observational study in Riyadh [20].

In contrast to another study from Saudi Arabia, the consanguinity rate was 32.6%, although in our study the rate was 26% [28]. Other risk factors included smoking; in our study, a positive history of smoking was found in one (out of five) of our patients, but a positive history of smoking was found in 11.1% of other Arab countries [28]. Similar to other studies in the Middle East, our study reported that haematochezia, diarrhoea, urgency, and tenesmus were the main presenting features of patients [28]. Concerning the time for diagnosis, studies in Saudi populations reported that the average time to diagnosis was nearly six months in > 90% of patients with UC; however, in our study, this time was more than 3 years 18 months. The most common site of colonic involvement among the included studies was the left colon [28]; however, in our study, pancolitis was found to be the most common site. The proportion of patients with pancolitis was notably higher among patients from Kuwait, Lebanon, and Saudi Arabia [28], which is similar to our study.

Approximately two-thirds of patients with CD had remission, and those with UC had mild/moderate disease severity (56%), similar to that reported in other studies [28]. Moreover, in a study in Riyadh, Al Harbi et al. showed that among patients with UC, 51.3% were in remission, 16.6% had mild UC, 23.4% had moderate UC, and 8.6% had severe UC [9].

Most patients had a good treatment response of approximately 85% to aminosalicylates and/or corticosteroids/immunomodulators with low use of biological factors (9%), as reported in other studies of Arab countries [28]. In Saudi Arabia, 21% of the time, biological factors are used for CD, and 6% for UC [6]. In our gastroenterology centre, biological mediators other than infliximab and adalimumab were not used because no specialised centre with an infusion unit for IBD was available. In addition, internists prescribed treatment to patients with IBD and followed their treatments. More than one-third of patients were referred to tertiary centres in Riyadh.

One of the limitations of our study is the small number of people in

the study sample and other potential factors, such as socioeconomic status, since our area is a rural province of Riyadh that may have either overestimations or underestimations of the incidence of IBD.

6. Conclusion

There is a growing incidence of IBD in Saudi Arabia; therefore, there is a need for specialised IBD units for these patients. Other experts, such as surgeons and dieticians, are also needed in Al-Kharj. Our findings cannot be generalised across countries. Further studies are needed to assess both paediatric and adult IBD cases in several geographical regions of Saudi Arabia.

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8. Conflict of Interest

No competing interests exist.

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