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ORIGINAL ARTICLE

Clinical and Epidemiological Characteristics of Patients with Intestinal Inflammatory Disease in Pernambuco, Northeast of Brazil

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ABSTRACT

AIM: Inflammatory bowel disease (IBD) is a chronic inflammatory autoimmune condition. Despite an increase in the number of cases of these diseases in Brazil, there is still a lack of research, especially in the northeast. The goal of this study is to describe the clinical-epidemiological profile of patients with IBD at Clínicas' Hospital, Federal University of Pernambuc.

MATERIALS AND METHODS: A prospective cohort study was performed. Demographic, social, and clinical data of patients in outpatient follow-up were collected from January 2011 to March 2012.

RESULTS: Of the 220 IBD patients studied, 65% had idiopathic ulcerative colitis (UC), 32.7% had Crohn's disease (CD), and 2.3% had undetermined colitis. Among cases of UC, 51.8% had pancolonic involvement. For CD cases, involvement of the terminal ileum occurred in 54.2% of patients and isolated colon occurred in 44%, with a stenosing and/or penetrating disease pattern present in 69.5% of patients. The time between onset of symptoms and diagnosis was, on average, 2 years and 4 months. There was a predominance of women, white and brown patients. The main extraintestinal manifestations were osteoarticular. Surgical procedures due to complications or clinical intractability occurred in 34.7% of patients with CD and 5.6% of those with UC.

CONCLUSION: The patients presented clinical and epidemiological characteristics similar to those found in the literature, highlighting, however, the preponderance of the most extensive forms of UC and the most complicated forms of CD. A long time for diagnosis was observed, which may have contributed to a more intense disease pattern.

Key words: Inflammatory Bowel Disease; Chron's disease; Ulcerative colitis; Epidemiology

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INTRODUCTION

Inflammatory bowel disease (IBD) is a broad term used mainly to refer to Crohn's disease (CD) and ulcerative colitis (UC), which are immunologically mediated diseases of recurrent course and responsible for some of the most severe manifestations of gastrointestinal disease[1-5]. They are characterized by chronic inflammation of the

mucosa, caused by a multifactorial etiology where different genetic, immunological, and environmental factors are involved but whose mechanisms have not yet been fully clarified[3,6-8].

The prevalence of IBD, initially described in North America and Europe, has increased around the world, with a progressive increase in publications on the subject in the last two decades and an increase in incidence in several countries in the Asia-Pacific axis and South America[9-13].

The gradual reduction of this interregional difference occurred in parallel with the greater industrialization/urbanization of cities, improvement of the population's living conditions, growth of purchasing power, change in hygiene habits, access to new diagnostic methods, among other factors[6,12,14-16].

Epidemiological studies in Brazil are few and, in general, restricted to a few regions, involving a series of cases and single hospital-based cohorts with a small number of cases[17,18,27,19-26]. More recently, an observational study using data from the Ministry of Health in a state in southeastern Brazil was conducted[28].

Prevalence and incidence rates are still unknown, although regional reports describe a significant increase in the number of cases and the emergence of outpatient units for specific care of these pathologies, as well as standardization of special medications by the health secretaries provided free of charge—indirectly indicating a probable increase in the number of cases[23,24,27-29].

Due to the limited number of publications in our region, this study aims to describe the clinical-epidemiological aspects of a cohort of patients with IBD treated at a university hospital in northeastern Brazil.

MATERIALS AND METHODS

The study is a prospective cohort of patients followed up at the outpatient clinic for inflammatory bowel disease at Clínicas' Hospital, Federal University of Pernambuco, recruited from January 2011 to March 2012. Pernambuco is the second most populous state in northeastern Brazil, with a population of about 9 million.

The diagnosis of IBD was based on the presence of clinical, radiological, endoscopic, and anatomopathological manifestations which are characteristic of CD and UC. Cases in which these characteristics were not able to distinguish one disease from the other were also included, being defined as indeterminate colitis (IC).

All patients were informed about the study and, after signing the informed consent form, were included in the study, without impairing their treatment if they declined to participate in the research.

The epidemiological aspects (demographic and social) included were: sex, age, race, place of residence (urban or rural area), and family income. Data on smoking history (current or previous) and on the existence of first-degree relatives affected by the disease were also included.

As for the clinical profile, data were extracted related to the location of the affected gastrointestinal tract segment and the disease behavior (30), the need for surgical interventions, and the presence of extraintestinal manifestations (which were classified as osteoarticular, ophthalmic, dermatological, vascular, hepatobiliary, and nephrological). The interval between the onset of symptoms and the definitive diagnosis was also addressed in this study. The proportion of individuals with Crohn's disease, ulcerative colitis, or indeterminate colitis was calculated for each of the described variables.

RESULTS

Two hundred and twenty patients were included in the study, of which 143 (65%) had idiopathic ulcerative colitis (UC), 72 (32.7%) had Crohn's disease (CD), and 5 (2.3%) had indeterminate colitis (IC). There was a predominance of females with UC and CD (Table 1). Participants' ages ranged from 12 to 84 years, with a mean age of 34.7 and 35.9 years for CD and UC respectively (Table 1). Minors under 20 years old represented 19.5% (14/72) of patients with CD; the age range with the highest number of patients was 21 to 40 years old (45.8%). For UC 13.9% of participants were under 20 years old and 53.2% were between 21 and 40 years old (Table 2).

As for race, 111 (50.4%) patients were mixed, 84 (38.2%) were white, and 25 (11.4%) were black.

Regarding place of residence, 38.6% came from the state capital (Recife), 19.9% came from the metropolitan region (Jaboatão dos Guararapes, Paulista and Olinda), and 41.5% from inland cities.

In the analysis of family income, the minimum wage in the region was considered as a reference at the time of $177 (R$ 622.00), with 129 patients (58.7%) with an income below minimum wage, 43 (19.5%) patients between 2 to 4 salaries, and 48 (21.8%) greater than four salaries.

Current or previous smoking history was reported by 33.3% (24/72) of patients with CD and 36.4% (52/143) of patients with UC. For patients with stenosing/penetrating and inflammatory forms, smoking history was present in 33% (18/50) and 22% (5/22) respectively.

Regarding family history, 5 (7.0%) patients with CD reported having first-degree relatives affected by the disease and, among cases of UC, 10 (6.9%) had first-degree relatives with the disease. No patients with IC reported a family history of the disease.

As for the interval between the onset of symptoms and a definitive diagnosis, an average of 29.3 months was observed in CD, with a median of 48 months, and an average of 27.1 months was observed in UC, with a median of 12 months.

According to the Montreal Classification of the disease in terms of the location of the affected gastrointestinal tract segment, colonic involvement in CD was most common and was present in 44.4% (23/72) of patients. Ileocolonic involvement was present in 32% (23/72) and isolated ileac in 12.5% (9/72) of patients (Table 2).

In the analysis of disease behavior, the stenosing form present in 30.5% (22/72) was most prominent, followed by the non-stenosing/non-penetrating or inflammatory form in 30.5% (22/72), penetrating isolated in 13.9% (10/72), associated with fistulas 19.5% (14/72) of patients, and mixed forms: stenosing and penetrating in 2.8% (2/72); 2.8% (2/72) with a stenosing and penetrating form with perianal involvement (Table 2).

With regard to the extent of disease involvement in UC, 51.8% (74/143) of patients had pancolitis, 42.6% (61/143) had left colitis, and 8 (5.6%) had proctitis (Table 5). Of the five individuals with IC, 1 (20%) had disease restricted to the rectum, 2 (40%) had left colitis, and 2 (40%) had pancolitis.

Extraintestinal manifestations were present in 112 (50.9%) patients with IBD, in 31 (43.6%) with CD, and in 77 (54.2%) with UC (Table 3), some of the patients with more than one extraintestinal manifestations.

Surgical history due to disease complications or clinical intractability was present in 25 (34.7%) patients with CD, in 8 (5.6%) patients with UC, and in one (16.6%) of those with IC. Five (3.5%) patients with UC received a total proctocolectomy.

DISCUSSION

IBD has been described in the USA and Europe—whose populations are predominantly Caucasian—as having a high incidence rate,

which was not described in developing countries on the Asia-Pacific axis or in South America. However, in recent years there has been a progressive increase in publications on the subject in these countries, indicating a possible increase in the incidence of the disease or a higher rate of diagnosis in these locations[5,13,31].

Although Brazil is a country with continental dimensions and more than 200 million inhabitants, there is still no estimate on the prevalence or incidence of inflammatory bowel diseases in the country. Studies that do exist have been hospital-based, with little representation, limited to a few regions of the country, evaluating different aspects of the disease, with no uniformity to establish a pattern of the disease[17,18,27,19-26]. In a study analyzing a database of government programs for the supply of medicines in São Paulo, Brazil between 2012 and 2015, prevalences of 24.5 and 28.5 per 100,000 inhabitants were found respectively for UC and CD[28]. In northeastern Brazil, another hospital-based study analyzed 252 patients and estimated a prevalence of 12.8 cases per 100,000 inhabitants[24]. However, the different methodologies for collecting information, combined with studies limited to a few locations, makes it challenging to estimate the real frequency of this disease in different regions of the country.

In addition, there are no official national data on the incidence or prevalence of the disease, as these are not compulsory reporting diseases, and accurate information on newly diagnosed cases is not available.

In this study, we describe the clinical-epidemiological pattern of 220 IBD patients recruited over a period of 14 months in a reference hospital in the state of Pernambuco, located in northeastern Brazil. In the same region, there are two other large public hospitals that have reference outpatient clinics for the care of IBD patients, which suggests that this is not a rare disease in our country and reinforces the need for further studies.

There was no correlation between racial phenotype and the occurrence of IBD, with a predominance of non-whites (mixed and blacks) and with 38.2% of the white race. These findings are in line with the general population of this region (with high miscegenation) and are similar to other studies carried out in the Northeast[20,23,24]. Despite the prevalence of the disease described among Caucasians, the increase in cases in different ethnic groups has been reported in Asia and Latin America[11-13,32].

In the present study, a majority of cases were RCU (65%) compared to CD (32.7%), consistent with most national and international studies[11-13]. The incidence of UC is greater than that of CD worldwide except in Canada and some places in Europe[10,13,32]. These results are consistent with a study by Parente, *et al* conducted in another region of northeastern Brazil, involving 252 patients, with 60.3% diagnosed with UC. In another study conducted in southeastern Brazil, the frequency of UC was slightly lower, accounting for 53.8% of the cases analyzed[23,28].

As for gender distribution, females outnumbered males in this study, significantly for UC.

The literature reports an equal occurrence of the disease for both genders, or a slight predominance of CD in women and UC in men[10,32,33]. However, these data are not uniform, with large variations according to the age group analyzed, and with reports of a higher incidence of UC in men in Europe and North America in the 45 and older age group[31]. In the Asia-Pacific region, population studies show that both UC and CD are more common in men than in women[11,31].

This study found a ratio of approximately 2:1 between women and men with UC, similar to the results described by Parente *et al* in Piauí (also in the northeast region of Brazil)[24]. A study carried out with 178 patients at a university hospital in southeastern Brazil showed no statistical differences despite the predominance of gender[24,27]. These results are in contrast with the results of Gasparini *et al* who found a statistically significant predominance of females, both with CD and UC, representing 57.9% and 61.3% of the cases respectively[28]. There is no clear evidence for the emergence of gender differences between regions with genetic factors, hormonal factors, and environmental exposure influencing the differences[31,34,35].

There was a predominance in this study of whites and mixed patients (who represent the ethnic majority in the region), which is consistent with other national studies[18,22,24,27]. Santana *et al* studied patients with CD in Salvador-Bahia—the Brazilian state with the highest number of Afro-descendants—and found a predominance

Table 1 Demographic and clinical characteristics of patients with IBD.

Demographic variables		IBD Phenotype			
		UC† [N (%)]	CD‡ [N (%)]	IC§ [N (%)]	Total [N (%)]
Gender	Male	52 (36)	35 (49)	3 (60)	130 (59)
	Female	91 (64)	37 (51)	2 (40)	90 (41)
Age	Average				
	≤ 20 years	20 (13.9)	14 (19.5)	1 (20)	35 (15.9)
	21 to 40 years	76 (53.2)	33 (45.8)	2 (40)	111 (50.5)
	41 to 60 years	42 (29.4)	23 (31.9)	2 (40)	67 (30.5)
	> 60 years	5 (3.5)	2 (2.8)	0	7 (3.2)
Race	Mixed	71 (49.7)	36 (50)	4 (80)	111 (50.5)
	White	49 (34.3)	34 (47.2)	1 (20)	84 (38.2)
	Black	23 (16)	2 (2.8)	0 (0)	25 (11.4)
Family history of IBD¶	Positive	10 (6.9)	5 (7)	0	15 (6.8)
	Negative	106 (74.2)	45 (63.4)	3 (50)	154 (70)
	NI	27 (18)	21 (29.6)	3 (50)	51 (23.2)

†: ulcerative colitis; ‡: Chron's disease; §: indeterminate colitis; ¶: inflammatory bowel disease. UC: ulcerative colitis CD: Chron's disease IC: indeterminate colitis IBD: inflammatory bowel disease.

Table 2 Clinical characteristics of patients with CD‡ and UC† according to the Montreal Classification.

Clinical phenotype		N	%
	Crohn's disease		
Age at diagnosis	A1: ≤ 16 years	8	11.1
	A2: 17-40 years	39	54.2
	A3: >40 years	25	34.7
Location of the disease	L1: ileal	9	12.5
	L2: colonic	32	44.4
	L3: ileocolonic	23	32
	L4: isolated upper disease	0	0
	L1+L4	4	5.5
	L2+L4	1	1.4
	L3+L4	3	4.2
Disease behaviour	B1: non-stricturing, non-penetrating	22	30.5
	B2: stricturing	22	30.5
	B3: penetrating	10	13.9
	B3+p: penetrating + perianal	14	19.5
	B2 + B3	2	2.8
	B2+B3p	2	2.8
	Ulcerative colitis		
Extent	E1: ulcerative proctitis	8	5.6
	E2: left sided UC	61	42.8
	E3: extensive UC (pancolitis)	74	51.8

†: ulcerative colitis; ‡: Chron's disease.

of the disease in the non-white population (67.7%) compared to the white population (32.3%). These studies present an ethnic profile similar to the population residing in the region, in a country with continental dimensions and variable miscegenation with no apparent correlation of racial phenotype with the occurrence of IBD[21].

Regarding family history of IBD, only 6.9% of those with UC and 7.0% of those with CD had an affected first-degree relative. In European countries and the United States, this frequency can be greater than 15-20%, with frequencies less than 10% in eastern countries[8,36-38]. Although the study found frequencies similar to those in Asian countries, the low frequency of affected relatives may also be related to the difficulty of accessing this population's public health network, depriving symptomatic individuals of a possible diagnosis.

The period between the onset of symptoms and a definitive diagnosis was quite long, with an average of 29.3 months for CD and 27.1 months for UC. Patients with CD had a longer interval between the onset of symptoms and their diagnosis compared to patients with UC. The results are above the average described in studies in developed countries[5,39,40]. In a multicenter study in Western Europe, the average was 2 months for UC and 4.6 months for CD[5]. A study in the southeastern region of Brazil diagnosed IBD in less than a year, but another study in the northeast had results similar to the present study with an average of 25.1 months[26,27,28].

One factor that may have contributed to the delay in the diagnosis of CD and UC is the precariousness of public health care in the northeastern region, which has few referral services, few trained professionals, and a lack of diagnostic tests, making patients wait longer than necessary for the nosological definition of their case.

When assessing the age distribution at the onset of symptoms, patients in this series were predominantly young adults between 21 and 40 years old, with a second peak in the 40 to 60 age group, similar to epidemiological studies in Asia-Pacific and Brazil[11,28,41].

The affected gastrointestinal location in patients with CD was predominantly colonic (44.4%), in contrast to data from other countries where the ileocolonic form was most common[13,42-44]. Results similar to those in the literature have also been reported by Brazilian studies where ileocolonic (L3) or isolated ileal (L1) types were most common, followed by colonic (L2)[19,21,45]. This differs from the study by Parente et al, where colonial involvement was predominant[24].

This study found a predominance of the penetrating form and its associations (B3, B3p, B2 + B3, B2 + B3p), with the perianal fistula most associated with the penetrating disease (B3p). These findings are similar to the studies by Santana *et al* in Bahia (located in northeastern Brazil), with 55.4% of patients presenting the B3 form. In the literature, there is a predominance of the inflammatory pattern in CD, exceeding 60%. This study also found that 37.7% of patients with CD have already undergone some surgical procedure due to the presence of complications[5,8,13,24,41,45].

It is possible that these findings occurred due to the late diagnosis, which resulted in a delay in treatment and unfavorable evolution of the condition (associated with the fact that participating patients came from a referral service where patients with more aggressive disease are referred). In the multicenter study, Cantoro found that delayed diagnosis for more than 24 months was associated with a higher risk of more aggressive behavior (B2 + B3) of the disease[40].

As to the extent of UC involvement, this study found that the majority (51.8%) of patients had pancolitis (E3), which is in contrast with the literature, where pancolitis represents 20 to 30% of UC cases[5,27,42]. Other studies in Spain and Australia found that pancolitis predominated[37,46]. One reason for the difference in these results may be related to the fact that participants in this study belong to a reference outpatient clinic in IBD, where patients with a more aggressive disease are referred.

Table 3 Occurrence of extraintestinal manifestations in patients with CD‡ and UC†.

Manifestation type		CD n (%)	UC n (%)
Osteoarticular	Arthralgia	11 (15.2)	50(34.9)
	Arthritis	12(16.6)	19(13.2)
	Ankylosing spondylitis	1(1.4)	1(0.7)
	Sacroiliitis	1(1.4)	2(1.4)
Ophthalmic	Uveitis	3(4.2)	0
	Conjunctivitis	0	1(0.7)
	Episcleritis	0	0
Dermatological	Canker sores	3(4.2)	0
	Erythema nodosum	4(5.5)	2(1.4)
	Psoriasis	0	0
	Gangrenous pyoderma	1(1.4)	3(2.1)
Vascular	Thrombotic phenomena in the lower members	1(1.4)	7(4.9)
Hepatobiliary	Biliary lithiasis	4(5.5)	0
	CEP	0	13(9.1)
Nephrological	Renal lithiasis	3 (4.2)	4 (2.8)
Total		72	143

†: ulcerative colitis ‡: Chron's disease.

The present study identified frequent extraintestinal involvement in cases of CD (43.6%) and UC (54.2%). Extraintestinal manifestations occur in 5 to 47% of patients with IBD, increasing morbidity in patients who may manifest it along with intestinal symptoms or have the extraintestinal symptoms preceding the intestinal by months to years and often requiring a high degree of diagnostic suspicion[32,42,43,45,47,48]. Studies carried out by Torre *et al* and Souza *et al* in São Paulo, Brazil found extraintestinal manifestations of 16% and 26.9% respectively[27,45].

Arthralgia and arthritis were the most frequent manifestations found in 31.4% of patients with CD and 48.1% of patients with UC. Primary sclerosing cholangitis (PSC) was observed only in 13 patients (9.1%) with UC. This frequency is higher than the 1 to 5% of IBD cases reported in the literature[5,37,43,49,50].

The results of this study showed a predominance of UC, with a higher frequency of females with both UC and CD, with the majority of cases affecting individuals under 40 years of age, followed by individuals aged 40 to 60 years. The time elapsed between the onset of symptoms and the definitive diagnosis was quite long; this delay may be related to difficulty in accessing the public health system in the northeastern region.

The gastrointestinal location in patients with CD was predominantly colonic, with a predominance of the penetrating form and its associations, which differs from findings in other countries and which may be a consequence of late diagnosis and treatment. In UC, there was a predominance of pancolitis. Extraintestinal manifestations occurred in more than 40% of patients, with articular manifestations most common and an increased frequency of primary sclerosing cholangitis.

The study provided important information on the clinical-epidemiological profile of patients seen at a health unit located in northeastern Brazil, reinforcing the need to trace the profile of the disease in different regions in a country with continental dimensions in order to improve understanding of these diseases, to foster strategies that reduce delays in diagnosis, and to promote an effective therapeutic approach to treatment.

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