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Epidemiological Profile of IBD in the Northern Region: "Pilot Study"

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Abstract **Original Research Article**

Inflammatory bowel disease (IBD) refers to three chronic inflammatory disorders, ulcerative colitis (UC), Crohn disease (CD) and indeterminate colitis. Classically IBD is described as a disease of rich countries, and historical data on the geographical distribution of IBD around the world have shown a high incidence and prevalence in high-income countries, like Northern Europe and the USA. More recently, IBD emerged with increasing frequency in many parts of the planet especially in developing countries [1], including Morocco, becoming a global infection. UC remains more frequent than CD except in certain countries including France [2]. Although progress has recently been made, particularly in the genetic field, in understanding their physiopathology, the cause(s) of these two diseases remains unknown to date. A better knowledge of the descriptive epidemiology of IBD, in particular the differences in incidence in relation to time, age or geographical distribution, can lead to etiological leads. Study the epidemiology of IBD is a challenge, in part because it is difficult to diagnose, but it is important because of its direct and indirect costs. Data from Moroccan studies remain rare. Our study on the epidemiology of inflammatory bowel disease (IBD) is the first in the northern region.

Keywords: Chronic Inflammatory Bowel Diseases (IBD), Crohn's disease (CD), ulcerative colitis (UC), Epidemiology.

INTRODUCTION

Chronic Inflammatory Bowel Diseases (IBD), practically Crohn's disease (CD) and ulcerative colitis (UC) are multifactorial chronic inflammations of the digestive tract reaching exclusively the rectum and the colon for UC and the gastrointestinal tract anywhere from mouth to anus, with an ileocecal predilection for CD. They affect people of all age groups around the world. Although the incidence of the disease is stabilizing or decreasing in most countries of the Western world, it continues to increase in developing countries. In Morocco, IBD are not notifiable diseases. Therefore, we have no data on the incidence and prevalence of CD and the CU. The creation of a national register of IBD, by Moroccan Society of Digestive Tract Diseases SMMAD, has just been created and our data will be useful for having a pilot epidemiological vision at the level of the northern region. The aim of the present study was to describe, for the first time, the epidemiological characteristics of IBD in north region of morocco.

PATIENTS AND METHODS

A descriptive epidemiological study, retrospective and prospective, spread over three years between March 2019 and March 2022. Patients residing in the northern region presenting symptoms compatible with IBD confirmed by endoscopy, histology and radiology are included, and those known to have IBD referred from other university hospitals for follow-up for reasons of proximity. Clinical, endoscopic and radiological data are extracted from medical records through the operating form. The phenotypic characteristics of the disease were classified according to the Montreal IBD classification. The severity of the disease flare is assessed by True loves score for inaugural colitis, the clinical CDAI and Mayo score for CD and UC, respectively. The data was conducted using SPSS software.

RESULTS

During the study period, a total of 164 cases were diagnosed for IBD. They were divided into 78 women and 86 men sex ratio 1, 1. The mean age at diagnosis was 35 years [9–75 years] (Figure 1 A); six were children (4%), one patient had a history of a brother with IBD. Most of our patients are from urbain areas 70% and 30% from rural areas (Figure 1 B), patients have the RAMED as coverage in 70 % (n=115), only 30% (n=49) have the CNOPS or the CNSS. Total of 100 cases (61%) were diagnosed

crohn's disease, with a female predominance of 62%, ulcerative colitis (UC) in 44 patients (27%), predominant in men 80%, and indeterminate colitis was present at 12% (n=20) (Figure 2A, 2B). 35% (n=58) patients are smokers or have a history of smoking, among those 69% have Crohn's disease and 31% have UC (Figure 3a). 12% of our patients (n= 20) were appendectomized and are diagnosed with Crohn's disease in 80% (Figure 3b).

According to our study, diarrhea proved to be the main symptom in all forms of the disease, IBD [UC (90%) and CD (70%)] and indeterminate colitis (60%) followed by abdominal pain such as the syndrome de Koening in 68% of CD, rectal bleeding in 87% of patients with UC, dysenteric syndrome reported by 56% and 40% of our patients with UC and CD respectively. The presence of mucus in the stool is mainly observed during Crohn's disease (40%), vomiting is present in 35% of our patients, constipation in 72%, loss of appetite and weight in respectively 51 % and 65% during the first push (Table 1).

CD was ileocolic (L3) in 60%, colonic (L2) in 23%, ileal (L1) in17 % (Figure 4 A), and had a stenosing (B2) or fistulizing (B3) phenotype in 30% and 23% respectively. 27patients (27%) had anoperineal manifestations. Among those with UC, 10 patients had pancolic involvement (23%), Distal involvement was present in 12% (n=5), left colitis in 65%of cases (n=29) (Figure 4 B).

According to Truelove and Witts score, the initial attack was considered severe in 21% of cases (n=35), moderate in 47% (n=78) and the rest of the patients who consulted for follow-up with inactive disease (Figure 5 A). The average duration of diagnosis is 6 months, its better than3 months in 114 patients, between 1 month and 3 months in 35 and only 15 patients were diagnosed before one month (Figure 5 B).

The treatment of the severe attack was based on injectable corticosteroids, antibiotic therapy, iron and albumin supplements and nutritional support in the majority of patients, associated with topical treatment in 23 % (n= 8) patients with UC. Nine were treated with biotherapy; recourse to surgery is envisaged in only one patient with CD. The duration average stay was 5 days with extremes ranging from 3 days to 5 weeks (Figure 6 A).

For maintenance treatment, 50% of patients were put on azathioprine, 10% on 6-mercaptopurine, 4% on methotrexate, 26% on aminosalicylates, and only 10% who are on biotherapy despite it being indicated in 66% of cases (Figure 6 B).

Over an average surveillance period of one year, 79% of patients remained in remission, 12% developed corticosteroid dependence. 9% (n=15) had complications: refractory proctitis in a single patient, 7 patients with active fistulizing crohn and 5 others with stenosing phynotype which are operated (n=4) in the absence of means to procure biotherapy, and sadly we had 2 deaths (CD) in our serie (Figure 7).

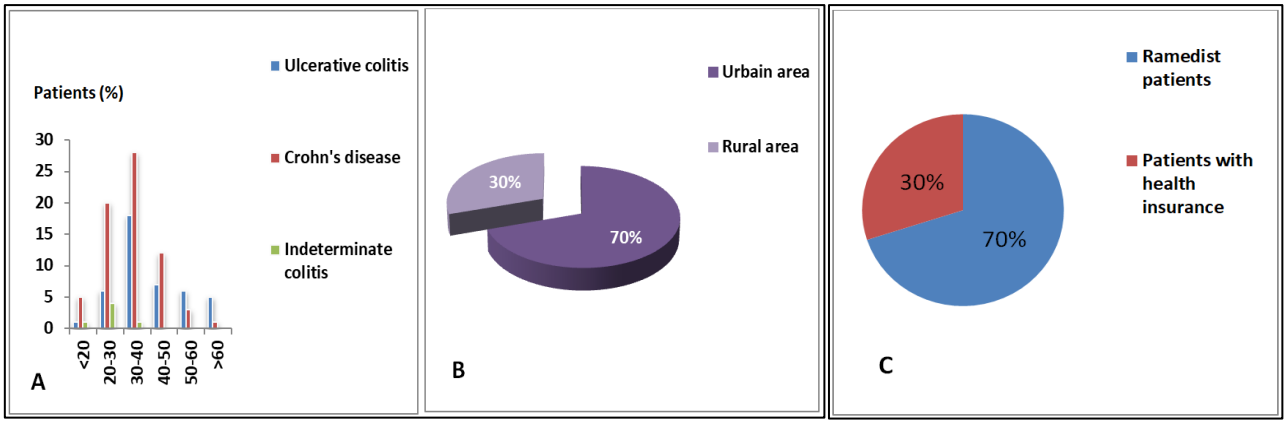

Figure 1: **Distribution of patients according: A) their age (years). B) Type of disease and living environment. C) Medical cover**

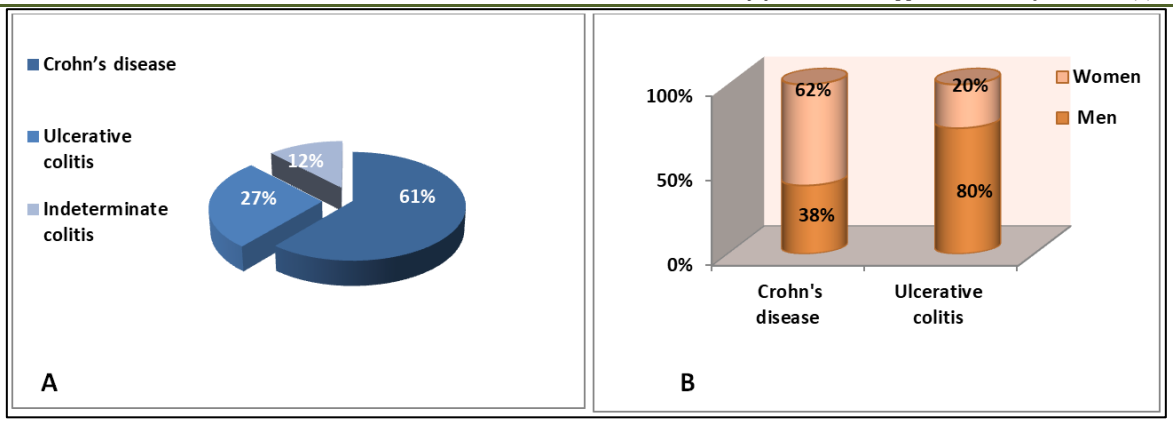

Figure 2: Distribution of patients according to: A) type of disease. B) Gender

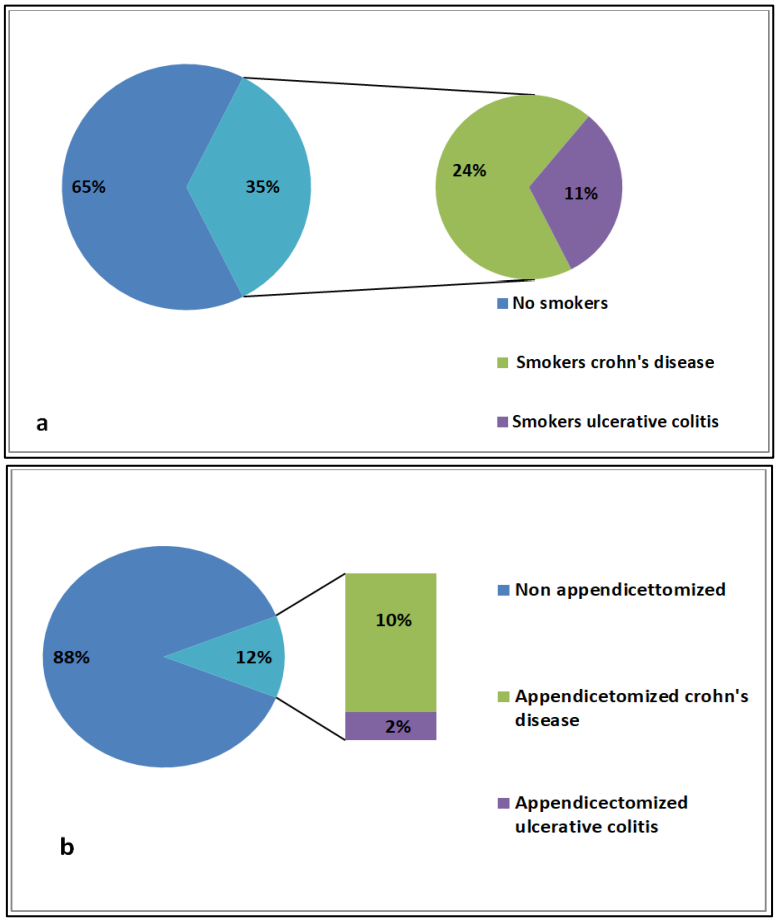

Figure 3: Distribution of patients according to: a) tobacco profile. b) appendectomized status.

Table 1: Distribution of patients according to the incidence of clinical manifestations

Constipation	Ulcerative colitis (%)	Crohn's disease (%)	Indeterminate colitis (%)
Diarrhea	90(n = 148)	705(n=114)	60(n=98)
Koening syndrome	0	68(n=111)	70(n=114)
Dysenteric syndrome	56(n=92)	40(n=66)	20(n=33)
Rectal bleeding	87(n=143)	12(n=20)	5(n=8)
Mucus in stool	10(n=16)	40(n=66)	25(n=41)
Constipation	12(n=20)	20(n=33)	40(n=66)
Vomiting	5(n=8)	15(n=25)	15(n=25)
Weight loss	20(n=33)	35(n=57)	10(n=16)
loss of appetite	15(n=25)	30(n=49)	6(n=10)

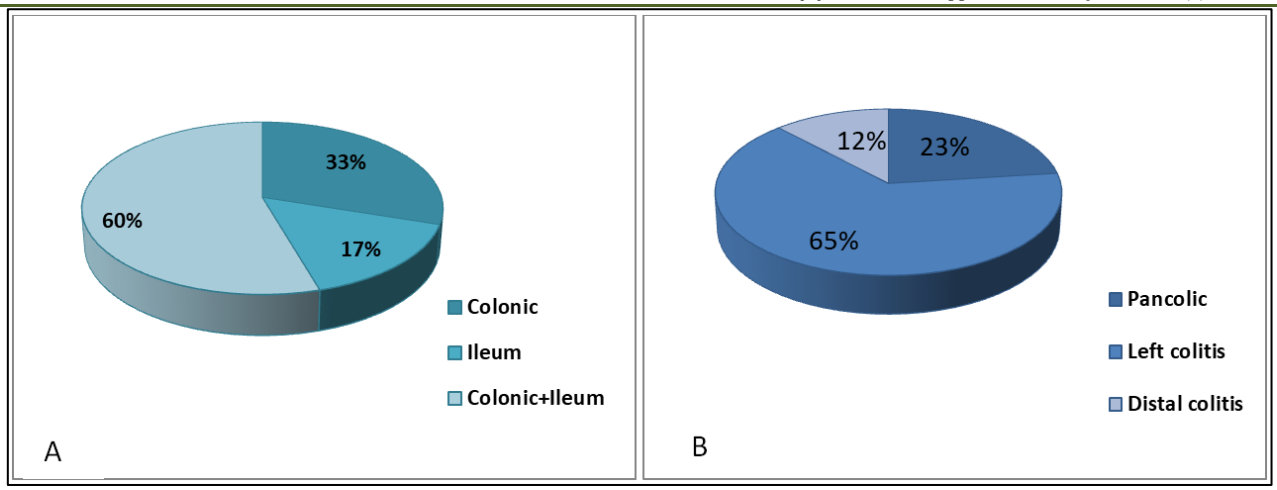

Figure 4: Distribution of patients according to the location of Crohn's disease (A), and ulcerative colitis (B)

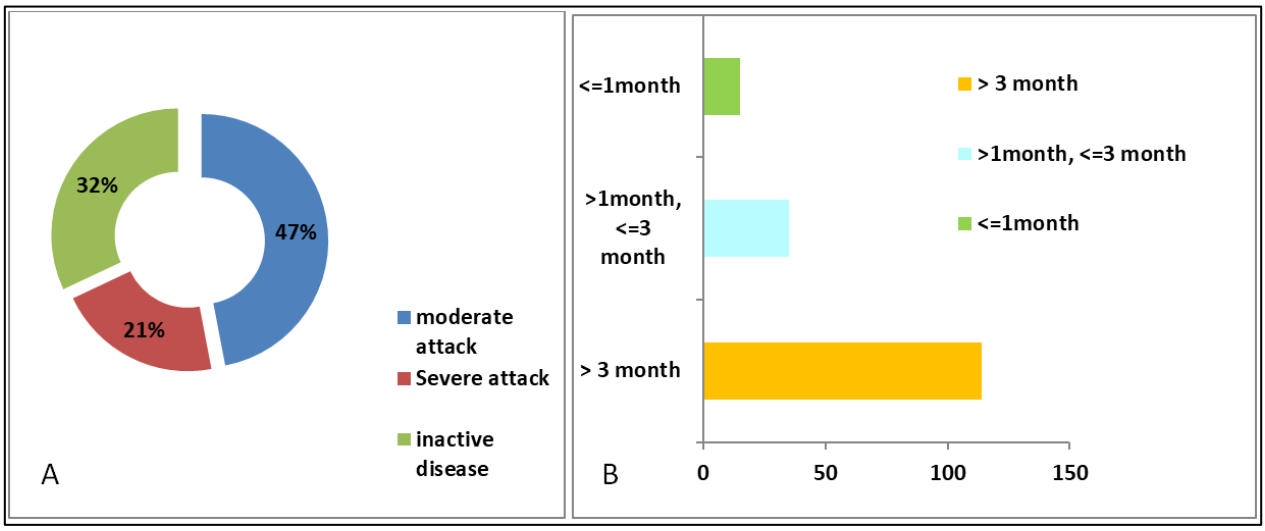

Figure 5: A) Activity of the first push according to the score of true loves. B) The diagnostic delay: time elapsed between the first attack and the diagnosis

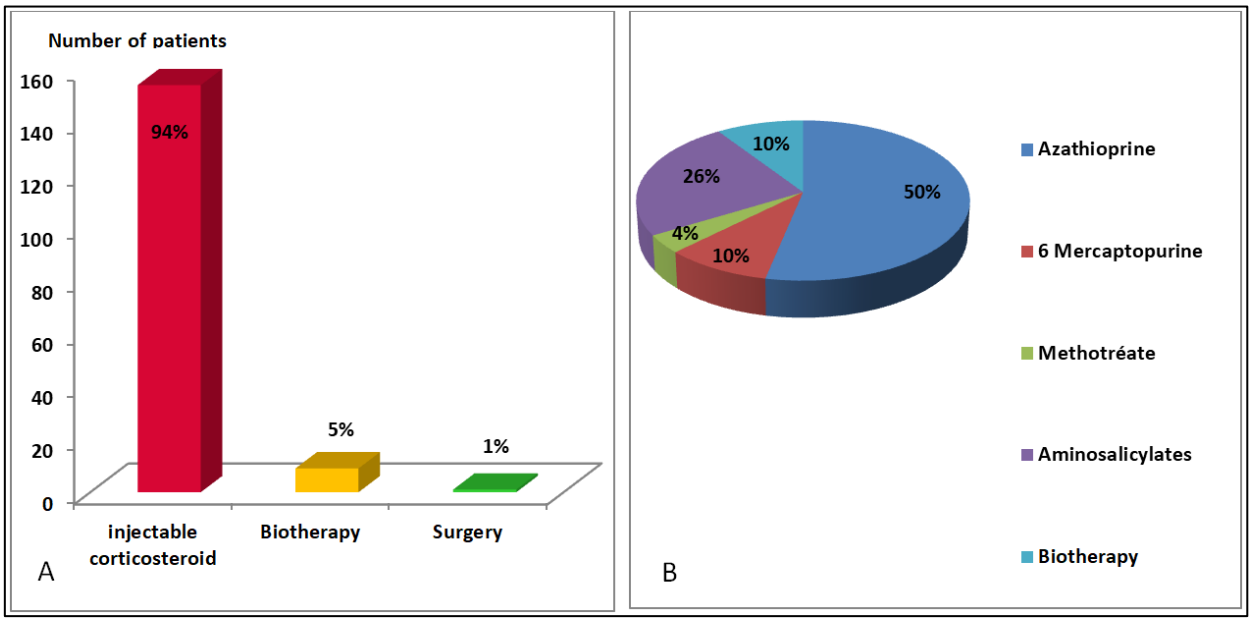

Figure 6: Treatment modalities: A) for the first flare-up. B) Maintenance

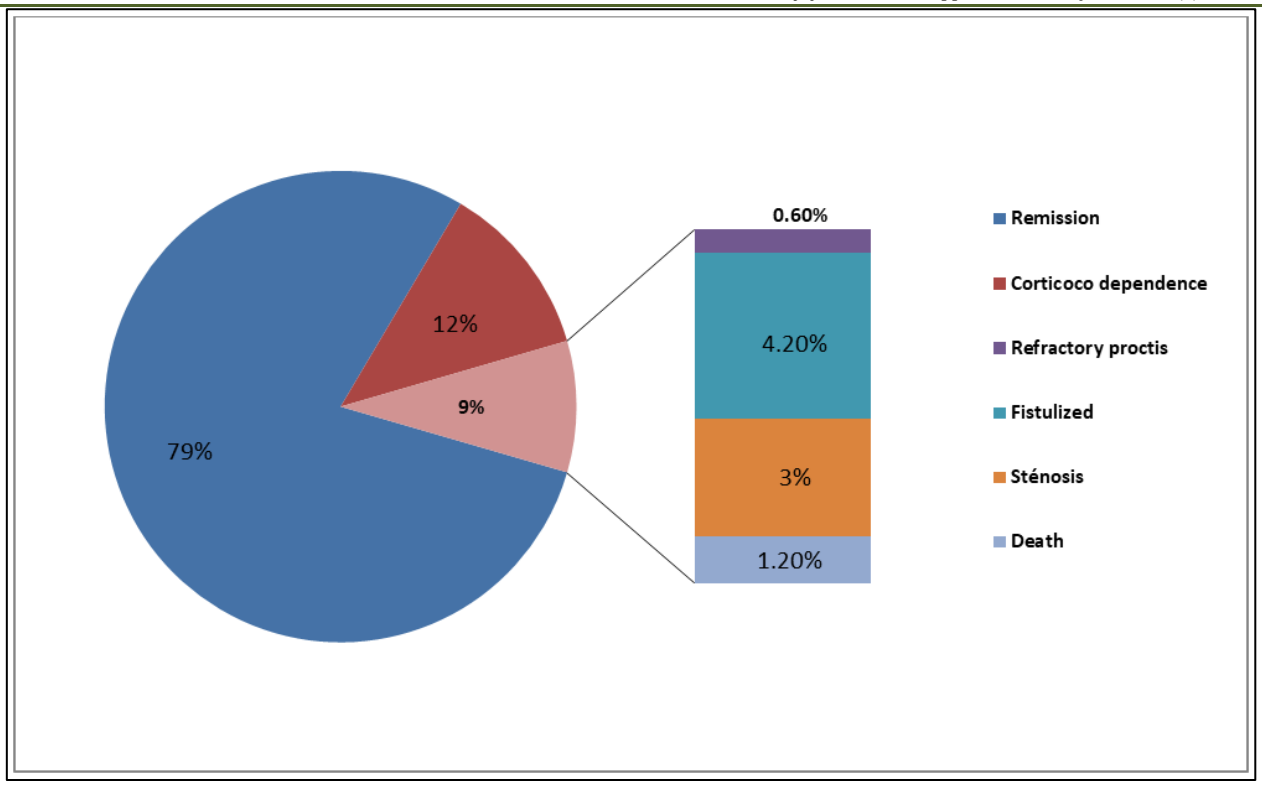

Figure 7: Evolution of the disease during one year of surveillance

DISCUSSION

The geographical distribution of IBD in the world has changed in recent years, while it was more frequent in industrialized countries; recent studies show an emergence of IBD low- and middle-income countries [3].

Our study shows that CD (61%) is more predominant than UC (27%), in 12% it is not possible to decide during the first attack between the diagnoses of CD and UC on the arguments usual endoscopic and histological examinations this entity is labeled according to the Montreal classification of indeterminate colitis or unclassified IBD. This makes the difference with Europe for example where the average prevalence of CD on the latest data in the general population is around 200/100,000 inhabitants while that of UC is significantly higher, around 250/100,000 inhabitants, exept France where CD is more common than UC with incidences of 7.8 and 4.8/10^5habitants respectively [4, 5].

This is consistent with a study conducted in the hepato-gastro-enterology department of the CHU IBN-SINA in Rabat “medical clinic B” about 300 cases which reported a higher prevalence of CD (58%) compared to UC (42%) [6]. These differences between countries can be explained by the emergence and increase in the incidence of CD while that of UC has remained stable since the 1980 [7] and may reflect the involvement of environmental risk factors and genetic predispositions, such as the NOD2 mutations implicated in the occurrence of CD [8].

The average age at diagnosis was 35 years with a peak frequency between 20 and 40 years, the patients were mostly aged 30 to 40 years. The highest frequency was at 20-30 years for CD, 30-40 for UC, in patients older than 50 years UC showed a trend of increased incidence compared to CD unclassified IBD is observed mainly during the first period between 20-30 years. The pediatric population represents 4% of our series, which joins the studies made on IBD in pediatric populations whose threshold does not exceed 10% of IBD diagnoses with an incidence that continues to increase [9, 10].

These results are consistent with those of national and international studies, which show that IBD are diseases that usually begin in the second-to-third decade of life [3, 6, 11, 12].

Regarding the gender distribution of patients with IBD, our patients were divided into 78 women and 86 men sex ratio 1.1, there is a female predominance in the CD group and mal predominance for UC; Ulcerative colitis (UC) [M: F: 35 (80%): 9 (20%)] and Crohn's disease (CD) [M: F: 38 (38%):62 (62%)], which joins the global results with female predominance in Crohn's disease and male predominance for UC [13] which led to the hypothesis of the role of endogenous or exogenous hormonal factors in CD pathophysiology.

In our study, a high incidence of IBD was reported among the population from urban areas as compared to rural areas (70% &30 %), which pleads for the protective effect of rurality on the risk of IBD, which is greater in the case of rurality induring the first 5 years of life [14]. However Saurabh *et al.,* reported that there was not much significance of residency factor in the distribution of prevalence of UC and CD [15]. The socio-economic level is low, thus 70% of cases benefit from RAMED as social coverage, and from CNOPS and CNSS in 15% each.

Our series, presents a frequency of smoking at 35% distributed in 24% (n= 40) in CD, UC in 11% (n= 18), joining most of the studies, which have shown the protective role of tobacco in the UC [16] and its risk which is twice as high as in non-smokers in CD; this risk is independent of the quantity of cigarettes consumed, and it decreases as soon as you quit smoking but only disappears after 4 years of weaning [17, 18]. Tobacco use worsens the course of the disease and increases the number of flare-ups. Many theories have been proposed to explain the role of tobacco in IBD and its opposing effects on UC and Crohn's disease. The effects of tobacco depend on genetic terrain and may vary depending on the susceptibility genes present in a given individual. Tobaccoexposure of mice deficient in interleukin (IL)-10 or NOD2 accelerates the development of colitis or ileitis, but has no effect in normal mice [18]. Tobacco constituents and products of its consumption/combustion, such as carbon monoxide orfree radicals, is among the factors proposed to explain its deleterious effect. Smoking can lead to epi-genetic modifications altering the expression of certain genes involved in immune responses and autophagy. It can also modify the composition of the microbiota. Carbon monoxide inhibits secretion of pro inflammatory cytokines. Tobacco and nicotine increase endoplasmic reticulum stress, and reduce the production ofpro-inflammatory cytokines (IL-8, TNFα), IL-2 and IL-10.During UC, there is a decrease in the production of mucus glycoproteins and an increase in colonic permeability. Tobacco increases mucus thickness and reduces colonic mucosal permeability, which may help protect patients with UCor likely to have it [19].

Regarding the distribution of appendectomies of patients with IBD, we observed that 12% of our patients (n= 20) were appendectomized at the time of diagnosis, among those 80% are with CD versus 20% with UC. However, the determination of the age of appendectomy was difficult since the patients forgot the age at which they underwent the intervention. This result joins studies showing the protective role of appendectomy on the occurrence of UC, especially if it is performed before the age of 20; [20, 21]. Once UC is declared, the benefit of an appendectomy performed with the aim of attenuating the disease is not established. In the case of Crohn's disease, studies have shown that patients with ileocecal involvement more often an appendectomy in the months or years preceding the diagnosis, suggesting that the surgical indication is carried for an ignored Crohn's disease, and the appendectomy has no protective role against Crohn's disease [22].

The clinical presentation is pleomorphic. according to our study diarrhea proved to be the most frequent clinical manifestation in all forms of the disease, IBD [CU (90%) and MC (70%)] and non-IBD (60%) followed by abdominal pain such as Koening syndrome in 65% of CD, rectal bleeding in 87% of patientswith UC, dysenteric syndrome and weight loss are reported respectively by 56% and 40% of our patients. the presence of mucus in the stool (25%), vomiting (20%) was present in(20%), constipation in12%, and all our patients report loss of appetite and weight during the first push. These results were comparable to literature studies reported by various other authors [23, 24].

For patients admitted for inaugural symptoms, the attack was classified according to the Truelove and Witts score severe in 21 (n=35), moderate in 47% (n=78), the rest of the patients consulted for monitoring of their diseases which were scored inactive. The median delay between onset of symptoms and diagnosis was 6months. This lengthened delay compared to that of other studies (3 months) [25], is probably due to the difficult access to care and proximity to hospital structures of the rural population which is dominant in our series.

The ileocolic L3 localization of CD is the most frequent (60%) followed by the pure colonic L2 form (23%) and the ileal L1 form in 17%. The phynotype is stenosing in 30%, fistulizing in 23%. 27% of patients had anoperineal manifestations. This result is consistent with the Moroccan study[6], which showed a predominance of ileo-colic topography, whereas in most series of the literature ileo-colic, colonic, and ileal involvement occur in equal proportions [26]. Perianal involvements are initially observed in less than a quarter of patients, according to data from the literature [27, 28].

Among patients with UC, 10 patients had pancolicE3 involvement (23%), distal E1 involvement was present in 12% (n=5), left colitis E2 in 65% of cases (n=29); In the literature [29] the distal form is the most frequent 65%, followed by left involvement 15% and then pancolic UC 20%, The clear dominance of the left colic form of UC in our study is explained by the extended diagnostic delay allowing time for the inflammatory process to extend into the colon retrogradely from the rectum.

In terms of treatment, severe attacks were controlled by injectable corticosteroids, antibiotic therapy, iron and albumin supplements in the majority of patients, associated with topical treatment in 23% (n = 8) of patients with UC. Nine were treated with biotherapy after failure of the previous protocol; recourse to surgery is envisaged in a single patient with CD. The average length of hospital stay was 5 days. Maintenance treatment is essentially based on azathioprine in 57% of our patients, 10% were put on 6-mercaptopurine, 4% on methotrexate, 26% on aminosalicylates and only 10% are on biotherapy when it is indicated in 66% of cases, given that most patients do not have the means to obtain biotherapy.

After one year by monitoring, 79 % of patients remained in remission, 12% developed corticosteroid dependence. 9 %(n=15) had complications: refractory proctitis in a single patient, 7 patients with active fistulizingcrohn and 5 others with stenosingphynotype which are operated (n=4) in the absence of means to procure biotherapy, and sadly we had 2 deaths (CD) in our serie; they had severe malnutirition with extensive localization of the disease.

In terms of mortality, the data from other series did not show any excess risk in the event of UC compared to the healthy population [30], while Crohn's disease slightly increases the risk of mortality, particularly in relation to extensive forms of hail, malnutrition, surgical complications, cancer, tobacco which is frequent in this population.

CONCLUSION

According to our study CD is more common than UC; women are more affected by Crohn's disease, men by ulcerative colitis. The young population is frequently affected. The fistulizing phenotype with ano-perineal manifestations is quite frequent requiring biotherapy which constitutes a major financial challenge in our practice, other studies are necessary for a good epidemiological approach at the end of IBD in Morocco, in order to orient the visions of health programs towards these conditions which affect an active population.

Abbreviations:

- IBD: Inflammatory bowel disease.
- UC: Ulcerative colitis.
- CD: Crohn's disease.
- SPSS: Statistical Package for Social Sciences.
- RAMED: Medical assistance scheme for the economically underprivileged.
- CNOPS: The national fund of social security organizations.
- CNSS: National Social Security Fund.
- CDAI score: Clinical disease activity score.

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