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Clinical Profile and Analysis of Biological Markers (Fecal Calprotectin and CRP) during Relapse of Inflammatory Bowel Diseases in a Population of Adults

Asma Nassar [a*], Amina Alliouch -kerboua [a], Hacene Meriche [a], Nassima Sabiha Gadiri [a] and Frida Chettab [b]

[a] Department of Immunology, Clinique Saint Therese UHC, Annaba, Algeria.
[b] Department of Gastroentero-Hepatology, Hospital Ibn Sina UHC, Annaba, Algeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Inflammatory bowel diseases (**IBD**) are increasingly common pathologies, affecting both adults and children. This study investigates the clinical and epidemiological characteristics of IBD among patients at the gastroentero-hepatology department of Annaba University Hospital. Conducted from

**Corresponding author: E-mail: nassarasma20@gmail.com;*

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February 2023 to September 2024, the prospective descriptive analytical study included 77 patients diagnosed with IBD, focusing on the role of biological markers, specifically C-reactive protein (CRP) and fecal calprotectin (FC), in non-invasive disease assessment.
Inclusion criteria were based on clinical, endoscopic and histological assessments. Demographic data, clinical manifestations, CRP and **FC** levels were analyzed.
Among the 77 patients, 53 patients or 68.9% had Crohn's disease (**CD**), while 24 patients or 31.1% suffered from ulcerative colitis (**UC**). The most prevalent symptoms were abdominal pain and chronic diarrhea. Among CD patients, ileal involvement was common in 21 cases (39.62%) with 25 cases (32,47 %) experiencing complications
The study found that 34 or 46.57% of patients had elevated CRP levels, with a higher prevalence in those with CD compared to UC. A statistically significant association was observed between CRP levels and IBD type.
Additionally, the analysis revealed that among patients experiencing relapse, 20 cases or 52.63% had positive FC results, compared to 14 cases or 35.9% in remission, indicating a significant correlation between relapse status and FC levels (P=0.018). However, no significant association was found between relapse status and CRP levels, although a significant difference in mean CRP levels between active and remission states in UC was noted (P=0.03). A weak positive correlation (r =0.12) between CRP and FC during active phases was also identified.
The findings underscore the clinical and epidemiological profile of IBD in this population, highlighting the importance of FC as a valuable marker for monitoring disease activity and relapse status in IBD patients.

Keywords: Fecal calprotectin; inflammatory bowel disease; crohn's disease; ulcerative colitis; C-reactive protein.

1. INTRODUCTION

Chronic inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic and progressive pathologies responsible for irreversible destruction of the digestive tract, leading to significant alteration in quality of life. Diagnosis of IBD is often difficult in clinical practice, due to pathognomonic symptoms and considerable overlap with those of irritable bowel syndrome (Ulcerative colitis - PubMed, 2024; Torres et al., 2017)

Although endoscopy has been the mainstay of IBD assessment, the feasibility of using ileo colonoscopy repeatedly for long-term follow-up is limited by its availability, invasiveness, patient tolerance and cost. There is therefore considerable interest in using non-invasive biomarkers to monitor IBD activity (Ma et al., 2019).

FC, a neutrophil-derived protein, is the most sensitive biomarker of intestinal inflammation. FC levels correlate well with endoscopic scores in CD and UC. Today, FC is used in a variety of clinical settings, notably for the initial diagnosis of IBD (D'Amico et al., 2021).Although FC and CRP are the most studied biomarkers in this field, there are concerns about the sensitivity and specificity of CRP in IBD patients. Moreover, patients often prefer blood tests to stool collection, which limits the acceptability of FC. Finally, the optimal thresholds for FC to predict disease activity vary according to IBD phenotype and the tests used (Swaminathan & Day, 2024).

Our study aims to assess the clinical and epidemiological profile of IBD in adult population. It also explores the correlation between CRP levels and FC in the context of IBD, to better understand their usefulness as biological markers in monitoring intestinal inflammation.

2. MATERIALS AND METHODS

The present study was conducted in the Immunology Laboratory at Annaba University Hospital, Annaba/Algeria, over a period of 19 months, from February 9, 2023, to September 30, 2024. This is a prospective descriptive-analytical study involving a sample of 77 adult patients referred by the gastroenterology and hepatology department at Annaba University Hospital. The sample consisted of 29 males and 48 females, with an average age of 39.7 ± 17.47 years, a median age of 34 years, and a mode of 34 years. The age range was from 17 to 82 years, resulting in a male-to-female ratio of 0.6.

Inclusion Criteria

Patients included in our study represent those whose diagnosis of IBD (UC/CD) was confirmed

on the basis of clinical, endoscopic, and histological criteria (Montreal Classifications) and referred to the immunology laboratory for immunological work-up: Determination of FC and CRP.

Exclusion Criteria

Patients whose diagnosis of IBD has not been confirmed (still under investigation).
Patients with incomplete or unusable clinical records.
Patients diagnosed with indeterminate colitis.
77 patients met the criteria and consented to participate in the study

2.1 The Included Immunological Analysis Techniques

Included among the immunological analysis techniques were:

– Determination of the FC using the sandwich ELISA technique (enzyme-linked immunosorbent assay from INOVA DIAGNOSTICS) on stool samples

– Determination of CRP by FAI (fluorescence Immunoassay) on a serum samples.

2.2 Data Collection and Statistical Analysis

Statistical analyses were conducted using SPSS software. The following statistical tests were employed to compare the different subgroups:

- ✓ Chi-square test: Used for comparing qualitative variables.
- ✓ Student's t-test and Analysis of Variance (ANOVA): Utilized for comparing means across groups.
- ✓ Spearman's rank correlation: Applied to assess the correlation between FC levels and CRP levels.

A significance level of 0.05 was established for all analyses.

3. RESULTS

3.1 Study Population Description

The study population consisted of 77 patients referred by the gastroenterology department. Among the included patients, 53 (68.9%) were diagnosed with Crohn's disease (CD) and 24 (31.1%) with ulcerative colitis (UC). Specifically, CD was identified in 20 men (25.97% of cases) and 33 women (42.85% of cases), resulting in a male-to-female ratio of 0.6. UC was diagnosed in 15 women (19.48% of patients) and 11 men (11.68% of patients), yielding a male-to-female ratio of 0.73. No significant association was found between gender and type of IBD (UC or CD).

In our cohort of CD cases, ileal localization was the most prevalent, accounting for 21 cases (39.62%), followed by colonic localization, which involved 14 patients (23.81%). Additionally, 5 patients (5.3% of the cohort) were active smokers.

Regarding disease activity, 38 patients (49.35%) were in the relapse phase, including 24 with CD; however, no statistically significant association was observed.

In terms of treatment, 15 (19, 5 %) of patients received anti-TNF therapy, 12 (15, 6 %) were on a combination of therapies, 11 (14.3%) were treated with corticosteroids, while 8 (10.4%) received immunosuppressants and 6 (7.8%) were treated with salicylates. (Table 1)

Complications of IBD: The results suggest that the obstructive tableau is more frequent in patients with CD, with a statistically significant difference ($P = 0.04$).

There is a trend towards a difference for fistulas, although not significant ($P = 0.07$).

Other complications (stenosis, abdominal mass) show no significant differences between CD and UC patients (Fig. 1).

Digestive manifestations : Digestive manifestations were dominated by abdominal pain in 55 cases (71.43%), followed by chronic diarrhea in 50 cases (64.93%), rectal bleeding in 15 cases or 19.48 % (14.28 of cases with UC), purulent diarrhea and false needs in 7 cases (9.09%) and constipation in 3 cases (3.9%). Rectal bleeding is significantly more frequent in UC patients ($P< 0.0001$), consistent with this disease.

Other symptoms (abdominal pain, chronic diarrhea, false needs, purulent diarrhea, and constipation) showed no significant differences between CD and UC patients. (Table 2)

Extra-digestive manifestations: None of the extra-intestinal manifestations evaluated (peripheral arthritis, axial rheumatism, uveitis, erythema nodosum, oral ulcerations, steatosis) showed any statistically significant difference between UC and CD patients. (Table 3)

Table 1. Description of study population

	Sample size	Percentage	Pearson Chi-square test
Type of IBD			
CD	53	68,9%	
UC	24	31,1%	
IBD by Gender			
CD			
Man	20	25,97%	
Woman	33	42,85%	*P*=0,98
UC			
Man	9	11,68%	
Woman	15	19,48%	
Localization (CD)			
Ileal	21	39,62 %	
Ileocolic	13	24,52 %	
colonic	14	26,41 %	
Smoking Factor			
Smoker	5	5,3%	
IBD in Relapse Phase			
CD	24	31,17%	*P*=0,28
UC	14	18,18%	
Treatments			
Corticosteroids	11	14,3 %	
Immunosuppressants	8	10,4 %	
Anti-TNF	15	19,5 %	
Aminosalicylates (5-ASA)	6	7,8 %	
Combination Therapy	12	15,6 %	

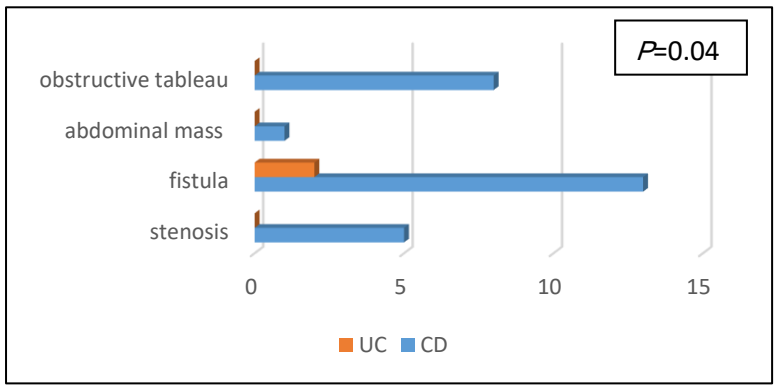

Fig. 1. IBD population distribution based on complications

Table 2. IBD cases distribution based on digestive symptoms

	Abdominal pain	Chronic diarrhea	Rectal bleeding	False needs	purulent diarrhea	Constipation
CD	40 (51, 9%)	35(45, 45%)	4(5, 19%)	6(7,79%)	5(6,49%)	1(1,3%)
UC	15(19,5%)	15(19,5%)	11(14,28%)	1(1,3%)	2(2,6%)	2(2,6%)
Total	55	50	15	7	7	3
%	71,43	64,93	19,48	9,09	9,09	3,9
P	0,24	0,76	<0,0001	0,30	0,87	0,17

Table 3. Population distribution based on extra-digestive symptoms

	Peripheral arthritis	Axial rheumatism	Uveitis	Erythema nodosum	Oral ulcerations	Steatosis
UC	3(3,9%)	2(2,6%)	2(2,6%)	0	4(5,2%)	0
CD	20(25,97%)	7(9,09%)	6(7,8%)	3(3,9%)	12(15,6%)	3(3,9%)
Total	23	9	8	3	16	3
%	29,87	11,69	10,39	3,9	20,78	3,9
p	0,25	0,53	0,69	0,23	0,54	0,23

3.2 FC and CRP Assay Results

3.2.1 Population distribution based on FC findings

Among the 77 patients, 34 (44.2%) were FC positive, 36 (46.8%) were FC negative and 7 (9.1%) were FC equivocal (Table 4).

3.2.2 FC results in relapse/non-relapse status

The results show a significant difference between relapsing and non-relapsing patients in terms of FC.

Patients in relapse had a higher proportion of positive FC (20 patients or 52.63%) compared with patients not in relapse (14 patients or 35.9%), and none of the patients in relapse had an equivocal FC.

This difference is confirmed by a *P*-value of 0.018, indicating a significant association between relapse status and FC. (Table 5)

3.2.3 FC results according to IBD

The results indicate that, although there are differences in FC between the relapse and remission phases, these differences are not statistically significant, with a *P*-value of 0.10 for both CD and UC patients. (Table 6)

The comparison between UC and CD during the relapse phases yielded a *P*-value of 0.27, also non-significant. (Table 7).

Table 4. Population distribution based on FC findings

	Positive FC	Negative FC	Equivocal FC	Total
Number of patients	34	36	7	77
%	44,2	46,8	9,1	100

Table 5. FC results in relapse/non-relapse status

	Positive FC	Negative FC	Equivocal FC
Relapse	20(52,63%)	18(47,37%)	0
Non- relapse	14(35,9%)	18(46,15%)	7(17,9%)
Total	34(44, 2%)	36(46, 8%)	7(9, 1%)
Pearson Chi-square test	*P*= 0,018		

Table 6. FC results according to the type of IBD and active/inactive Status

	Positive FC	Negative FC	Equivocal FC	Pearson Chi-square test
CD (Relapse) 24 cases	11(45,83%)	13(54,17%)	0	*P*=0,10
CD (non -Relapse) 29cases	11(37,93%)	13(44,83%)	5(17,24%)	
UC(Relapse) 14 cases	9(64,29%)	5(35,71%)	0	*P*=0,10
UC (non -Relapse) 10 cases	3(30%)	5(50%)	2(20%)	
Total (77)	34(44,2%)	36(46,8%)	7(9,1%)	

Table 7. Comparison of FC results between UC and CD during relapse phase

	Positive FC	Negative FC	Equivocal FC	Pearson Chi-square test
CD (relapse) 24 cases	11(45,83%)	13(45,17%)	0	*P*=0,27
UC (relapse) 14 cases	9(64,29%)	5(35,71%)	0	
Total (38)	20(52,63%)	18(47,37%)	0	

3.2.4 Distribution of the population according to CRP Levels

In our study, 34 patients (46.57%) had a CRP level of ≥ 6 mg/L, while 39 patients (53.42%) had a CRP level of < 6 mg/L. Patients with CD had a higher proportion of positive CRP compared to patients with UC. The Fisher's exact test showed a statistically significant association (*P*=0.007) between CRP levels and the type of IBD (Fig. 2).

3.2.5 CRP Results according to active/inactive disease status

The results suggest that there is no significant link between disease status (active or inactive) and CRP levels (<6 and ≥6), according to Fisher's exact test (*P* = 0.48). (Table 8)

3.2.6 CRP Results According to the Type of IBD

In patients with CD, no significant difference in CRP levels was observed between the active and remission phases (*P* = 0.80). For UC, there is a trend toward a difference, but it is not statistically significant (*P* = 0.08). (Table 9)

The comparison between patients with active CD and those with active ulcerative colitis UC also yields a non-significant result (*P* = 0.17). (Table 10).

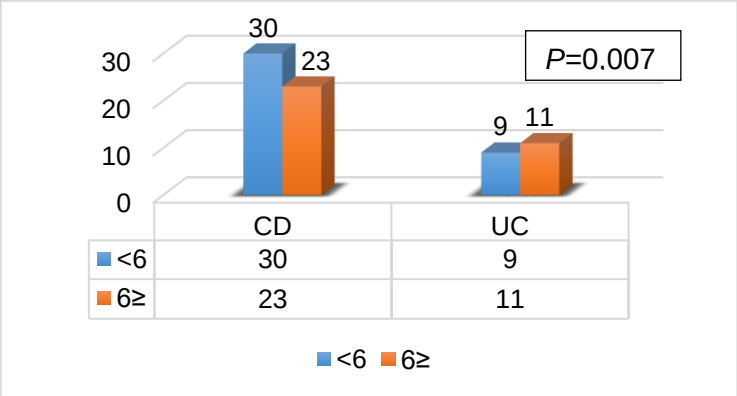

Fig. 2. Distribution of the Population According to CRP Levels

Table 8. CRP Results According to Active/Inactive Disease Status

	CRP <6 mg/l	CRP≥ 6mg/l	Fisher's exact test
relapse 37 cases	18 (48,65%)	19 (51,35%)	
Non –relapse 36 cases	21 (58,33%)	15 (41,67%)	*P*=0,48
Total (73)	39 (53,42%)	34 (46,57%)	

Table 9. CRP Results According to the Type of IBD

	CRP <6mg/l	CRP≥6mg/l	Pearson Chi-square test
CD (relapse) 24 cases	14(58,33%)	10(41,67%)	
CD (non-relapse) 29 cases	16(55,17 %)	13(44,83%)	*P*= 0,80
UC (relapse) 13 cases	4(30,77%)	9(69,23%)	
UC (on-relapse) 7 cases	5(71,42%)	2(28,6%)	*P*=0,08
Total (73)	**39 (53,42%)**	**34(46,57%)**	

Table 10. Comparison of CRP Results between CD and UC in Active Phase

	CRP <6mg/l	CRP≥6mg/l	Pearson Chi-square test
CD (relapse) 24 cases	14(58,33%)	10(41,67%)	
UC (relapse) 13 cases	4(30,77%)	9(69,23%)	
Total (37)	**18(48,65%)**	**19(51,35%)**	*P*= 0,17

3.2.7 CRP /FC Results According to Different Locations in Crohn's Disease

There is no statistically significant difference between FC results and the different localization in CD (Table 11).

The results indicate that there is no statistically significant difference in CRP levels (≥ 6 or < 6) for ileal and ileocolonic locations. However, there is a suggestive trend in the colonic location with a *P*-value of 0.06 (Table 12).

3.3 Comparison of the Average Rate of FC and CRP

3.3.1 Comparison of the average rate of FC between CD and UC during flare-up

The average rate of FC is higher during UC than in CD, however these results do not establish a significant distinction between UC and CD in terms of FC (*P*=0.09). (Table 13)

3.3.2 Comparison of the Mean FC levels between active and remission states in UC

The mean FC levels are higher in patients in the 'active' state (531 mg/L) compared to those in 'remission' (412.6 mg/L). However, the standard deviations are very high in both groups (751.71 for patients in the active state and 879.82 for those in remission), suggesting a large variability in individual values. This could indicate a heterogeneous distribution of FC levels within each group.

Despite this difference in means, the comparison between the two groups does not reveal a statistically significant difference (*P*=0, 73) (Table 14).

Table 11. FC Results according to different locations in crohn's disease

	Ileal localization	Ileocolic localization	Colonic localization
Positive FC	10(47,62%)	3(23,1)	7(50%)
Negative FC	10(47,62%)	8(61,54%)	6(42,86%)
Equivocal FC	1(4,8%)	2(15,38%)	1 (7,14%)
P value	0,56	0,27	0,74

Table 12. CRP results according to different locations in crohn's disease

	Ileal localization	Ileocolic localization	Colonic localization
CRP≥6 mg/l	8(38,1%)	5(38,46%)	9(64,29%)
CRP <6 mg/l	13(61,9%)	8(61,54%)	5(35,71%)
P value	0,58	0,67	0,06

Table 13. Comparison of the average rate of FC between CD and UC during Flare-Up

	IBD	N	Mean (mg/kg)	Standard Deviation
FC	UC	14	531,11	780,1
	CD	24	249,88	326,24
Student's t-test	*P*=0,09			

Table 14. Comparison of the Mean FC levels between active and remission states in UC

	Clinical status	N	Mean (mg/Kg)	Standard Deviation
FC	In a flare-up	14	531	751,71
	In remission	10	412,6	879,82
Student's t-test	*P*=0,73			

3.3.3 Comparison of the Mean FC levels between active and remission states in CD

The mean FC levels are very close between the two groups: 250 mg/L during the active phase and 258 mg/L in remission. However, the standard deviations reveal greater variability in the remission group (555.53) compared to the active group (320), indicating that the FC values are more dispersed among patients in remission.

The Student's t-test indicates that there is no statistically significant difference between the mean FC levels based on clinical status (*P*=0, 95). (Table 15)

3.3.4 Comparison of the Mean CRP levels between CD and UC during the active phase

The Student's t-test yielded a *P*-value of 0.88, indicating that the difference between the mean CRP levels of the two groups is not statistically significant. (Table 16)

3.3.5 Comparison of the Mean CRP levels between active and remission states in UC

The difference between the mean CRP levels in the two clinical states is statistically significant (*P*=0.03). (Table 17)

3.3.6 Comparison of the Mean CRP levels between active and remission states in CD

Patients in the "active" state have a slightly higher mean CRP level (19.62 mg/L) compared to those "in remission" (12.06 mg/L). However, the Student's t-test (*P* = 0.37) indicates that this difference is not statistically significant. (Table 18)

3.3.7 Comparison of the Mean FC levels according to disease location in CD

Although there are differences in the mean fecal calprotectin (FC) levels based on the location of the disease (ileal, ileocolonic, colonic), these differences are not statistically significant (*P*=0, 53). (Table 19)

Table 15. Comparison of the Mean FC levels between active and remission states in CD

	Clinical status	N	Mean (mg/Kg)	Standard Deviation
FC	In a flare-up	24	250	320
	In remission	29	258	555,53
Student's t test	*P*=0,95			

Table 16. Comparison of the Mean CRP levels between CD and UC during the active phase

	IBD	N	Mean (mg/L)	Standard Deviation
CRP	UC	14	18,12	15,76
	CD	24	19,7	38,88
Student's t-test	*P*=0,88			

Table 17. Comparison of the Mean CRP levels between active and remission states in UC

	Clinical status	N	Mean (mg/L)	Standard Deviation
CRP	In a flare-up	13	17,73	15,54
	In remission	7	6,84	5,76
Student's t-test	*P*=0,03			

Table 18. Comparison of the Mean CRP levels between active and remission states in CD

	Clinical status	N	Mean (mg/L)	Standard Deviation
CRP	In a flare-up	24	19,62	38,12
	In remission	29	12.06	14,63
Student's t-test	*P*=0,37			

Table 19. Comparison of the Mean FC levels among different locations in CD

	Ileal localization	Ileocolic localization	Colonic localization
Mean FC rate (mg/kg)	269,13	127,40	403,21
Standard Deviation	325,9	146,84	843,10
ANOVA test	*P*= 0,53		

Table 20. Comparison of the Mean CRP levels among different locations in CD

	Ileal localization	Ileocolic localization	Colonic localization
Mean CRP rate (mg/l)	7,99	13,44	20,67
Standard Deviation	11,1	13,15	23,82
ANOVA test		*P*=0,38	

3.3.8 Comparison of the Mean CRP levels According to disease location in CD

Although there are differences in the mean CRP levels based on the location of the disease (ileal, ileocolonic, colonic), these differences are not statistically significant (*P*=0, 38). (Table 20)

3.4 Correlation Test between FC and CRP during the active phase

The correlation between CRP and FC is weak and positive (r = 0.12). This means that as the FC variable increases, CRP tends to increase as well, but only very slightly. However, since *P* = 0.48, this correlation is not statistically significant.

In practical terms, this indicates that CRP and FC should be used complementarily and not interchangeably to assess inflammation in adult patients with inflammatory bowel disease (IBD). A low CRP does not necessarily indicate low intestinal inflammation, highlighting the importance of measuring FC for an accurate evaluation. (Fig. 3).

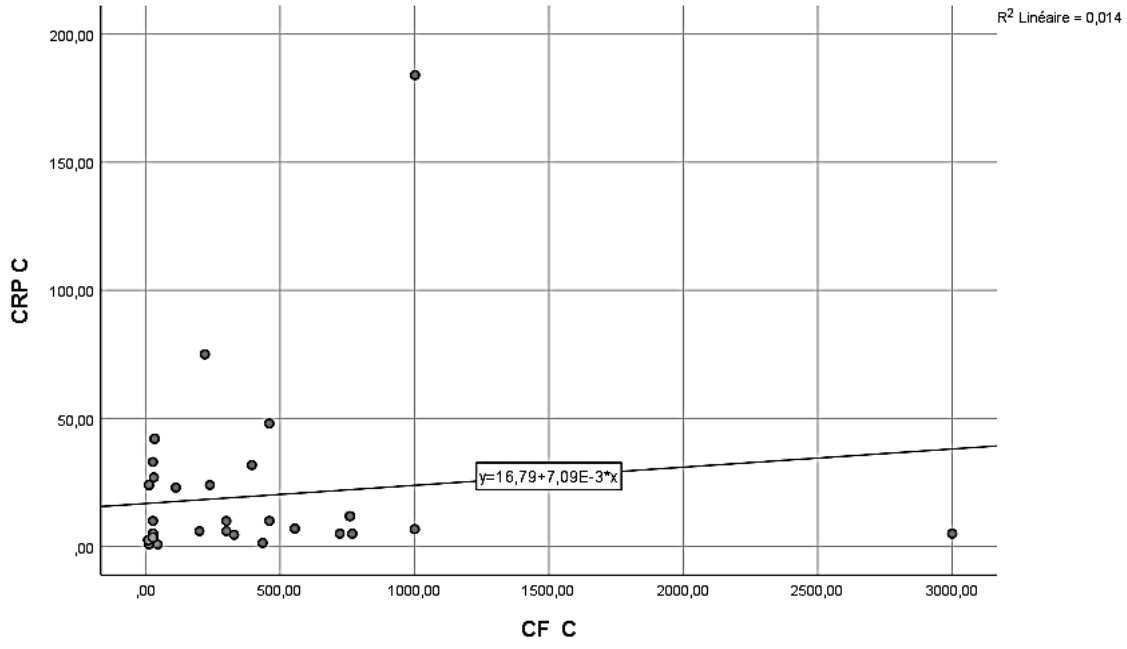

Fig. 3. Scatter Plot of correlation between FC and CRP during the active phase

Spearman correlation test	*P*= 0,48 *r*=0,12

4. DISCUSSION

4.1 Description of the Studied Population

Inflammatory Bowel Diseases (IBD) do not appear to have a gender preference (Cosnes et al., 2011). However, according to Delmondes LM and al., a general female predominance has been observed in IBD cases, with a male-to-female ratio of 0.641 (Lm et al., 2015). A cohort study conducted in Canada in 2017 involving 45567 patients showed similar results. Lima Martins and al. also reported this finding in their study in 2018 (Benchimol et al., 2017 ; LM et al., 2018). Conversely, a study by Wang ZZ and al. in 2017 highlighted a male predominance in IBD cases (Jm et al., 2018).

In a German study, the peak incidence for both Crohn's Disease (CD) and Ulcerative Colitis (UC) was observed in patients aged 30 years or younger (Kostev et al., 2018). The average age in the Oranian study was reported as 31.2 ± 3.4 years (Masson, 2024).

In a study by Huguet J and al. in 2018, nearly 69% of patients were over 60 years old (Jm et al., 2018).

In our series, the mean age was 39.7 years ± 17.47 years.

In a Moroccan study, CD accounted for 46.67% of cases (IBD , n.d.). In our series, we noted a clear predominance of CD, comprising 68.9% of cases. CD can affect any part of the gastrointestinal tract but shows a preference for the ileocecal region. The Montreal classification is widely used by gastroenterologists for lesion topography (Satsangi et al., 2006).

According to literature data, the small intestine and colon are preferred sites for CD.

In our case series of CD, ileal localization was the most common, representing 39.62% of cases, followed by colonic localization at 26.41%. The observed differences may be linked to geographical, environmental, or genetic factors influencing the presentation of IBD.

Fistulas are among the most frequently encountered complications in CD (Management of acute ano-perineal Crohn’s disease, 2024).

Our results suggest that obstructive presentations are more common in patients with CD, with a statistically significant difference (*P*= 0.04). This discrepancy with existing literature may arise from geographical variations, access to care, or differences in follow-up and treatment practices.

A Dutch population study by Smids C and al. found that 44% of patients with CD smoked, compared to 20% with Crohn's Disease Indeterminate (CDI) and 7% with UC (Smids et al., 2017).

Among our patients, 5.3% were smokers, all diagnosed with CD. Our findings do not align with the literature and may be biased due to our small sample size; however, smoking appears more prevalent in CD cases than in UC.

According to research by Casellas F and al., studying disease activity among a population of 117 IBD patients, among those with CD, six subjects experienced at least one relapse compared to 58 who were in remission. For UC cases, four patients had relapses while 49 showed no disease activity (Nahon et al., 2018).

In our series, 38 patients (49.35%) were experiencing flare-ups, with 31.17% having CD. The increase in flare-ups within our series may be attributed to the small sample size.

A Moroccan study reported abdominal pain in 20 patients with CD (33.3%) and in 14 patients with UC (23.3%). False needs were reported in 32 patients (53.3%), including ten with CD (16.67%) and twenty-one with UC (35%). Rectal bleeding was noted in 25% of patients with UC (IBD, n.d.).

In our series, digestive manifestations were dominated by abdominal pain in 51.95% of patients with CD and in 19.48% of those with UC. Chronic diarrhea was present in 45.45% of CD cases and in 19.48% of UC cases; rectal bleeding occurred in 19.48% of cases (14.28% with UC), and false needs were reported in 9.09% of cases (7.79% with CD). These results are consistent with literature data.

An Iranian study conducted by Zobeiri M and al. highlighted that extra-digestive symptoms were marked by musculoskeletal signs (51.9%), followed by ocular signs (27.9%), and skin signs (22.7%) (Gao et al., 2017).

In our study, articular signs were present in 41.55% of patients; ocular manifestations occurred in 10.4%, and skin signs were seen in

3.9%. Our results align well with those reported in other studies.

4.2 Results of FC and CRP testing

In a Chinese study, CRP levels were found to be higher among patients with CD (Wang et al., 2013).

In our series, 34 patients (46.57%) had CRP levels ≥6 mg/L (with 29.87% having CD). Our findings are consistent with existing literature.

Schoepfer and al. reported a higher correlation between the endoscopic activity of UC and FC levels (r = 0.8) compared to CRP (r = 0.5) (Schoepfer et al., 2024). A study conducted at the gastroenterology clinic of RSUD Dr. Soetomo Hospital in Surabaya from March to August 2020 included 30 participants with UC. This cross-sectional analytical study aimed to evaluate colitis activity through CRP and FC measurements. During flare-ups, FC was positive in 20 patients (67%), while CRP was positive in 13 patients (43%). A significant relationship was observed between FC and CRP, with a correlation coefficient (r) of 0.57 (P = 0.01) (Anindita et al., 2023).

In our study, patients in flare had a higher proportion of positive FC (52.63%) compared to patients in remission (35.9%), and none of the patients in flare had equivocal FC results. This difference was confirmed by a P-value of 0.018, indicating a significant association between flare status and FC levels.

Our results suggest that although there are differences in FC between flare and remission phases, these are not statistically significant with a P-value of 0.1 for patients with CD and UC. Furthermore, the comparison between CD and UC during flare phases yielded a P-value of 0.27, which is also not significant. This supports the notion that FC is a good biomarker for inflammation in the context of inflammatory bowel diseases (IBD), consistent with previous studies.

A study conducted between 2018 and 2019 involving 49 patients with CD and 31 healthy controls recruited from the gastroenterology and hepatology department at the University Hospital in Krakow, Poland, found significantly higher serum CRP levels in the CD group compared to the control group. Additionally, in patients with CD, serum CRP concentrations were markedly higher during active disease than during inactive disease (Słowińska-Solnica et al., 2021).

A study conducted in 2006 in Italy, in 76 IBD patients (29 CD and 47 UC) fecal calprotectin has been evaluated by a commercial ELISA kit. Results demonstrate that levels of this protein in the stool are significantly more elevated in active CD and UC patients than in normal volunteers. Moreover, in CD patients levels of calprotectin are higher than in UC (Amati et al., 2006).

Our results reveal no significant link between flare status (flare or non-flare) and CRP levels (<6 and ≥6) (P = 0.48). In CD patients, no significant difference in CRP was observed between flare and remission phases (P = 0.8). For UC, a trend towards a difference was noted, although it was not statistically significant (p = 0.08).

Differences in disease location in CD may account for some of the inter-individual variation in FC. However, FC and other stool biomarkers have been found to have low sensitivity in detecting isolated small bowel involvement seen on wireless capsule endoscopy (Sands, 2015).

Gecse and al. demonstrated that patients with large ulcerations (>5 mm) in the ileum had significantly lower FC concentrations compared to those with ileocolonic or colonic disease (297 vs. 1,523 µg/g, P < 0.0001).

A study involving 120 patients with CD examined disease activity using biological markers as well as endoscopic and radiographic methods. FC concentration was measured in stool samples. Among these patients, 45% had ileocolonic CD, 36.5% had small bowel CD, and 18.5% had colonic CD. In small bowel CD patients, FC was significantly correlated with CRP (P = 0.03), endoscopic activity (P < 0.0001), and radiographic assessment (P = 0.03). Similarly, in colonic CD patients, FC correlated with CRP (P = 0.0009) and endoscopic activity (P = 0.0002). However, among small bowel CD patients, the Crohn's Disease Activity Index (CDAI) and inflammatory markers were not correlated with endoscopic and radiographic evaluations.

For ileocolonic CD patients, FC showed a significant correlation with endoscopy (P=0.006), radiographic assessment (P = 0.04), CDAI (P = 0.0006), as well as most biological markers. The concentration of FC reflects inflammatory activity more accurately in patients with lesions in both

the small intestine and colon compared to those with isolated small bowel disease (Sands, 2015).

A study involving 273 CD patients, including 41 with ileal disease and 189 with ileocolonic disease, showed that FC was significantly correlated with CDAI; correlation coefficients were 0.711 for ileal disease patients and 0.687 for ileocolonic disease patients (Gecse et al., 2015).

In our study, although there are differences in average FC levels based on disease location (ileal, ileocolonic, colonic), these differences are not statistically significant, possibly due to sample size or individual variations.

According to a study including 88 patients with an average age of 34±10.8 years, twelve (13.6%) had negative CRP results. While location did not serve as a significant predictor, all patients with negative CRP had ileal involvement (Stawczyk-Eder et al., 2015).

In our study, results indicate no statistically significant difference between CRP levels (≥6 or <6) for ileal and ileocolonic locations; however, there is a suggestive trend for colonic location with a *P*-value of 0.06.

There is an emphasis on the similarity regarding the absence of significant predictors related to location, suggesting that despite variations across studies, there is a general trend indicating that ileal location does not appear to be strongly correlated with CRP levels.

4.3 Comparison Between the Average Levels of FC / CRP

In a prospective study involving patients recruited from the inflammatory bowel disease unit at the University Hospital of Saint Etienne between June 2017 and June 2018, patients were followed for 12 months or until relapse. The measurement of FC and CRP showed that median FC levels progressively increased in patients who relapsed during the follow-up period, rising from 26 µg/g at baseline to 105 µg/g at three months, 177 µg/g at six months, and 292 µg/g at the time of relapse (p = 0.049 between baseline and relapse) 1.

Serum CRP levels fluctuated during follow-up, but a significant difference in median CRP levels was observed between baseline and relapse (1.5 mg/L vs. 3.3 mg/L, respectively; *P* = 0.008). However, median CRP levels remained normal below 5 mg/L (Li et al., 2023).

A study involving twenty-six patients with inflammatory bowel disease, including five with Crohn's disease and twenty-one with ulcerative colitis, revealed no significant correlation between FC and CRP (*r* = 0.2) (Sousa et al., 2017).

In another observational prospective study of fifty-nine patients with ulcerative colitis, eighteen patients (30.5%) exhibited signs of active histological inflammation. These patients had a significantly higher median FC level (278 µg/g), while the average CRP level was 16 mg/L (Veyrard et al., 2022).

A study conducted on 273 patients with Crohn's disease at the gastroenterology division of Tongji Medical College in Wuhan, China, found median FC levels in patients in endoscopic remission, mildly active, and moderately to severely active stages to be 26.94, 66.77, and 327.22 µg/g respectively, with significant differences observed (*P* < 0.001). Median CRP levels in clinically remission, mildly active, and moderately to severely active groups were respectively 3.30, 6.30, and 30.30 mg/L (Gecse et al., 2015).

In our study, the average FC level in patients with active Crohn's disease was 250 µg/g, while it was 258 µg/g in remission. Average CRP levels were 19 mg/L during flare-ups and 12 mg/L in remission. This difference may be attributed to individual variability in inflammatory response or the presence of confounding factors such as the use of immunosuppressive medications.

A separate study on fifty patients with ulcerative colitis aged between twelve and seventy-four years measured FC and CRP levels based on disease severity. Patients with mild activity had an average FC level of 207.46 g/kg and an average CRP level of 11.37 mg/L; those with moderate to severe activity had an average FC level of 729.85 g/kg and an average CRP level of 29.38 mg/L. A statistically significant difference was observed between the two groups for both FC (*P* = 0.001) and CRP (*P*= 0.0001), indicating that both markers increase significantly with the severity of ulcerative colitis (Kyle et al., 2021).

Rodriguez-Moranta and al. found that FC is better correlated with the degree of inflammation than other clinical indicators and serological

markers (Guardiola et al., 2014). Moreover, it could also be useful for predicting mucosal healing and the risk of relapse.

According to a study by Mohamed and al., there was a highly significant increase in average FC values among active ulcerative colitis patients compared to inactive ones; similarly, there was a significant increase in average FC values among inactive ulcerative colitis patients compared to controls (Ahmed et al., 2017).

In our study, the average FC level among patients with active ulcerative colitis was found to be 531 µg/g while it was 412.6 µg/g in remission. The Student's t-test yielded a non-significant p-value of 0.73 for comparing these two groups regarding FC levels. Average CRP levels were found to be 17.73 mg/L during flare-ups and 6.84 mg/L in remission; the Student's t-test yielded a significant *P*-value of 0.03 when comparing the two groups for CRP.

A retrospective analysis of records from inflammatory bowel disease patients followed between January 2012 and October 2014 at a gastroenterology care center in Mumbai included sixty-three patients (32 with ulcerative colitis and 31 with Crohn's disease). Erythrocyte sedimentation rate (ESR), CRP, and FC were compared against endoscopic results to evaluate inflammation.

Patients with ulcerative colitis exhibited higher FC levels than those with ileocolic Crohn's disease (median FC: 1800 mg/g vs. 619 mg/g; $P = 0.04$). Additionally, FC levels were correlated with CRP ($r = 0.4$; $P < 0.001$). Among the sixty-three patients showing signs of inflammation upon endoscopic examination, a higher proportion (86.9%) had positive FC concentrations compared to those showing positive CRP results (65.6%; $P < 0.01$) (Rodríguez-Moranta et al., 2013).

In our study, average FC levels were higher in ulcerative colitis than in Crohn's disease; however, these results did not significantly distinguish between ulcerative colitis and Crohn's disease concerning FC levels. The Student's t-test applied to average CRP levels yielded a *P*-value of 0.88, indicating no statistically significant difference between the average CRP levels of both groups.

Finally, the correlation between CRP and FC was weakly positive ($r = 0.12$; $P = 0.48$). Previous studies have shown that both FC and CRP significantly increase in correlation with inflammation severity; however, our analysis reveals a weak and non-significant correlation within our cohort ($r = 0.12$; $P = 0.48$). This suggests that within our cohort, CRP and FC do not act together to reflect inflammation effectively (Badawy et al., 2014;Samant et al., 2015).

5. CONCLUSION AND PERSPECTIVES

Our study has provided a clearer definition of the clinical and epidemiological profile of inflammatory bowel diseases (IBD) in adults, highlighting the distinctive characteristics of Crohn's disease (CD) and ulcerative colitis (UC). The results indicate a higher prevalence of IBD among adult women. In terms of biomarkers, C-reactive protein (CRP) and final concentration (FC) have proven relevant for monitoring intestinal inflammation, with significantly elevated levels of FC during flare-ups, confirming its utility as an inflammation indicator. However, the absence of a significant correlation between FC and CRP during flare-ups suggests that these biomarkers reflect distinct aspects of inflammation.

An integrated assessment, combining these biomarkers with clinical scores and imaging, remains essential for optimal monitoring. In conclusion, this study highlights clinical and biological differences based on the type of IBD, the location of lesions (ileal, ileocolic, or colonic), and the nature of complications, emphasizing the importance of a personalized approach to managing IBD that incorporates specific biomarkers (CRP, FC) and patient profiles. Larger comparative studies exploring genetic and environmental factors are necessary to refine diagnostic tools and further tailor treatments. Additional research will help validate these findings and optimize clinical follow-up protocols for more precise and tailored care.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT AND ETHICAL APPROVAL

Informed consent was obtained from all participants after they were fully informed about

the study's objectives, procedures, and measures to ensure confidentiality and data protection. The study protocol was conducted in accordance with ethical standards.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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