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Extraintestinal Manifestations In Inflammatory Bowel Disease: Prevalence, Clinical Features, And Comparative Analysis In A Moroccan Tertiary Cohort

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Abstract
Background and Aims: *Extraintestinal manifestations (EIMs) constitute a frequent and clinically significant dimension of inflammatory bowel disease (IBD), extending its morbidity well beyond the gastrointestinal tract. This study aimed to determine the prevalence and clinical spectrum of EIMs in a cohort of IBD patients managed at a Moroccan tertiary referral centre, and to examine differences between Crohn's disease (CD) and ulcerative colitis (UC).*
Methods: *A retrospective descriptive analysis was conducted on 210 patients followed between 2019 and 2022, comprising 133 with CD and 77 with UC. Clinical, demographic, and laboratory data were systematically extracted from medical records.*
Results: *EIMs were identified in 49% of the cohort, occurring more frequently in CD than UC (55.6% vs. 36.8%). The median patient age was 34 years, with an approximately equal sex distribution. Musculoskeletal involvement was the most prevalent EIM, noted in 24.4% of cases and encompassing both peripheral arthritis and axial disease, including ankylosing spondylitis. Peripheral arthritis was strongly associated with active intestinal disease, with 85% of affected patients experiencing a concurrent flare ($p = 0.001$). Densitometric evaluation in 75 patients revealed osteopenia in 21 and osteoporosis in 14. Dermatologic and mucosal manifestations were observed in 7.7% of patients, ocular involvement in 2.9%, hepatobiliary manifestations in 2.9%, and thromboembolic complications in 6.2%. Rare manifestations included acute pancreatitis, nephrolithiasis, and renal amyloidosis. Bone mineral density impairment was significantly more frequent in CD ($p = 0.033$).*
Conclusion: *EIMs affect nearly half of IBD patients and are more prevalent in CD. Their diverse clinical expressions and variable relationship with intestinal activity underscore the systemic character of IBD and reinforce the value of systematic multidisciplinary screening.*
Keywords: *Inflammatory bowel disease; Crohn's disease; ulcerative colitis; extraintestinal manifestations; musculoskeletal manifestations*

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I. Introduction

Inflammatory bowel diseases (IBD)—comprising Crohn's disease (CD) and ulcerative colitis (UC)—are chronic, relapsing inflammatory disorders of the gastrointestinal tract whose etiology involves a complex interplay of genetic susceptibility, dysregulated immune responses, and environmental factors [1,2]. Although the gastrointestinal tract constitutes the principal site of pathological involvement, the systemic inflammatory milieu characteristic of IBD renders it a genuinely multiorgan condition. Extraintestinal manifestations (EIMs) involving the musculoskeletal system, skin, eyes, and hepatobiliary tract are recognised complications that may precede, coincide with, or follow the onset of intestinal disease, and that can substantially influence disease course, health-related quality of life, and long-term prognosis [3,4].

The reported prevalence of EIMs varies considerably across studies, ranging from approximately 25% to over 50% of IBD patients, a disparity partly attributable to heterogeneity in case definitions, diagnostic criteria, and study populations [1]. Despite growing recognition, the burden of EIMs remains incompletely characterised in North African and Moroccan patient populations, where IBD registries are still in their early development.

The present study was undertaken to evaluate the prevalence and clinical characteristics of EIMs in a cohort of IBD patients managed at a tertiary university hospital in Tangier, Morocco. Secondary objectives included examining EIM-related demographic and disease-related associations, and contextualising the findings within the existing international literature.

II. Materials And Methods

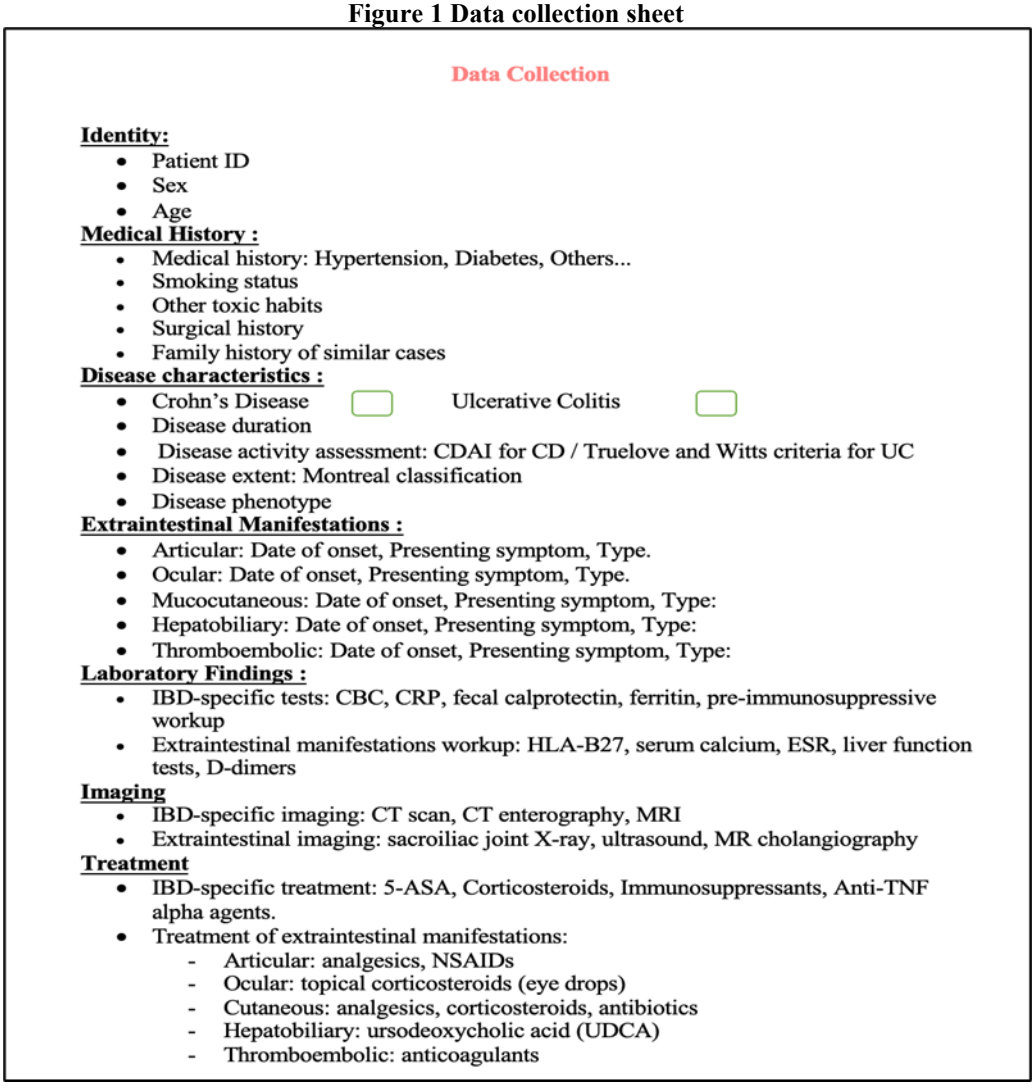
Study Population

This retrospective descriptive study was conducted over a four-year period spanning 2019 to 2022 and encompassed all patients under active follow-up for IBD at our institution. The study population comprised 210 patients, of whom 133 carried a diagnosis of CD and 77 of UC.

Data Collection

Clinical and laboratory data were retrieved from standardised medical records using a purpose-designed data collection form (Figure 1). Variables recorded included patient age, sex, smoking history, family history of IBD, disease subtype, presence and type of EIMs, and disease activity status at the time of EIM occurrence.

Figure 1 Data collection sheet



Data Collection

Identity:
- Patient ID
- Sex
- Age

Medical History :
- Medical history: Hypertension, Diabetes, Others...
- Smoking status
- Other toxic habits
- Surgical history
- Family history of similar cases

Disease characteristics :
- Crohn's Disease ☐ Ulcerative Colitis ☐
- Disease duration
- Disease activity assessment: CDAI for CD / Truelove and Witts criteria for UC
- Disease extent: Montreal classification
- Disease phenotype

Extraintestinal Manifestations :
- Articular: Date of onset, Presenting symptom, Type.
- Ocular: Date of onset, Presenting symptom, Type.
- Mucocutaneous: Date of onset, Presenting symptom, Type:
- Hepatobiliary: Date of onset, Presenting symptom, Type:
- Thromboembolic: Date of onset, Presenting symptom, Type:

Laboratory Findings :
- IBD-specific tests: CBC, CRP, fecal calprotectin, ferritin, pre-immunosuppressive workup
- Extraintestinal manifestations workup: HLA-B27, serum calcium, ESR, liver function tests, D-dimers

Imaging
- IBD-specific imaging: CT scan, CT enterography, MRI
- Extraintestinal imaging: sacroiliac joint X-ray, ultrasound, MR cholangiography

Treatment
- IBD-specific treatment: 5-ASA, Corticosteroids, Immunosuppressants, Anti-TNF alpha agents.
- Treatment of extraintestinal manifestations:
  - Articular: analgesics, NSAIDs
  - Ocular: topical corticosteroids (eye drops)
  - Cutaneous: analgesics, corticosteroids, antibiotics
  - Hepatobiliary: ursodeoxycholic acid (UDCA)
  - Thromboembolic: anticoagulants

Statistical Analysis

Statistical analyses were performed using SPSS version 26.0. Between-group comparisons of CD and UC were carried out using the Chi-square test for categorical variables and Student's t-test for continuous variables. A p-value of ≤ 0.05 was considered statistically significant.

III. Results

Patient Characteristics

Of the 210 patients included, 103 (49%) presented with at least one EIM: 74 cases (72%) occurred in CD and 29 cases (28%) in UC. The median age of the cohort was 34 years (IQR: 26–45; range: 9–76), and the sex distribution was virtually equal, with 106 males (50.5%) and 104 females (49.5%). A history of smoking was documented in 16% of patients, and a family history of IBD in 7%. EIMs were isolated in 26% of patients and multiple in 23% (Table 1).

Table 1. Demographic and clinical characteristics of the study cohort.

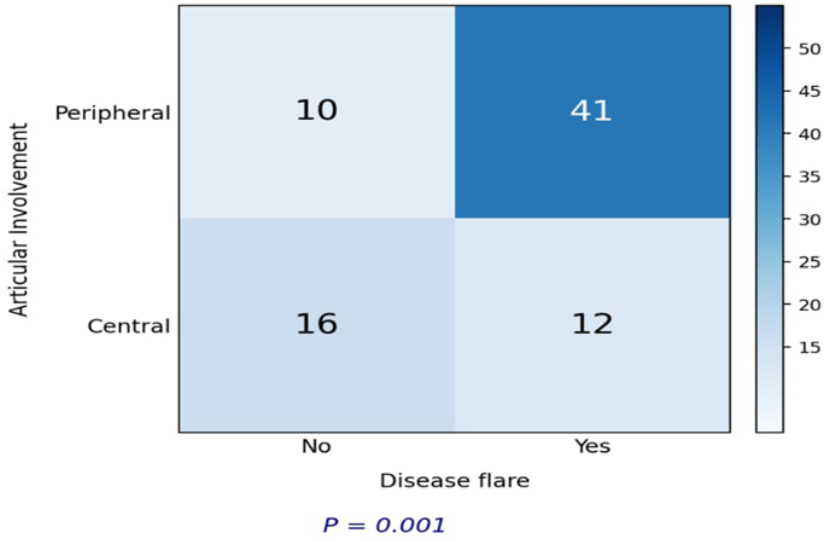
Variable	Value
Total patients, n	210
Disease type	
Crohn's disease (CD)	133 (63.3%)
Ulcerative colitis (UC)	77 (36.7%)
Patients with EIMs, n (%)	103 (49%)
CD with EIMs	74 (72%)
UC with EIMs	29 (28%)
Age (years) – Median [IQR]	34 [26–45]
Age range (years)	9–76
Sex	
Male	106 (50.5%)
Female	104 (49.5%)
Smoking history, n (%)	34 (16%)
Family history of IBD, n (%)	15 (7%)
EIM pattern	
Isolated EIMs	55 (26%)
Multiple EIMs	48 (23%)

Musculoskeletal Manifestations

Peripheral joint involvement was identified in 24.4% of patients (n = 51), with 33 cases in CD and 18 in UC. Axial arthropathy, predominantly ankylosing spondylitis, was documented in 15 CD patients and 2 UC patients. Isolated sacroiliitis was recorded in 4.8% of the cohort (8 CD and 2 UC cases). Concurrent axial and peripheral involvement was noted in 2 CD patients.

A statistically significant association was demonstrated between disease activity and the type of musculoskeletal involvement. Among patients with peripheral arthritis, 85% were experiencing an active intestinal flare at the time of musculoskeletal presentation, compared with only 42% of patients with axial involvement (p = 0.001). This differential relationship with intestinal disease activity is illustrated in Figure 2.

Figure 2 Disease activity and type of musculoskeletal involvement



Bone mineral density assessment by dual-energy X-ray absorptiometry (DXA) was performed in 75 patients. Osteopenia was identified in 21 cases and osteoporosis in 14 cases (Figure 3).

Dermatologic and Mucosal Manifestations

Dermatologic or mucosal EIMs were present in 7.7% of patients (n = 16). The observed manifestations comprised erythema nodosum (n = 4), pyoderma gangrenosum (n = 3), oral aphthosis (n = 3), psoriasis (n = 3), lichen pigmentosus (n = 1), pachyonychia (n = 1), and cutaneous lupus erythematosus (n = 1), as detailed in Figure 3.

Ocular Manifestations

Ocular involvement was recorded in 2.9% of patients (n = 6). Anterior uveitis was the predominant form, accounting for five cases, with a single case of dry eye syndrome (Figure 3).

Hepatobiliary Manifestations

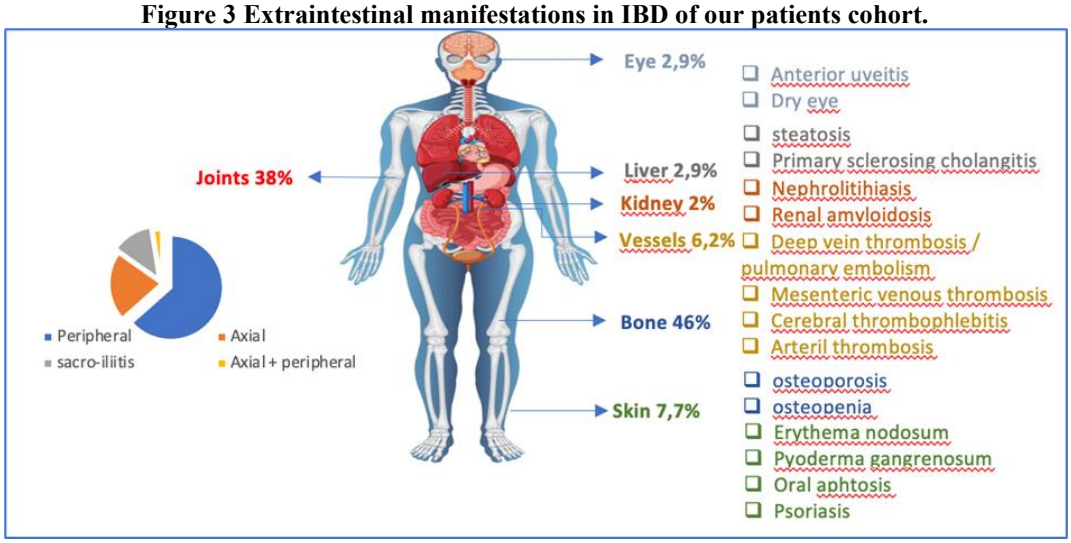
Hepatobiliary involvement was identified in six patients. Hepatic steatosis was observed in five CD patients, and primary sclerosing cholangitis (PSC) was documented in one CD patient (Figure 3). These findings occurred in the absence of consistent correlation with intestinal disease activity, consistent with the recognised capacity of hepatobiliary EIMs to follow an independent course.

Vascular and Other Manifestations

Thromboembolic complications were identified in 6.2% of patients and comprised deep vein thrombosis (n = 5), pulmonary embolism (n = 3), renal vein thrombosis (n = 1), superior mesenteric vein thrombosis (n = 1), cerebral thrombophlebitis (n = 1), and arterial thrombosis (n = 2), as summarised in Figure 3.

Less frequent manifestations included acute pancreatitis (n = 3), nephrolithiasis (n = 2), and renal amyloidosis (n = 2).

Figure 3 Extraintestinal manifestations in IBD of our patients cohort.



Comparative Analysis: Crohn's Disease vs. Ulcerative Colitis

EIMs were significantly more frequent in CD than in UC (55.6% vs. 36.8%; p = 0.031). Joint involvement—both peripheral and axial—was more prevalent in CD (43.6% vs. 28.9%), though this difference did not attain statistical significance (p = 0.076). Bone mineral density impairment was significantly greater in CD (82% vs. 17%; p = 0.033). No statistically significant intergroup differences were observed for dermatologic, ocular, hepatobiliary, or vascular manifestations (Table 2).

Table 2. Comparison of selected extraintestinal manifestations between Crohn's disease and ulcerative colitis.

	Any EIM	Joint involvement	Bone involvement
Crohn's disease	55.6%	43.6%	82%
Ulcerative colitis	36.8%	28.9%	17%
p-value	0.031	0.076	0.033

IV. Discussion

Extraintestinal manifestations are well-established features of IBD, reflecting its systemic character beyond the gastrointestinal tract. Their pathogenesis remains incompletely understood but appears to involve immune dysregulation, shared antigenic epitopes between intestinal mucosa and extraintestinal tissues, genetic susceptibility loci, and the systemic propagation of intestinal inflammatory signals [5,6]. The clinical significance of EIMs is considerable: they contribute independently to patient morbidity, influence therapeutic decisions, and represent an important dimension of the overall disease burden in IBD [4,7].

The overall EIM prevalence of 49% observed in the present cohort falls within the range of 25–50% reported across the international literature [6,8]. A large multicentre cohort study reported an EIM prevalence of approximately 40% [6], and population-based investigations have corroborated that nearly half of IBD patients develop at least one EIM during their disease course [8]. The higher prevalence in CD relative to UC, as observed here, is consistent with findings from several prior reports, although some authors have not found a statistically significant difference between the two phenotypes [9].

Musculoskeletal involvement, comprising peripheral arthritis and axial arthropathies, represented the most prevalent EIM category in our cohort, a finding aligned with existing reviews documenting arthritis as the most common EIM in IBD, with estimates ranging from 5% to 20% depending on the diagnostic criteria applied [10]. The strong association between peripheral arthritis and active intestinal disease (85% of cases in flare, $p = 0.001$) corroborates the widely held pathophysiological distinction between activity-dependent and activity-independent EIMs, wherein peripheral arthritis is classified among the former and ankylosing spondylitis among the latter [7].

Alterations in bone mineral density were frequent, with osteopenia and osteoporosis detected in substantial proportions of assessed patients. This is consistent with published data reporting osteopenia in 20–50% and osteoporosis in 5–37% of IBD patients [11,12]. The underlying mechanisms encompass chronic systemic inflammation, prolonged corticosteroid use, impaired intestinal calcium absorption, and vitamin D deficiency—factors that are particularly pronounced in CD, accounting for the significantly higher bone involvement observed in CD patients in the present study [11].

Dermatologic manifestations were present in 7.7% of patients, slightly below the 10–15% reported in broader series [6,13]. Erythema nodosum typically parallels intestinal disease activity, while pyoderma gangrenosum pursues a more autonomous and potentially refractory course [13]. The concurrent presence of psoriasis further implicates shared immunological pathways linking IBD to other systemic inflammatory conditions.

Ocular involvement in 2.9% of patients is consistent with prevalence estimates of 2–10% in the literature [14]. Anterior uveitis was the predominant form and, notably, may evolve independently of intestinal activity, necessitating vigilant ophthalmological surveillance given the risk of vision-threatening sequelae [14].

Hepatobiliary EIMs, including hepatic steatosis and primary sclerosing cholangitis, were identified in 2.9% of patients. PSC, the archetypal hepatobiliary EIM, carries a reported prevalence of 2–7% and is more closely associated with UC in most series [15], though the single PSC case in our cohort occurred in a CD patient. Hepatic steatosis is increasingly recognised in IBD and may reflect a composite of metabolic, nutritional, and inflammatory factors [15].

Thromboembolic events were documented in 6.2% of patients, at the upper margin of the 1–6% range reported in most published series [16]. This finding is consistent with the well-characterised hypercoagulable state associated with IBD, which arises from a convergence of systemic inflammation, endothelial dysfunction, platelet activation, and abnormalities in the coagulation cascade [16]. The clinical implication is that thromboembolism risk should be assessed systematically, particularly during disease flares.

Rare manifestations—acute pancreatitis, nephrolithiasis, and renal amyloidosis—were also documented, consistent with prior descriptions of the extended systemic reach of IBD [17]. Although individually uncommon, their cumulative occurrence reinforces the necessity of broad clinical vigilance.

Strengths and Limitations

The strengths of this study include a relatively large, well-characterised single-centre cohort and a systematic, comprehensive approach to EIM assessment across multiple organ systems. Its limitations are inherent to the retrospective design, which is susceptible to underascertainment of EIMs and selection bias. The single-centre setting, while enabling detailed data extraction, may restrict the generalisability of findings to broader or community-based IBD populations.

Clinical Implications and Future Directions

These results support the integration of systematic EIM screening into routine IBD management protocols, with particular attention to musculoskeletal, bone metabolic, and thromboembolic complications. Future prospective studies should aim to identify predictive biomarkers, refine phenotypic classifications of EIMs,

and assess the extent to which biologic therapies with dual intestinal and extraintestinal efficacy modify the natural history of EIMs in IBD.

V. Conclusion

Extraintestinal manifestations represent a clinically and epidemiologically significant dimension of IBD, affecting nearly half the patients in this cohort. Their heterogeneous clinical presentation, variable relationship to intestinal inflammatory activity, and potential for independent and severe progression collectively underscore the systemic nature of the disease. Musculoskeletal involvement predominates and is tightly coupled to disease activity, whereas other EIM categories, while less frequent, may follow courses dissociated from intestinal flares. The greater prevalence of EIMs—particularly musculoskeletal and bone involvement—in CD suggests a more pronounced systemic inflammatory burden compared with UC, though inter-study variability warrants cautious interpretation.

Collectively, these findings advocate for a proactive, multidisciplinary model of IBD care in which systematic EIM screening is embedded in routine practice. Early recognition and targeted, organ-specific management remain pivotal to improving patient outcomes and quality of life. Prospective multicentre investigations are needed to further elucidate the pathophysiological determinants of EIMs and to optimise therapeutic strategies across the expanding spectrum of available IBD treatments.

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