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Original Research Article

Frequency of Extra-Intestinal Manifestations of Ulcerative Colitis in Patients Presenting in A Tertiary Care Hospital

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Abstract: *Ulcerative Colitis (UC) is a chronic inflammatory bowel disease primarily affecting the colon and rectum. However, a significant proportion of patients also experience extra-intestinal manifestations (EIMs), which may involve the musculoskeletal, dermatological, ocular, and hepatobiliary systems. These manifestations can complicate the clinical course and significantly impact the patient's quality of life.* ***Objective:*** *To determine the frequency and distribution of extra-intestinal manifestations in patients with UC presenting at a tertiary care hospital and assess associations with demographic and clinical factors.* ***Methods:*** *This cross-sectional study was conducted over three months from January to March 2025, at the Department of Medicine, Shalamar Hospital, Lahore. A total of 125 patients with a confirmed diagnosis of UC were enrolled using non-probability consecutive sampling. Data were collected through a structured proforma, with confirmation of EIMs by relevant specialists. Statistical analysis was performed using SPSS version 23. Chi-square and t-tests were applied to assess associations, with a p-value < 0.05 considered significant.* ***Results:*** *Out of 125 patients, 47 (37.6%) exhibited extra-intestinal manifestations. Musculoskeletal involvement was the most common (25.6%), followed by dermatological (12.0%), hepatobiliary (11.2%), and ocular (10.4%) manifestations. A statistically significant association was observed between longer disease duration and the presence of EIMs (mean duration: 8.2 ± 2.4 years vs. 5.6 ± 2.1 years, p = 0.0004). No significant gender difference was found, although musculoskeletal symptoms were more common in males and dermatological conditions were more frequent in females.* ***Conclusion:*** *EIMs are a common and clinically significant aspect of UC, affecting over one-third of patients in this study. The findings highlight the importance of early recognition and multidisciplinary management of EIMs, particularly in patients with longer disease duration. Routine screening and inter-specialty coordination can facilitate timely diagnosis and enhance patient outcomes. Further multicenter longitudinal studies are warranted to explore the long-term impact and progression of EIMs in diverse populations.*

Keywords: Ulcerative Colitis, Extra-Intestinal Manifestations, Inflammatory Bowel Disease

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Introduction

Clinical manifestations of ulcerative colitis (UC) are not limited to the gastrointestinal tract; a significant proportion of patients also experience involvement of other organ systems. Musculoskeletal extra-intestinal manifestations (EIMs) are the most common, followed by mucocutaneous, ocular, hepatobiliary, and vascular complications. (1,2) However, any organ system, including dermatologic, hepatobiliary, pulmonary, renal, and endocrine systems, may be affected. (3) This diverse involvement poses a significant challenge for physicians managing patients.

Approximately 7% to 60% of patients with UC develop one or more EIMs, which can be more debilitating than the underlying intestinal disease itself. (4,5) Some EIMs, such as pulmonary embolism, can be catastrophic if left untreated, while others, such as primary sclerosing cholangitis and uveitis, may lead to prolonged morbidity. Joint involvement is particularly associated with poor quality of life. Notably, EIMs may be active even when UC is in remission, or they may precede intestinal symptoms altogether. (6,7) Except for primary sclerosing cholangitis and a subset of spondyloarthropathies, most EIMs tend to follow the clinical course of intestinal disease. Uveitis, however, is a notable exception, often occurring independently of bowel activity.

The pathogenesis of EIMs in UC is multifactorial and remains incompletely understood. It may involve an intricate interaction of gut microbiota, innate immune responses, IL-17 axis cytokines, and mechanical stress. EIMs may reflect subclinical inflammation in UC patients, emphasizing the importance of early recognition to reduce associated morbidity and mortality. (8,9)

In one study involving 100 patients with an average age of 34 years, EIMs were observed in 11% of participants. [10] Another recent study, involving 120 participants, reported musculoskeletal symptoms in 24% of patients, including sacroiliitis (12.1%), peripheral arthritis (7.3%), episcleritis (2.1%), erythema nodosum (1.9%), and primary sclerosing cholangitis (1.1%). (11)

A multicenter study by Isene et al. (2014) involving 1,145 patients with inflammatory bowel disease (IBD) found that UC patients exhibited the following EIMs: arthritis (5.5%), sacroiliitis (1.5%), ankylosing spondylitis (1.0%), other rheumatological conditions (8.1%), iridocyclitis/uveitis (0.6%), other ophthalmological issues (0.6%), pyoderma gangrenosum (0.5%), erythema nodosum (0.8%), dermatological conditions (1.3%), and sclerosing cholangitis (0.4%). (12)

Factors such as age at diagnosis, family history, gender, smoking history, nutritional status, and disease extent are key prognostic indicators. (13) Additionally, biodemographic factors, including gender, age, disease duration, and smoking history, also impact the occurrence of EIMs. (14)

The rationale for this research proposal focuses on the urgent need to improve our understanding of the extraintestinal manifestations (EIMs) of ulcerative colitis (UC), which remain only partially understood despite their significant impact on patient morbidity and mortality. As the global prevalence of UC continues to increase, the burden of its systemic manifestations is becoming more apparent. This study aims to address gaps in existing knowledge by assessing the frequency and types of EIMs among patients at a tertiary care center. Building on insights from

previous studies, which report varying prevalence rates and a wide range of EIMs, including musculoskeletal, dermatological, and ophthalmological conditions, this research will develop a detailed epidemiological profile specific to a local population. The findings will help guide clinical practice by supporting the development of comprehensive management strategies, targeted patient education, and more effective allocation of healthcare resources. Ultimately, this study intends to improve patient outcomes and enhance the quality of life for individuals living with UC. The aims and objectives of our research were to determine the frequency of extraintestinal manifestations of ulcerative colitis in patients presenting at a tertiary care hospital and to compare the frequencies of extraintestinal manifestations of Ulcerative Colitis among patients in different demographic groups, identifying any associations.

Methodology

A cross-sectional study was conducted in the Department of Medicine at Shalamar Hospital, Lahore, over three months from January to March 2025. A sample size of 125 patients was determined based on the prevalence of extra-intestinal manifestations (EIMs) in Ulcerative Colitis (UC), which is 11% (10), with a 95% confidence level and a 5% margin of error. Non-probability consecutive sampling was used to recruit participants. A total of 125 cases of diagnosed UC were included in the study. The inclusion criteria were: patients aged 18 to 70 years, a confirmed UC diagnosis according to the operational definition, and both males and females were eligible. The exclusion criteria included patients with Crohn's disease or indeterminate colitis based on clinical history and medical records; individuals with a history of colectomy for UC; those with other significant systemic illnesses that might affect the study outcomes, such as rheumatoid arthritis or systemic lupus erythematosus; and patients with substantial co-morbidities like advanced liver disease or severe cognitive impairment.

Data was collected using a structured questionnaire (Data Collection Proforma) designed to assess the frequency of extraintestinal manifestations (EIMs) in patients with ulcerative colitis (UC) at a tertiary care hospital. The questionnaire included sections on patient demographics, disease history, smoking status, and the presence of specific EIMs such as arthritis, uveitis, and primary sclerosing cholangitis (PSC). Following ethical approval from the institutional review board, a cross-sectional observational study was conducted. Informed consent was obtained from all participants who met the inclusion criteria. Patients presenting to the outpatient department (OPD) or admitted to the inpatient department, with a previously established diagnosis of UC, were enrolled in the study. Baseline information, including age, gender, and duration of UC symptoms or diagnosis, was recorded using the proforma. A detailed physical examination was performed to identify any EIMs. Suspected dermatological manifestations, such as erythema nodosum and pyoderma gangrenosum, were confirmed by a consultant dermatologist. Musculoskeletal manifestations, including peripheral arthritis, axial spondylitis, and enthesitis, were confirmed by a rheumatologist. Ophthalmological findings, such as episcleritis and scleritis, were diagnosed by an ophthalmologist, while a gastroenterologist confirmed suspected cases of PSC. All data were documented by the primary researcher using a structured pro forma.

The data were analyzed using SPSS version 23. Quantitative variables, such as age and duration of symptoms, were reported as the mean ± standard deviation. Categorical variables, including gender and extraintestinal manifestations, were shown as frequencies and percentages. The data were stratified according to age, gender, and duration of symptoms. Post-stratification, the Chi-square test was used to assess the effect of these potential confounding variables on the outcome. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 125 patients diagnosed with Ulcerative Colitis were included in the study. The cohort consisted of 53 males (42.4%) and 72 females (57.6%).

Table 1: Population Demographics

Characteristic	Value
Total Patients	125
Mean Age (years)	41.26 ± 10.12 years
Mean Duration of Disease (years)	6.65 ± 4.3 years

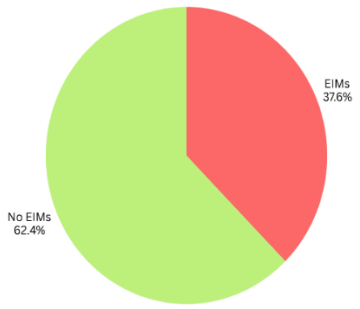

Image 1: Frequency of Extra-Intestinal Manifestations.

Among the 125 patients diagnosed with Ulcerative Colitis, extra-intestinal manifestations (EIMs) were identified in 47 individuals (37.6%). Musculoskeletal involvement was the most common, reported in 32 patients (25.6%). Of these, 22 (17.6%) had peripheral arthritis, while 10 (8.0%) showed features consistent with spondyloarthropathy. Ocular manifestations were noted in 13 patients (10.4%), with uveitis in 8 (6.4%) and episcleritis in 5 (4.0%). Dermatological issues affected 15 patients (12.0%), including erythema nodosum in 10 (8.0%) and pyoderma gangrenosum in 5 (4.0%). Four patients (3.2%) also had other skin conditions such as psoriasis and dermatitis. Hepatobiliary involvement was noted in 14 patients (11.2%), with 12 (9.6%) diagnosed with primary sclerosing cholangitis (PSC).

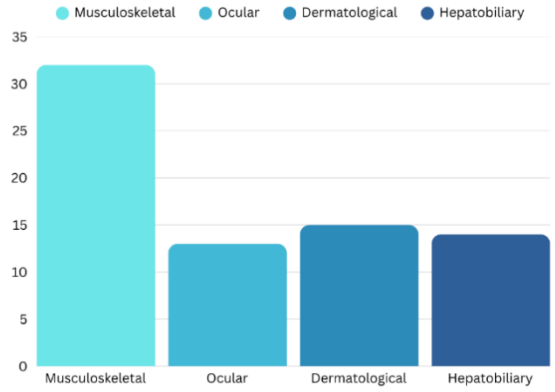

Image 2: Distribution of Extra-Intestinal Manifestations

To evaluate the relationship between disease duration and the occurrence of extra-intestinal manifestations (EIMs), the study population was divided into two groups based on the presence or absence of EIMs. The average disease duration for patients with EIMs was 8.2 ± 2.4 years, compared to 5.6 ± 2.1 years for those without EIMs. The difference in duration between the two groups was statistically significant ($p = 0.0004$, independent t-test), indicating that patients with a more extended history of Ulcerative Colitis are more likely to develop extraintestinal complications.

Table 2: Correlation of Average Disease Duration with the presence or absence of EIMs.

Group	Average Disease Duration	P value
EIMs present	8.2 ± 2.4 years	0.004
EIMs absent	5.6 ± 2.1 years	

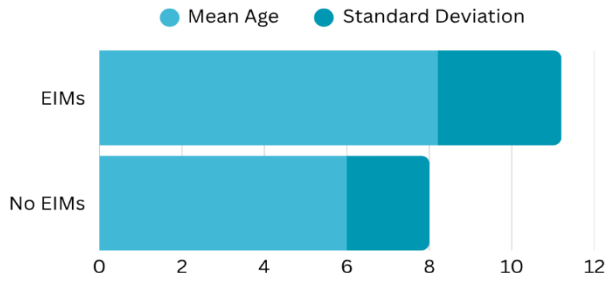

Image 3: Mean Age ± Standard Deviation across groups

No statistically significant difference was found in the overall prevalence of extraintestinal manifestations between male and female patients. However, musculoskeletal involvement was more common among males, while dermatological manifestations were more frequent in female patients.

Discussion

Ulcerative colitis is a chronic inflammatory condition affecting the colon and rectum. The symptoms of this persistent condition extend beyond the gut and may also involve several other organ systems. The findings of this study emphasize the impact of UC beyond the gastrointestinal system, with 37.6% of the study population experiencing extra-intestinal manifestations associated with UC. This aligns with other studies conducted in different regions, which report similar EIM rates in UC patients (11, 15, 16). Recognizing and understanding these extraintestinal manifestations is crucial for delivering effective patient care, as they present unique challenges in both diagnosis and management due to their high prevalence.

Among the EIMs, musculoskeletal involvement was the most common (25.6%), followed by dermatological (12.0%), hepatobiliary (11.2%), and ocular (10.4%) involvement. These findings are consistent with global literature, which identifies musculoskeletal symptoms, particularly peripheral arthritis and axial spondyloarthropathies, as the most frequent EIMs associated with UC. (11,12, 17, 18) Although no statistically significant difference was found in the overall frequency of EIMs based on gender, an interesting trend emerged: musculoskeletal symptoms were more prevalent in males. At the same time, females exhibited dermatological manifestations more frequently. This observation aligns with other similar studies. (12, 16) While these trends are not statistically significant, they may help clinicians remain alert to potential differences based on patient demographics.

A particularly noteworthy finding of this study was the significant association between longer disease duration and the presence of EIMs. Patients with EIMs had a mean disease duration of 8.2 ± 2.4 years,

compared to 5.6 ± 2.1 years in those without EIMs (p = 0.0004). This underscores the increased risk of developing EIMs over time and highlights the importance of regular monitoring of systemic complications through a multidisciplinary approach in patients with long-standing UC, a finding also supported by previous literature. (19, 20)

From a clinical perspective, these findings have significant implications. Early detection and proactive management of EIMs are crucial not only to prevent long-term complications but also to enhance overall quality of life. Many EIMs, such as primary sclerosing cholangitis, uveitis, and arthritis, can initially be subtle or misattributed to unrelated conditions, leading to delays in appropriate treatment. In some cases, EIMs may precede gastrointestinal symptoms, serving as a potential early indicator of underlying inflammatory bowel disease. Therefore, clinicians, including dermatologists, ophthalmologists, rheumatologists, and general practitioners, should be aware of the systemic nature of UC and maintain a high level of suspicion when encountering patients with unexplained extraintestinal symptoms. Incorporating multidisciplinary care is also vital, as managing EIMs often requires coordinated efforts across different specialties. Prompt referral and collaborative management can prevent complications, improve treatment outcomes, and boost patients' quality of life. Additionally, educating patients about the potential for extraintestinal involvement is essential, as it encourages early reporting of symptoms that might otherwise go unnoticed.

Despite the strengths of this study, like a well-defined patient cohort and specialist-confirmed diagnoses, certain limitations should be recognized. First, the study was conducted at a single tertiary care center, which may restrict the generalizability of the results to the broader population. Second, the cross-sectional design prevents causal inference or evaluation of the temporal relationship between disease activity and EIMs. Additionally, reliance on clinical suspicion and specialist assessment may have led to underdiagnosis of subclinical or asymptomatic EIMs, particularly in the hepatobiliary and ocular areas. Lastly, the absence of endoscopic severity scores or laboratory inflammatory markers (e.g., CRP, ESR) hinders the ability to link disease activity with systemic involvement.

Conclusion

This study highlights the significant burden of extra-intestinal manifestations in patients with Ulcerative Colitis, commonly affecting musculoskeletal, dermatological, ocular, and hepatobiliary systems. The findings emphasize the importance of early detection and multidisciplinary management of EIMs to prevent long-term complications and improve patient outcomes. Since a link exists between longer disease duration and a higher frequency of EIMs, regular screening and ongoing follow-up are crucial components of comprehensive UC care. Although the results align with existing research, more multicenter, long-term studies are necessary to understand better the underlying mechanisms and progression of EIMs, especially in diverse populations. Increasing awareness among healthcare providers about the systemic nature of UC can lead to earlier diagnosis, timely referrals, and ultimately enhance the quality of life for those affected by UC.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-MMS-033-24)

Consent for publication

Approved

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Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

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All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the integrity of the study.

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