CLINICAL AND HISTOLOGICAL FEATURES OF RELAPSED PATIENTS OF ULCERATIVE COLITIS

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Abstract:
Objectives:
To determine the clinical and histological features observed in patients experiencing relapses of ulcerative colitis.
Materials and Methods: This cross sectional study was conducted at Department of Medicine, Ziauddin University, Karachi, Pakistan. We have enrolled 192 patients with ulcerative colitis. The study was conducted from 1st January, 2023 to 31 December, 2023. Mucosal tissue biopsies underwent processing in an automatic tissue processor over a period of 16 hours overnight. The tissues were dehydrated using ethyl alcohol, cleared with xylene, and impregnated with paraffin wax, after which tissue blocks were formed. Subsequently, hematoxylin and eosin stains were applied.
Results: The mean age of the 192 patients was 41.54 ± 10.25 years. Among them, 110 (57.3%) were male, and 82 (42.7%) were female. The primary presenting complaint in UC patients is vague abdominal pain (53.1%), predominantly observed in the 36-50 age group, followed by per rectal bleeding (39.6%), which is more frequently reported in the same age range. The two most prevalent histological features observed are cryptitis, present in 100.0% of patients across all age groups, followed by chronic inflammation, present in 188 cases (97.9%).
Conclusion: It was concluded that in relapsed cases, vague abdominal pain is the main presentation, with cryptitis as the most common histological feature in ulcerative colitis.

Key words: ulcerative colitis, histological features, vague abdominal pain, cryptitis

INTRODUCTION:

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by mucosal inflammation and ulceration in the colon and rectum.(1) Despite advancements in medical therapy, a significant proportion of patients with UC experience disease relapse, leading to a substantial burden on healthcare resources and patient quality of life. The reported incidence and prevalence rates of ulcerative colitis (UC) in Asia vary across different regions and populations.(2) According to epidemiological studies, the incidence of UC in Asia typically falls within the range of 0.4 to 2.1 cases per 100,000 individuals per year.(3) Similarly, the prevalence rate of UC in Asia is reported to be between 6 to 30 cases per 100,000 population.(4) Indeed, despite the well-documented prevalence rates of ulcerative colitis (UC) in various regions globally, including Asia, the specific prevalence and clinical patterns of UC in Pakistan remain largely unknown.(5) UC has been observed in different parts of Pakistan, including major cities such as Karachi, Multan, Lahore, and Peshawar. (6, 7) UC is not confined to specific regions within the country but is recognized across various geographic locations. The etiology of ulcerative colitis (UC) remains elusive and complex, involving a combination of genetic, environmental, and immunological factors.(8) Understanding these multifaceted influences is crucial for comprehensively elucidating the pathogenesis of UC. Genetically, UC is recognized as a polygenic disorder, with genome-wide association studies (GWAS) revealing numerous susceptibility loci, including single nucleotide polymorphisms (SNPs) within genes implicated in immune regulation (e.g., ATG16L1, IRGM, IL23R, NOD2 receptor). Environmental factors such as smoking, diet, medications, socioeconomic status, and psychological stressors contribute significantly to UC pathogenesis. Notably, smoking exhibits a paradoxical effect, elevating the risk of UC development while potentially mitigating disease exacerbation. Dysregulation of the immune system is central to UC pathogenesis, characterized by an aberrant response against gut microbiota in genetically susceptible individuals, involving various mucosal immune cells and cytokine signaling pathways like interleukin-23 (IL-23) and tumor necrosis factor-alpha (TNF-α).(9) Additionally, certain medications like aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) may trigger or worsen UC by disrupting mucosal integrity and altering immune responses.(10) Understanding these multifaceted influences is crucial for elucidating UC's underlying mechanisms and developing tailored therapeutic approaches.(10)

Ulcerative colitis (UC) presents with a wide array of symptoms, encompassing both gastrointestinal and systemic manifestations, and is often associated with other autoimmune disorders.(11) Common clinical features include fever, appetite loss, weight loss, and fatigue, along with gastrointestinal symptoms like diarrhea, constipation, rectal bleeding, altered bowel habits, mucus discharge, tenesmus, and abdominal discomfort. UC can also coincide with autoimmune conditions such as Primary Sclerosing Cholangitis, Multiple Sclerosis, and Bullous skin disorders, indicating intricate immune system interactions. Interestingly, regional variations exist in symptomatology, with fewer extra-intestinal manifestations reported in UC patients from areas like Pakistan and India. (3, 12) Recognizing these diverse clinical presentations and regional differences is pivotal for precise diagnosis, effective management, and tailored care provision for individuals affected by UC.

Understanding the clinical and histological features of relapse in patients with UC is essential for optimizing disease management and improving outcomes. Clinical predictors such as disease extent, severity, smoking status, and treatment history can help identify patients at higher risk of relapse, guiding therapeutic decisions and monitoring strategies. Histological evaluation provides valuable insights into the underlying mucosal inflammation and may offer additional prognostic information beyond clinical assessments. Moving forward, efforts to achieve and maintain mucosal healing should be prioritized to reduce the burden of relapse and improve the long-term outcomes of patients with UC.

Objective:

To determine the clinical and histological features observed in patients experiencing relapses of ulcerative colitis.

MATERIALS AND METHODS:
Study Design: Cross sectional study
Study setting: Department of Medicine, Ziauddin University, Karachi, Pakistan.
Duration of the study: The study duration was One Year from (1st January, 2023 to 31 December, 2023).

Inclusion Criteria:
- Patients diagnosed with ulcerative colitis.
- Patients of age 18-65 years.
- Both gender.

Exclusion Criteria:
- Patients with other co-existing gastrointestinal disorders.
- Colorectal biopsies revealing dysplasia and neoplasia.
- Patients experiencing endoscopic and clinical remission.

Methods:
This study was conducted at Department of Medicine, Ziauddin University, Karachi, Pakistan after the approval of hospital ethical committee. A total of 74 patients with ulcerative colitis were enrolled in the study, and each patient was assigned a unique identification number following the acquisition of informed consent. Mucosal tissue biopsies underwent processing in an automatic tissue processor over a period of 16 hours overnight. The tissues were dehydrated using ethyl alcohol, cleared with xylene, and impregnated with paraffin wax, after which tissue blocks were formed. Subsequently, hematoxylin and eosin stains were applied. A predesign questionere were used to collect data. SPSS version 25 were used for statistical analysis.

RESULTS:
The mean age of 192 patients was 41.54+10.25 years (Table 1). Out of total, 110(57.3%) were male and 82(42.7%) were female. In the present study we have found that 95(49.5%) patients were of the 36-50 years age group, 59(30.7%) patients were of the 18-35 years age group, 28(14.6%) patients were of the 51-60 years age group and 10(5.2%) were of the >60 years age group. Table 2 and Table 3 present the distribution of patients based on age groups for both presenting complaints and histological features. The primary presenting complaint among UC patients is vague abdominal pain (53.1%), predominantly observed in the 36-50 age group, followed by per rectal bleed (39.6%), which is more frequently reported in the same age range. The two most prevalent histological features observed are cryptitis, occurring in 100.0% of patients across all age groups, followed by chronic inflammation, which is present in 188 cases (97.9%).

Table 2: Characteristic of all the enrolled patients *(n=192)*

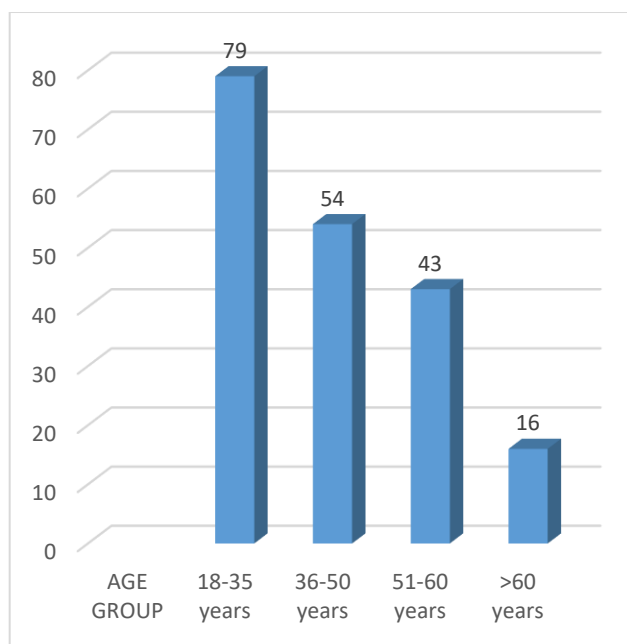| Variables	Frequency (Percentage)
Gender	
Male	110(57.3%)
Female	82(42.7%)
AGE GROUP	
18-35 years	59(30.7%)
36-50 years	95(49.5%)
51-60 years	28(14.6%)
>60 years	10(5.2%)
Mean age (years)	41.54+10.25

Fig 2: *Frequency of patients on the basis of age group*

Table 2: Distribution of patients with presenting complaints on the basis of age groups. (*n=192*)

	Age groups				
	18-35 years	36-50 years	51-60 years	>60 years	Total
Vague Abdominal Pain	31 (52.5%)	49 (51.6%)	16 (57.1%)	6 (60.0%)	102 (53.1%)
Per Rectal Bleed	27 (45.8%)	38 (40.0%)	10 (35.7%)	1 (10.0%)	76 (39.6%)
Diarrhea	35 (59.3%)	48 (50.5%)	15(53.6%)	4 (40.0%)	102 (53.1%)
Mucus discharge	3 (5.1%)	8 (8.4%)	2 (7.1%)	0 (0.0%)	13 (6.8%)
Altered Bowel Habits	17 (28.8%)	25 (26.3%)	7 (25.0%)	3 (30.0%)	52 (27.1%)
Pale	7 (11.9%)	16 (16.8%)	8 (28.6%)	1 (10.0%)	32 (16.7%)
Anemia	4(6.8%)	6 (6.3%)	2(7.1%)	0 (0.0%)	12 (6.3%)
Passage of Mucus Stool	0 (0.0%)	1 (1.1%)	0 (0.0%)	0 (0.0%)	0 (0.5%)

Table 3: Distribution of patients with histological features on the basis of age groups (*n=192*)

	Age groups				
	18-35 years	36-50 years	51-60 years	>60 years	Total
Cryptitis	59 (100.0%)	95 (100.0%)	28 (100.0%)	10 (100.0%)	192 (100.0%)
Chronic inflammation	58 (98.3%)	94 (98.9%)	26 (92.9%)	10 (100.0%)	188 (97.9%)
Activity(Neutrophils in lamina propria)	39 (66.1%)	62 (65.3%)	19 (67.9%)	8 (80.0%)	128 (66.7%)
Crypt distortion	44 (74.6%)	66 (69.5%)	18 (64.3%)	7 (70.0%)	135 (70.3%)
Crypt Abscess	40 (67.8%)	55 (57.9%)	17 (60.7%)	8 (80.0%)	120 (62.5%)
Basal lymphocytosis	32 (54.2%)	41 (43.2%)	11 (39.3%)	5 (50.0%)	89 (46.4%)
Basal lymphoid aggregates	27 (45.8%)	27 (28.4%)	13 (46.4%)	4 (40.0%)	71 (37.0%)
Eosinophils in lamina propria	7 (11.9%)	15 (15.8%)	3 (10.7%)	1 (10.0%)	26 (13.5%)

Discussion: The present study aims to determine the clinical and histological features observed in patients experiencing relapses of ulcerative colitis. Ulcerative colitis (UC) is indeed a chronic, lifelong inflammatory bowel disease characterized by periods of remission and relapse. This fluctuating nature of the disease can significantly impact the quality of life of affected individuals, leading to periods of symptom remission followed by episodes of disease flare-ups. The unpredictable course of UC necessitates long-term management strategies aimed at achieving and maintaining remission, minimizing symptoms during relapses, and preventing disease complications. The identification of histological features in ulcerative colitis (UC) is crucial, but it should be complemented by a

comprehensive assessment that integrates clinical, endoscopic, and radiological findings. This holistic approach allows for a more accurate diagnosis, assessment of disease severity, and evaluation of treatment response. Additionally, the advent of biological therapies has revolutionized the management of UC, significantly improving patient outcomes and enhancing quality of life. These targeted treatments offer effective alternatives for patients who are refractory to conventional therapies or experience intolerable side effects.

In our study, the majority of patients (95, 49.5%) fell within the 36-50 years age group, followed by the age group 18-35 years, which comprised 59 (30.7%) patients, with the mean age of all patients being 41.54 ± 10.25 years. Comparison with existing literature reveals similar trends: Alain Bitton et al.(13) observed a mean age of 40 years over a one-year duration, while Robert V. Bryant et al.(14) reported a higher mean age of 50 years over a six-year follow-up period. Additionally, other authors such as Aranzazu Jauregi Amezaga et al.(15) noted a mean age of 38 years. Another study conducted by momina jehangir khan et al. stated the mean age of 39.98 years.(9) Age group appears to be a significant factor influencing both the clinical features and histological features observed in relapsed patients of ulcerative colitis (UC). Our study revealed distinct patterns in symptom presentation and histological findings across different age groups. Notably, certain clinical symptoms, such as vague abdominal pain and per rectal bleeding, were more prevalent in specific age ranges, while histological features like cryptitis and chronic inflammation showed consistent distribution across all age groups. This suggests that age may influence the manifestation and severity of UC symptoms, as well as the underlying mucosal pathology.

In our study, rectal bleeding emerged as the second most common presenting complaint, reported in 76 cases (39.6%). This finding underscores the significance of gastrointestinal bleeding as a prevalent symptom in relapsed UC patients. Following rectal bleeding, diarrhea was identified as the third most common complaint, noted in 70 cases (36.5%). This highlights the frequent occurrence of altered bowel habits in UC relapse. Additionally, the passage of mucoid stool was noted in 58 cases (30.2%), further emphasizing the diversity of gastrointestinal symptoms experienced by relapsed UC patients. Collectively, these findings underscore the importance of recognizing and addressing a wide range of gastrointestinal symptoms in the clinical assessment and management of UC relapse.

In our study, clinically relapsed patients of UC commonly presented with vague abdominal pain, observed in 102 cases (53.1%), which is consistent with findings from studies by Momina Jehangir Khan et al.(9) (105 cases, 55.3%) and Sang Hyoung Park et al.(16) (164 cases, 53.9%). In our study, the second most common presenting complaint was rectal bleeding, reported in 76 cases (39.6%), which contrasts with the findings of Sang Hyoung Park et al.(16) (276 cases, 90.8%). However, our study findings align with those of Momina Jehangir Khan et al., supporting the prevalence of rectal bleeding as a common complaint. Additionally, diarrhea was the third most common presenting complaint in our study, reported in 70 cases (36.5%), similar to the findings of Sang Hyoung Park et al. (16) and Momina Jehangir Khan et al. (9) Fourthly, the passage of mucoid stool was noted in 58 cases (30.2%) in our study, contrasting with Sang Hyoung Park et al. (16) where it was reported in 168 cases (55.3%).

In our study, cryptitis emerged as the most common histological feature, observed in all cases (100.0%), which contrasts with the findings of other studies such as those conducted by Joshua E. Melson et al. (46%),(17) Sheenam Azad et al. (53.33%),(18) and Alain Bitton et al. (24%).(13) However, our study findings were supported by the presence of cryptitis reported in 189 cases (99.5%) in the study by Momina Jehangir Khan. (9) Additionally, crypt distortion was noted in 135 cases (70.3%) in our study, which is consistent with findings from studies conducted by Aman et al.,(19) Alain Bitton et al., and Momina Jehangir Khan. (9) In contrast, other studies reported a higher prevalence of crypt distortion, with Sheenam Azad et al.(18) observing it in all cases (100%), Joshua E. Melson et al(17). in 92% of cases, and SA Riley et al.(20) in 100% of cases. These variations underscore the diversity in histological findings across different studies and highlight the importance of considering multiple sources of evidence when interpreting study results. In our study, we observed several other microscopic indices commonly associated with ulcerative colitis (UC), including crypt abscesses, basal lymphocytosis, basal lymphoid aggregates, and eosinophils in the lamina propria,

which was supported by Momina Jehangir Khan et al.(9) the identification of these microscopic indices in our study provides further insights into the histopathological features of UC, aiding in the characterization of disease severity, assessment of treatment response, and understanding of underlying inflammatory processes. These findings contribute to a comprehensive understanding of UC pathology and may inform clinical management decisions for affected patients.

Conclusion: In relapsed UC, vague abdominal pains predominate, reflecting diverse symptomatology, while cryptitis is the primary histological feature, indicating active mucosal inflammation. A multimodality surveillance approach, combining clinical evaluation, endoscopy, histopathology, and imaging, is crucial for comprehensive disease monitoring and management.

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