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Serum Syndecan-1 Levels and Its Relationship to Disease Activity in Patients with Ulcerative Colitis Disease

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ABSTRACT

Background: Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) characterized by recurrent inflammation and ulceration of the colon and rectum.

Aim of the work: This study aimed to investigate the relationship between **serum** Syndecan-1 levels and disease activity in patients with UC.

Patients and Methods: This observational cross-sectional study included 84 participants, divided into three equal groups, (n=28 each): the Active Diseased Group with active UC; the Remission Group in UC remission; and the Normal Population Control Group of healthy individuals. The study compared clinical and biochemical parameters across these groups.

Results: Clinical assessments, laboratory tests, and colonoscopy were performed, and data were analyzed using SPSS version 23. A strong positive correlation was found between serum **Syndecan-1 levels** and **colonoscopy findings**, particularly in inflamed areas. The active disease group showed moderate to severe inflammation, while the remission and control groups had minimal or no inflammation. These findings suggest that serum Syndecan-1 is a reliable marker for assessing mucosal inflammation and overall disease severity.

Conclusion: This study indicates that **serum Syndecan-1** is a potential biomarker for evaluating UC disease activity and severity. Elevated levels were strongly correlated with increased inflammation, as evidenced by clinical symptoms, fecal calprotectin, ESR, CRP, and colonoscopy. These correlations suggest that serum Syndecan-1 could be a reliable **non-invasive marker** for monitoring disease progression and treatment response in UC patients.

Keywords: Serum Syndecan-1, Disease Activity, Ulcerative Colitis Disease.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) that primarily affects the colon and rectum. It is characterized by recurrent episodes of inflammation and ulceration in the lining of the colon. It is considered as one of the two major types of IBD, with the other being Crohn's disease [1].

UC presents with a range of symptoms that can vary in severity. Common symptoms include diarrhea (often with blood or mucus), abdominal pain, urgency to have a bowel movement, and rectal bleeding. Other systemic symptoms like fatigue, weight loss, and fever can also occur during disease flares. The symptoms tend to occur in episodes of active disease, which are interspersed with periods of remission when the symptoms subside [2]. The exact cause of UC is not fully understood, but it is believed to result from an abnormal immune response in genetically predisposed individuals [3]. The diagnosis of UC typically involves a combination of medical history assessment, physical examination, and diagnostic tests. Endoscopy and colonoscopy are key diagnostic tools that allow healthcare providers to directly visualize the colon's lining and take biopsies for analysis. Blood and stool tests as well as imaging studies may also be performed to rule out other conditions and assess the extent of inflammation [2].

Serum Syndecan-1 levels refer to the measurement of Syndecan-1, a cell surface proteoglycan, in the bloodstream, they are often observed in conditions characterized by tissue damage and inflammation, such as ulcerative colitis [4]. Higher Serum Syndecan-1 levels are often associated with more severe inflammation and mucosal damage in the colon, suggesting a direct link between the degree of disease activity and the concentration of Serum Syndecan-1 in the bloodstream. This relationship has sparked interest in Serum Syndecan-1 as a potential non-invasive biomarker for assessing the status of UC and monitoring changes in disease activity over time [5].

Understanding the dynamics of Serum Syndecan-1 in relation to UC disease activity may have broader implications for patient care. It could enable clinicians to make more informed decisions regarding treatment strategies and interventions [6]. Serum Syndecan-1 levels may contribute to a better understanding of the molecular mechanisms underlying UC pathogenesis, potentially leading to the development of targeted therapies aimed at modulating Syndecan-1 shedding or its downstream signaling pathways [7].

So the aim of the present study was to investigate the relationship between **serum** Syndecan-1 levels and disease activity in patients with UC.

METHODS

This observational cross-sectional study included 84 participants, after ethical committee approval and informed consent approval; participants were selected and classified into three equal groups.

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- **Group A (Active Diseased Group)**: 28 individuals currently experiencing active ulcerative colitis (UC).
- **Group B (Remission Group):** 28 individuals who have UC but are currently in remission.
- **Group C (Control Group):** 28 healthy individuals.

Participants with other significant gastrointestinal disorders (as Crohn's or celiac disease), pregnant or breastfeeding individuals, severe comorbid conditions (as., severe cardiovascular disease, kidney disease, or malignancies) or those who underwent recent gastrointestinal surgery were excluded from the study population.

All participants were subjected to: Detailed medical history and clinical examination, Laboratory investigations including: Complete blood count (CBC), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) , Albumin (Alb.), Fecal calprotectin (FCP), serum syndecan-1 level and Colonoscopies with biopsies to detect pathology.

Data collection:

Demographic and Clinical Information: Detailed demographic information (age, gender) and relevant clinical data (disease duration, treatment history) are collected through structured interviews with participants.

Blood Sample Collection:

Blood samples are collected from all participants during both active disease phases, periods of remission and from healthy control group. This allows for comparative analysis of Syndecan-1 levels. Standardized procedures are followed to ensure proper sample handling, preventing degradation or contamination.

Serum Isolation:

Blood samples are processed in a laboratory setting to isolate serum, the liquid portion of blood. Serum contains various biomolecules, including Syndecan-1, that can be measured to assess disease activity.

Syndecan-1 Level Measurement:

Enzyme-linked immunosorbent assays (ELISA) are employed to quantify Syndecan-1 levels in the collected serum samples. ELISA kits specifically designed for Syndecan-1 detection are used, ensuring accurate and standardized measurements.

Ethical approval

This study was performed in accordance with the ethical standards of the Faculty of Medicine, Ain Shams University Ethical Committee. Approval was taken before starting the study, and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. A written consent was obtained from each participant. Committee's reference number: FWA 000017585.

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as mean± standard deviation and ranges when their distribution was parametric (normal) while non-normally distributed variables (non-parametric data) were presented as median with inter-quartile range (IQR). Also, qualitative variables were presented as number and percentages. Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test.

The p-value was considered significant as the following: P-value $\leq$0.05 was considered significant, p-value $\leq$0.01 was considered as highly significant, p-value >0.05 was considered non-significant.

RESULTS

This study included 28 healthy participants (control group) and 56 ulcerative colitis patients (case group), which was further classified into 2 subgroups according to activity and remission of the disease: group A (activity) while group B (remission). All patients were sex and age matched with average age of 35 years.

There is a strong positive correlation between Serum Syndecan-1 levels and the number of motions indicating that higher Syndecan-1 levels are associated with increased bowel movements. Similarly, significant positive correlations are observed between Serum Syndecan-1 and both bleeding per rectum and pain, suggesting that elevated levels may reflect more severe clinical symptoms, table (1).

Table (1): Correlation of Serum Syndecan-1 with Clinical Symptoms in Patient Groups

	Serum Syndecan-1	
	r	**p-value**
Motions	**0.547**	**<0.001**
Bleeding Per Rectum	**0.412**	**<0.001**
Pain	**0.412**	**<0.001**
Arthralgia	-0.168	0.205

Using: r: spearman correlation coefficient, p-value >0.05 is non-significant; p-value <0.05 is significant; p-value <0.01 is highly significant.

There is correlation between Serum Syndecan-1 and various hematological parameters. Significant positive correlations are found with TLC and Neutrophils, indicating that higher levels of Serum Syndecan-1 are associated with increases in these white blood cell counts. Conversely, there is a highly significant negative correlation with hemoglobin, table (2).

Table (2): Correlation of Serum Syndecan-1 with Hematological Parameters in Groups

	Serum Syndecan-1	
	r	p-value
TLC	**0.341**	**0.015**
Neutrophils	**0.280**	**0.049**
Lymphocytes	**0.228**	**0.111**
Hemoglobin (Hb)	**-0.369**	**0.008**
MCV	-0.013	0.929
MCH	-0.201	0.167
Platelet	-0.046	0.752

Using: r: spearman correlation coefficient, p-value >0.05 is non-significant; p-value <0.05 is significant; p-value <0.01 is highly significant.

Another correlation between Serum Syndecan-1 levels and various inflammatory markers revealed highly significant positive correlations between Serum Syndecan-1 and ESR, CRP, and Fecal Calprotectin. These findings suggest that elevated Serum Syndecan-1 levels are strongly associated with increased inflammatory activity in patients, table (3).

Table (3): Correlation of Serum Syndecan-1 with Inflammatory Markers in Patient Groups

	Serum Syndecan-1	
	R	p-value
ESR	**0.459**	**<0.001**
CRP	**0.417**	**<0.001**
Fecal Calprotectin	**0.790**	**<0.001**

Using: r: spearman correlation coefficient, p-value >0.05 is non-significant; p-value <0.05 is significant; p-value <0.01 is highly significant.

Table (4) presents the correlation between Serum Syndecan-1 levels and colonoscopy, including the cecum, ileum, right side, transverse, left side, sigmoid, anus, rectum, and overall pathological findings. The analysis demonstrates significant positive correlations across all segments, with the strongest associations observed with pathology ($p < 0.001$), anus and rectum ($p < 0.001$), and the sigmoid colon (left sided colon) ($p < 0.001$).

Table (4): Correlation of Serum Syndecan-1 with Colonoscopy in Patient Groups

	Serum Syndecan-1	
	r	p-value
Cecum	**0.287**	**0.010**
Ileum	**0.287**	**0.010**
Ascending Colon	**0.368**	**<0.001**
Transverse	**0.370**	**<0.001**
Descending Colon	**0.498**	**<0.001**
Sigmoid	**0.664**	**<0.001**
Anus &rectum	**0.759**	**<0.001**
Pathology	**0.811**	**<0.001**

Using: r: spearman correlation coefficient, p-value >0.05 is non-significant; p-value <0.05 is significant; p-value <0.01 is highly significant.

DISCUSSION

The relationship between Serum Syndecan-1 levels and disease activity in patients with ulcerative colitis (UC) has garnered significant attention due to its potential as a non-invasive biomarker for monitoring disease severity [8].

The comparison of symptom prevalence among the active diseased, remission, and control Groups reveals significant differences across all measured symptoms. The active diseased group exhibits a much higher average number of motions (9.14 ± 2.84) compared to the remission (2.93 ± 0.60) and control groups (2.64 ± 1.10), with a highly significant p-value (<0.001). Bleeding per rectum is present in 89.3% of the active diseased group, 53.6% of the remission group, and absent in the control group ($p < 0.001$). Pain is universal in the active diseased group (100%) but affects only 64.3% of the remission group and none of the control group ($p < 0.001$). Arthralgia follows a similar pattern, that being more prevalent in the active diseased group (46.4%) and significantly lower in the remission group (17.9%) and absent in the control group ($p < 0.001$). These findings indicate that symptoms such as increased motions, bleeding, pain, and arthralgia are much more pronounced in the active diseased group, reflecting the higher disease activity compared to the remission and control groups.

In accordance, it was found that while symptoms such as pain and joint pain (arthralgia) were more commonly reported in the active disease group, the differences in symptom prevalence did not reach statistical significance [5], contrasting with the significant findings in our study. Similarly, it was observed more frequent symptom reporting in patients with active disease, but the variations were not statistically significant, differing from the strong statistical correlations we found [9].

Elevated total leukocyte count (TLC) and Neutrophil levels in the active diseased group, compared to both the remission and control groups, reflect the heightened immune response during active disease, as seen with the significant p-value of 0.007 for TLC. These findings align with the studies by **Chen [10] and Cui [11],** which similarly demonstrate increased inflammatory markers during active UC phases.

The significant differences in lymphocyte counts, with higher values in the active diseased group ($p < 0.001$), mirror the immune response dynamics, where lower lymphocyte levels in the remission group suggest a return to immune homeostasis [12]. It's demonstrated that elevated inflammatory markers, such as ESR and CRP, are closely associated with active disease phases in UC [5], mirroring the significant increases observed in the active diseased group in our research. This further supports the notion that systemic inflammatory markers like ESR and CRP are reliable indicators of disease severity in UC. Fecal calprotectin, a key marker of intestinal inflammation, is significantly elevated in patients with active UC [13], which aligns with the

considerable rise in its levels seen in our active diseased group compared to the remission and control groups. **Hanafy *et al.* [14]** also emphasized the predictive value of non-invasive inflammatory markers, such as ESR and CRP, in assessing disease activity and remission, reinforcing their relevance as observed in our study where these markers clearly differentiated between active disease and remission phases. These external findings validate our study's conclusions regarding the utility of inflammatory markers and fecal calprotectin in monitoring UC progression.

In alignment with the findings of colonoscopy of this study, **Floer *et al*. [5]** similarly reported variations in colonic inflammation, with moderate to severe inflammation predominantly observed in patients with active UC, while those in remission exhibited minimal or no inflammation. This mirrors the pattern observed in our active diseased group, where significant inflammation was found across various segments of the colon, particularly in the sigmoid and rectum. **Yablecovitch *et al*. [4]** also documented extensive colonic inflammation during active disease phases, particularly in the lower colon, aligning with our findings of severe involvement in the sigmoid colon and anus/rectum. **Verstockt *et al.* [15]** further emphasized the distinction between active and remission phases of UC, with their work reinforcing the marked differences in endoscopic findings observed between our study groups.

The comparison of Serum Syndecan-1 levels and pathology severity among the active diseased, remission, and control groups reveals significant differences as it is markedly higher in the active diseased group (33.41 ± 15.72) compared to the remission group (15.58 ± 12.93) and the control group (1.22 ± 0.83), with a highly significant p-value (<0.001), indicating its potential role as a biomarker for active disease. This finding is supported by **Floer *et al.* [5]** who also demonstrated a strong association between elevated Syndecan-1 levels and active disease states in UC. The pronounced severity of pathology in the active diseased group aligns with the correlation of higher Serum Syndecan-1 levels with increased disease activity. In contrast, the remission group shows predominantly mild pathology and no severe cases. These statistically significant findings further support the potential of Serum Syndecan-1 as a biomarker for disease severity, reinforcing its importance as highlighted by studies from **Yablecovitch *et al.* [4], Verstockt *et al.* [15], and D'Amico *et al.* [16].** Elevated Serum Syndecan-1 levels are closely linked to inflammatory processes, contributing to symptom severity, particularly bowel-related symptoms such as pain and rectal bleeding. This aligns with the strong positive correlations observed in our study between Syndecan-1 levels and the number of motions, bleeding per rectum, and pain, further supporting the use of Syndecan-1 as a marker for active disease and symptom severity in ulcerative colitis (UC) [5]. Elevated Serum Syndecan-1 levels correlate with increased inflammatory activity in ulcerative colitis, particularly with intestinal inflammation. This supports the strong positive correlation observed in our study between Serum Syndecan-1 and fecal calprotectin, reinforcing its role as a marker of localized inflammation in severe cases [17]. There is also an association between Serum Syndecan-1 and systemic inflammatory markers such as ESR and CRP, aligning with our findings of moderate positive correlations between Serum Syndecan-1 and these markers [12]. Elevated Serum Syndecan-1 levels were significantly linked to severe inflammation in specific colon segments, particularly in the sigmoid and rectum, areas that are commonly affected in UC. This aligns closely with the strong correlations in our study, where Serum Syndecan-1 levels were most strongly associated with inflammation in the sigmoid and anus/rectum regions [5].

Similarly, **Derkacz *et al.* [12]** also reported a correlation between Serum Syndecan-1 levels and overall pathology severity, further supporting our findings of a very strong correlation between Serum Syndecan-1 and the extent of mucosal inflammation across all colon segments. Moreover**, Hanafy *et al.* [14]** reinforced the relevance of Serum Syndecan-1 as a non-invasive marker for UC severity, with findings correlating well with endoscopic assessments.

CONCLUSION

In conclusion, the findings from this study underscore the significant role of Serum Syndecan-1 as a potential biomarker for assessing disease activity and severity in patients with ulcerative colitis. Elevated Serum Syndecan-1 levels were strongly correlated with increased inflammation, as evidenced by both clinical symptoms and objective measures such as fecal calprotectin, ESR, and CRP. Additionally, the strong positive correlations between Serum Syndecan-1 levels and colonoscopy findings across various segments of the colon highlight its potential utility in reflecting the extent and severity of mucosal inflammation. These correlations suggest that Serum Syndecan-1 could serve as a reliable non-invasive marker for monitoring disease progression and treatment response in ulcerative colitis patients.

ABBREVIATIONS

Alb: Albumin
CBC: Complete blood count
CRP: C- reactive protein
ESR: erythrocyte sedimentation rate
ELISA: Enzyme-linked immunosorbent assays
FCP: Fecal calprotectin
IBD: Inflammatory bowel disease
Hb: Hemoglobin
MCV: Mean corpuscular volume
MCH: Mean corpuscular hemoglobin
NS: Non significant
PLT: platelet

S: Significant
SD: Standard deviation
SPSS: Statistical package for Social Science
TLC: Total leucocyte count
UC: Ulcerative Colitis

DECLARATIONS

- **Availability of data and material:** data are available with corresponding author to be presented upon request.
- **Competing interests:** the authors declare that they have no competing interests
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