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Serum Oncostatin M as a potential diagnostic biomarker of Ulcerative colitis Patients and Its Relation to Severity

Mohamed Gamal Mohamed[a], Shafiq Naguib Shafiq[a], Marwa Abdellah Shaker[b], Hany sayed Ahmed[a]

[a]*Internal Medicine Department, Beni-Suef University, Beni- Suef, Egypt.*

[b]*Tropical medicine Department, Beni-Suef University, Beni- Suef, Egypt.*

Abstract

Elevated serum levels of Oncostatin M (OSM) are linked to inflammatory process. Ulcerative colitis (UC) is a common inflammatory condition characterized by mucosal inflammation and associated with a burden of disability. The aim of this study is to investigate Oncostatin M levels as potential biomarkers for the diagnosis and severity of ulcerative colitis. Ninety people, thirty patients with ulcerative colitis, thirty patients with high fecal calprotectin without ulcerative colitis, and thirty patients in the control group were included in the study. In our study, we included patients who had been diagnosed with ulcerative colitis initially. Every patient underwent endoscopic scoring utilizing the Ulcerative Colitis Endoscopic Severity Index (UCEIS) and the Mayo endoscopic scoring (MES) methodology. Oncostatin M blood samples were obtained from the patients. There was a significant difference in Oncostatin M between the three groups With $p<0.05$, When comparing ulcerative colitis patients to controls with elevated fecal calprotectin and no signs of inflammation, serum Oncostatin M was considerably greater in these patients. Additionally, according to UCEIS, there is a significant difference in the severity and extension of the disease in patients with ulcerative colitis ($p<0.05$). In adult patients with UC, Serum Oncostatin M can be helpful in diagnosing ulcerative colitis (UC) and assessing its severity at the time of initial presentation.

Keywords: Ulcerative colitis, Oncostatin M, inflammatory, Severity

Full length article **Corresponding Author*, e-mail: *mohamedgm88@med.bsu.edu.eg ; mohamedgm1988@gmail*

1. Introduction

Ulcerative colitis (UC) is an idiopathic, chronic inflammatory illness of the colon that is characterized by continous, diffuse mucosal inflammation [1-2].With 505 new cases per 100,000 people, Europe now has the highest prevalence of UC, followed by North America with 249 new cases per 100,000 people [3]. With an annual percentage rise of +4.3% (6), it is becoming increasingly commonplace worldwide as more nations adopt Westernized lifestyles, leading to fast increases in incidence rates [4-5]. In Egypt, the diagnosis of UC has rising in the last 10 years and is more common than crohn's disease (CD), with the average patient age being in their late 20s at diagnosis. Females were more likely to have UC. UC is roughly 6:1 more frequent than Crohn's disease (CD) [6].

About 15–20% of UC patient has moderate to severe presentation and require hospitalization, with a risk of colectomy 10% [7].The pathogenesis of UC has not been elucidated yet, but it is supposed to be a consequence of unbalanced expression of molecules that have both anti- and pro-inflammatory properties [8]. The inflammatory markers erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and fecal calprotectin (FC) have been studied to determine the type of ulcerative colitis (UC), its severity, prognosis, and responsiveness to treatment [9]. FC is not a valid diagnostic indicator of gastrointestinal tract (GIT) inflammation, despite its sensitivity. Additionally, the same patient's stool samples taken on different days or on the same day may have different FC levels [10].

As a member of the interleukin 6 (IL-6) cytokine family, oncostatin M (OSM) can trigger signaling via the phosphatidylinositol-3-kinase (PI3K)-Akt pathway, mitogen activated protein kinase (MAPK) cascades, and the JAK-STAT pathway (containing JAK1, JAK2, STAT1, STAT3, STAT5, and possibly STAT6) [11]. According to many research, OSM appears to cause intestinal inflammation by causing gut-resident stromal cells to express large levels of the OSM receptor-β (OSMR), adhesion factor, cytokine, and chemokine. In this work, we sought to assess the use of Oncostatin M level in patients with UC, ascertaining the degree and character of the illness and its correlation with various disease severity ratings by contrasting it with fecal calprotectin (FC) [11].

2. Materials and Methods

2.1. Study design

Ninety individuals in all were selected from the gastrointestinal and endoscopy department at University Hospital for this case-control study [12]. Thirty patients with ulcerative colitis (Group 1), thirty individuals with increased FC but a normal colonoscopy and no evidence of UC and biopsies were taken during endoscopic assessment excluding other inflammatory processes as microscopic colitis, Crohn's disease or others made up Group 2, and thirty seemingly healthy volunteers as a control group (Group 3). The thirty UC patients were then divided based on several severity levels, such as the Mayo score and the Ulcerative Colitis Endoscopic Index of Severity (UCEI).

2.2. Ethical considerations

The Helsinki Declaration's ethical guidelines were adhered to in the current study. The Beni-Suef University Faculty of Medicine's Ethical Committee approved the study, giving it clearance number FMBSUREC/03102023/Mohamed. Written informed consent was acquired from every individual involved. The NCT05974332 clinical trial number was assigned.

2.3. Inclusion criteria

Patients, both male and female, who are over the age of 18 and were identified as having UC based on histological, clinical, and endoscopic criteria.

2.4. Exclusion criteria

Those with concomitant systemic inflammation as Rheumatoid arthritis(RA) and Bronchial asthma (BA), those with a history of malignancy, or those with other infection as common cold. Also, patients who were discovered to have microscopic colitis, Crohn's disease or other inflammatory process proved by pathological assessment of colonic biopsy.

2.5. Confidentiality of data

All participant data will be kept in locations with restricted access in locked file cabinets.

2.6. Statistical analysis

The data was analyzed using the statistical program for social science, version 20, known as SPSS. Quantitative variables are referred to as mean, SD, and range. Numerical values and percentages representing qualitative variables.

2.7. Methods

All patients enrolled in the study, will be subjected to

i. Carefully gathering medical history, including smoking, physical activity, age, sex, education, residency behavior, and medical history including fever, frequency of diarrhea.
ii. A clinical assessment: Patients were measured for temperature, pulse or signs of severity.
iii. The following lab tests were performed: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and complete blood count (CBC). Likewise Albumin.
iv. Evaluation via endoscopic examination: Mayo endoscopic score (MES) was utilized for evaluation the degree of mucosal inflammation in each portion of the colon. Remission (score 0-1), mild (score 2-4), moderate (score 5–6), and severe (scoring 7–8) were the four categories into which UCEI was categorized.
v. OSM serum level measurement using the sandwich enzyme-linked immunosorbent test (ELISA), supplied by ELK Biotechnology (China), in accordance with the manufacturer's instructions. The range of detection is 15.63–1000 ng/L.

3. Results and discussion

3.1. Results

- **Base line patient characteristics**

Table I presents the laboratory data and demographics of the study participants at the time of recruitment. The patients with ulcerative colitis had an average age of 32.17 ±9.52, whereas the control group and high FC groups had mean ages of 33.13 ±10.78 and 32.90±9.26, respectively. In terms of participant sex, men and women are roughly equal. Regarding age, sex, and smoking, there is no discernible difference between the research groups in Table 1. However, it demonstrates that there are statistically significant differences in CRP, ESR, albumin, hemoglobin level, white blood cells, platelets, fecal calprotectin, and oncostatin M across the study groups.
Table 2 shows that there was a statistically significant difference ($p<0.027$) in the severity of symptoms described by UCEIS between pancolitis patients, proctitis patients, and the left-distal group, but not between severity and MES.

Table 3 shows that there was a statistically significant difference with $p<0.001$ between OSM and with disease extension and disease severity in ulcerative colitis patients by UCEIS score.

Table 4 shows that there was a significant positive correlation between levels of Oncostatin M and fecal calprotectin. ($r2 = 0.083$) (Figs. 4). A positive and statistically significant association was found between OSM and FC in the patient group, as per the Spearman's Ranking association Coefficient analysis ($rspearman = 0.083$, $p < 0.01$).

3.2. Discussion

The most prevalent type of inflammatory bowel disease (IBD) that affects people globally is ulcerative colitis (UC) [12]. In 2023, it was predicted that there would be 5 million cases worldwide, and the incidence is rising. It is a chronic idiopathic inflammatory disease that is linked to bloody diarrhea and is characterized by diffuse friability and superficial colonic wall erosions [13]. Oncostatin-M (OSM) is a cytokine belonging to the interleukin-6 (IL-6) family. It was initially identified in 1986 from human histolytic lymphoma U937 cells [14]. It is involved in several inflammatory disorders, including bone remodeling, liver regeneration, and wound healing [15]. Numerous biological processes are impacted, including the PI3K/AKT, MAPK, JNK, and JAK/STAT pathways [16].

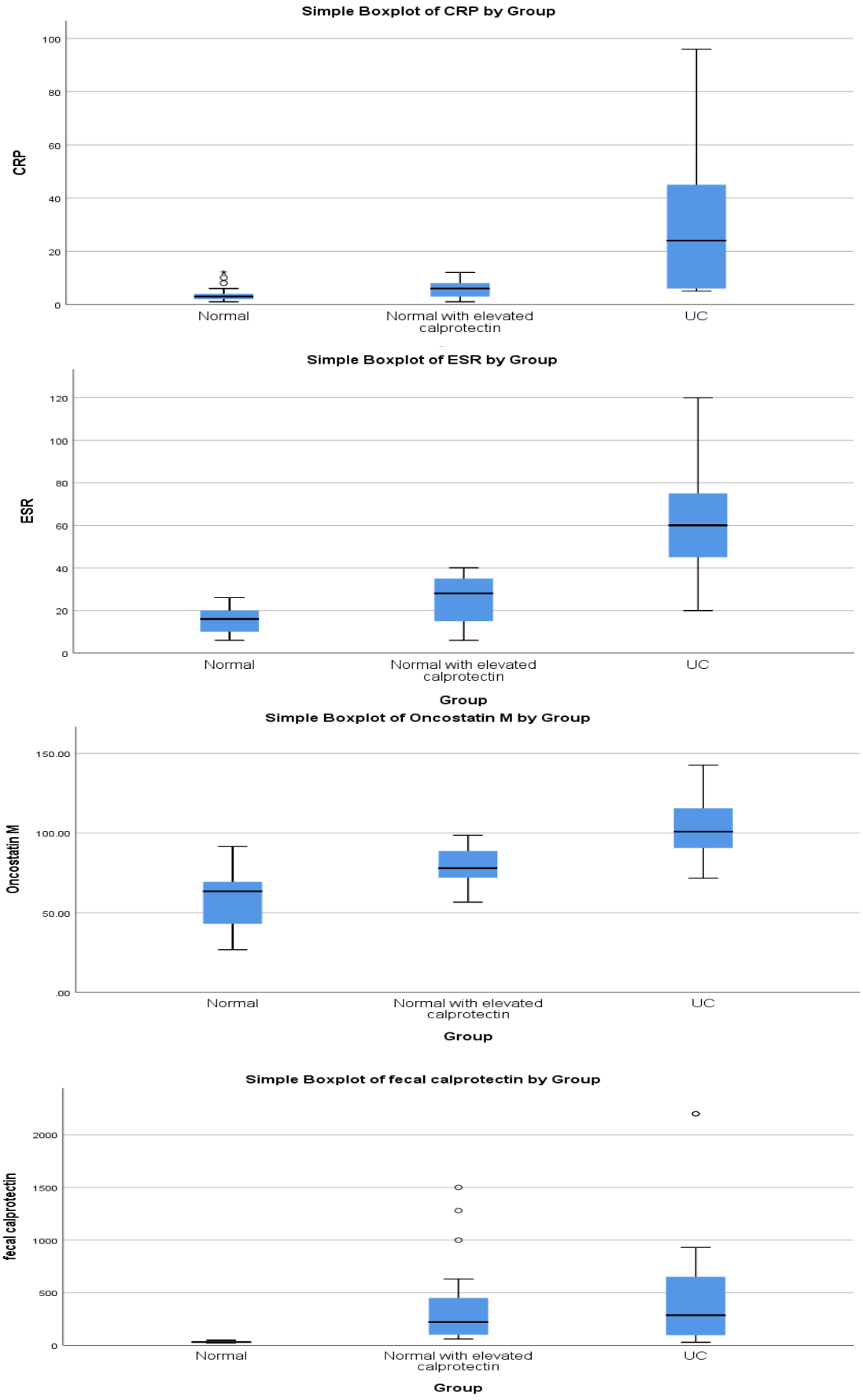

Figure 1: Difference between study groups regarding CRP, ESR, FC and Oncostatin M

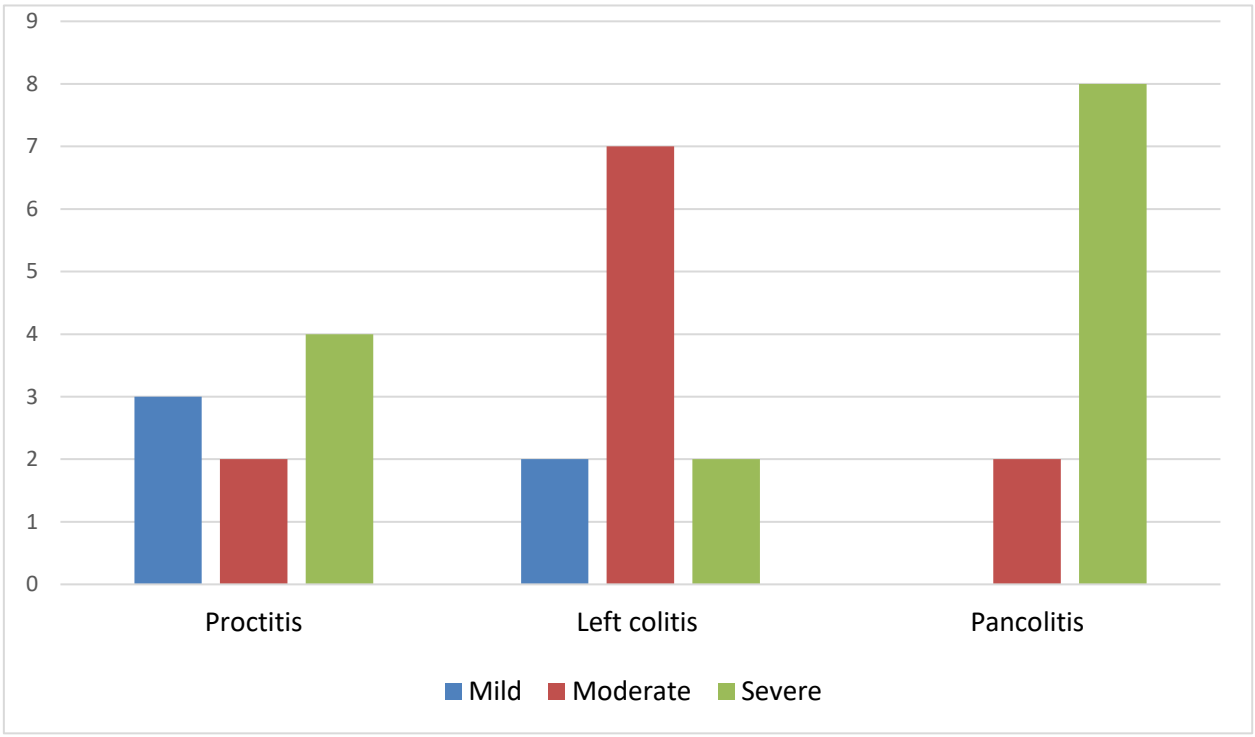

Figure 2: Relationship between disease extension and UCEIS score

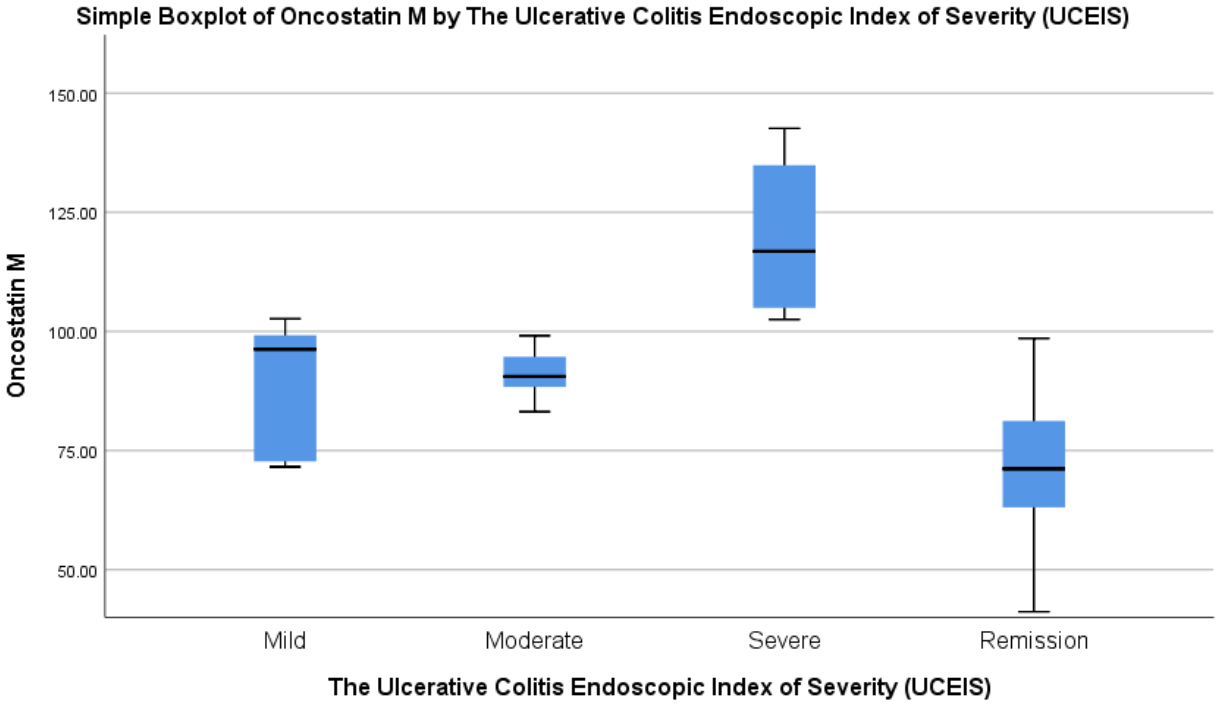

Figure 3: Relationship between Oncostatin M with disease severity by UCEIS score in ulcerative colitis patients.

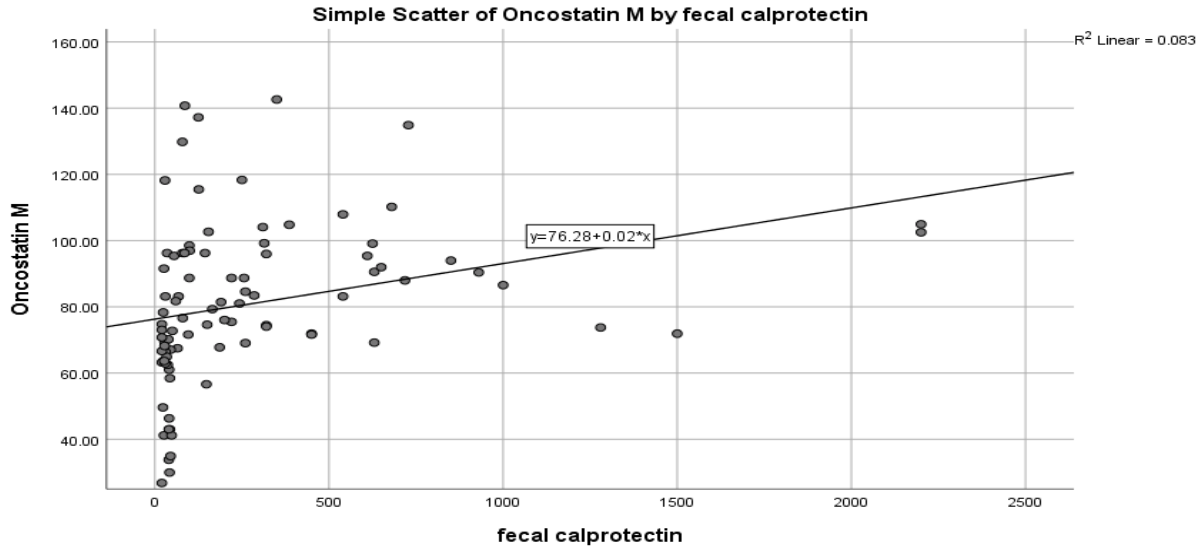

Figure 4: Correlation between Oncostatin M and fecal calprotectiz

Table 1: Comparison between Study groups regarding socio-demographic and laboratory characteristics

		Normal group (n=30)	**Normal with elevated calprotectin (n=30)**	**Ulcerative colitis group (n=30)**	**P value**	
Age [Mean ±SD]		33.13 ±10.78		32.90 ±9.26	32.17 ±9.52	0.925
Sex	Males [n (%)]	16 (35.6%)		15 (33.3%)	14 (31.1%)	0.875
	Females [n (%)]	14 (31.1%)		15 (33.3%)	16 (35.6%)	
Smoking	Smoker [n (%)]	11 (37.9%)		10 (34.5%)	8 (27.6%)	0.701
	Non-smoker [n (%)]	19 (31.1%)		20 (32.8%)	22 (36.1%)	

CRP[mg/L] [Mean ±SD]	3.80 ±2.55[c]	5.80 ±3.16[c]	26.27 ±24.34[a b]	**<0.001***
ESR[mm/h] [Mean ±SD]	15.03 ±5.89[b c]	25.47 ±10.56[a c]	64.67 ±25.26[a b]	**<0.001***
Albumin [g/L] [Mean ±SD]	4.26 ±0.49[c]	4.09 ±0.38[c]	3.42 ±0.67[a b]	**<0.001***
Hgb gm/dl [Mean ±SD]	11.50 ±1.29	12.05 ±1.063[c]	10.91 ±2.07[b]	**0.019***
WBCs [10^3/mm^3] [Mean ±SD]	8080 ±2641.89	7216.67 ±2016.16[c]	8890 ±2653.48[b]	**0.035***
Platelets [10^3/mm^3] [Mean ±SD]	252.87 ±64.83[c]	289.6 ±92.75[c]	370.87 ±134.99[a b]	**<0.001***
Fecal calprotectin [Mean ±SD]	31.90 ±9.26[b c]	345.13 ±353.89[a]	464.13 ±544.16[a]	**<0.001***
Oncostatin M[ng/ml] [Mean ±SD]	58.99 ±16.31[b c]	80.13 ±10.74[a c]	103.87 ±18.88[a b]	**<0.001***

(*): P value is significant
(a): Significant difference with normal group
(b): Significant difference with normal with elevated calprotectin group.
(c): Significant difference with ulcerative colitis group.

Table 2: Relationship between extensions of colitis with disease severity indices in ulcerative colitis patients.

		Proctitis (n=9)	Left colitis (n=11)	Pancolitis (n=10)	P value
Mayo endoscopic score	Mild [n (%)]	3 (33.3%)	4 (36.4%)	2 (20.0%)	0.813
	Moderate [n (%)]	3 (33.3%)	5 (45.5%)	4 (40.0%)	
	Severe [n (%)]	3 (33.3%)	2 (18.2%)	4 (40.0%)	
The Ulcerative Colitis Endoscopic Index of Severity (UCEIS)	Mild [n (%)]	3 (33.3%) [c]	2 (18.2%)	0 (0.0%) [a]	**0.027***
	Moderate [n (%)]	2 (22.2%)	7 (63.6%) [c]	2 (20.0%) [b]	
	Severe [n (%)]	4 (44.5%)	2 (18.2%) [c]	8 (80.0%) [b]	

(*): P value is significant (a): Significant difference with proctitis group.
(b): Significant difference with left colitis group (c): Significant difference with pancolitis group.

Table 3: Relationship between Oncostatin M with disease extension and disease severity in ulcerative colitis patients

		Oncostatin m level [Mean ±SD]	P value
Disease extension	Proctitis	103.26 ±19.08	0.651
	Left colitis	95.08 ±15.94	
	Pancolitis	114.08 ±18.23	
Mayo endoscopic score	Mild	93.96 ±15.68	0.170
	Moderate	108.73 ±19.04	
	Severe	107.28 ±19.73	
Ulcerative Colitis Endoscopic Index of Severity (UCEIS)	Mild	88.48 ±15.07[d]	**<0.001***
	Moderate	91.09 ±4.90[a d]	
	Severe	119.40 ±14.77[a b c]	

(*): P value is significant (a): Significant difference with remission UCEIS group.
(b): Significant difference with mild UCEIS group. (c): Significant difference with moderate UCEIS group.
(d): Significant difference with severe UCEIS group.

Table 4: Correlation between Oncostatin M and fecal calprotectin

	P value	Correlation coefficient r
Oncostatin M	**0.001***	**0.083**
Fecal calprotectin		

It has been demonstrated that OSM is expressed more frequently in inflammatory disorders than in healthy tissues. These diseases include inflammatory bowel disease, cardiovascular disease, skin disease, arthritis, and most recently, COVID-19 [16]. Therefore, the purpose of our study was to assess OSM's potential as a diagnostic serological marker for the diagnosis of UCC. Additionally, in order to potentially increase diagnostic accuracy, we correlated it with another well-recognized UC marker, fecal calprotectin (FC). In our case control study, UC individuals, individuals with elevated FC without inflammation and normal volunteers were enrolled. The results of our study indicate that there is a statistically significant difference (pvalue <0.001) in OSM between the UC group and the other two groups, suggesting that an increase in OSM level will be linked to UC.

Also, we found a statistically significant difference between severity of symptoms defined by UCEIS between the pancolitis patients, the left-distal group, and those with proctitis ($p<0.027$). There is a statistically significant difference between severity of symptoms defined by UCEIS and OSM level, indicating that a rise in OSM level is associated with disease severity and extension. There is a significant positive correlation between levels of Oncostatin M and fecal calprotectin. ($r2 = 0.083$) (Figs. 4). OSM and FC had a positive and significant association, according to the patient group's Spearman's Ranking association Coefficient study ($rspearman = 0.288$, $p < 0.01$). Suggesting that when it comes to identifying UC and inflammation, OSM is more sensitive and specific than FC.

Consistent with earlier studies, we discovered that OSM outperformed FC and standard blood indicators in detecting intestinal inflammation, and that these two biomarkers—OSM and FC—were strongly correlated with clinical and endoscopic activity. In line with earlier findings on FC, a particular biomarker called OSM was identified as being significantly overexpressed in UC patients but not in non-UC patients or healthy controls. West et al., who observed higher expression levels of OSM in the colon of UC patients at the time of the patients' initial presentation, corroborated these findings and provided an explanation for this function [11].

Additionally, it was shown by Bertani et al [17], Lorenzo Bertani et al [18] and Minar,P [19] that OSM expression was significantly elevated in UC and may be involved in the physiopathology. These findings are consistent with the current findings. According to West et al., there is a link between high levels of intestinal OSM expression and the necessity of early IBD surgery as well as a higher rate of main biological therapy nonresponse [11]. Similarly, Verstockt, et al. reported that up regulation of OSM expression on inflamed colonic mucosa might take part in UC pathogenesis, Also, Patients with active UC have considerably higher serum OSM levels than controls [20]. These results corroborate those of Zhou et al [21], who observed that blood samples from UC patients who are actively ill have higher levels of OSM gene expression than do those who are in remission. Furthermore, Jostins et al [22] found that OSM and TNF work together to induce inflammatory signals in stromal cells.

4. Conclusions

In conclusion, our study's findings demonstrated a robust correlation between OSM and UC, and severity of the disease at presentation. The diagnostic power of OSM, a promising UC diagnostic marker, when combined with FC is significantly increased. Its serum concentration can be used as an effective, non-invasive marker for UC identification.

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No funding was obtained for this study.

Conflict of interest

The authors declare that there is no conflict of interest.

Author's contribution

Mohamed Gamal and Hany Sayed conceived the study and design the methodology. All the authors collected data. Mohamed Gamal and Sahafik Naguib analyzed the data and drafted the manuscript.Marwa Abdellah critically revised the manuscript. All the authors approved the final version.

Data availability statement

All data for this study is available within the manuscript

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