Environment and Social Psychology (2025) Volume 10 Issue 12 ISSN: 2424-8975 (O)
doi: 10.59429/esp.v10i12.4222 2424-7979 (P)

RESEARCH ARTICLE

Sex-related differences in serum Calprotectin, Acetate, and Zonulin as biomarkers for assessment of IBD

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ABSTRACT

Background: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and Ulcerative colitis (UC), is a chronic inflammation of the gastrointestinal tract. Early diagnosis and effective follow-up are essential for optimal outcomes. **Objectives:** This study aims to determine and compare the role of serum calprotectin, acetate, and zonulin as biomarkers for the assessment of IBD. **Methodology:** 96 patients aged 25-55 years with IBD diagnosis were based on clinical and endoscopic features at the Gastroenterology and Hepatology Specialized Hospital, located in Najaf, Iraq. Of these, 48 were healthy people (G1; men 24 and G2; women 24) and 48 were patients diagnosed with IBD disease (G3; men 24 and G4; women 24). The blood samples were analyzed using specific ELISA kits for calprotectin, Acetate, and Zonulin levels. **Results:** The level of serum calprotectin was significantly higher ($P<0.05$) in IBD patients than in healthy controls, and between genders of IBD patients, the serum calprotectin increased in men more than in women. However, the level of serum acetate was significantly lower ($P<0.05$) in IBD patients than in healthy controls, and between genders of IBD patients, the serum acetate increased in men more than in women. The level of serum zonulin was significantly higher ($P<0.05$) in IBD patients than in healthy controls, and between genders found that serum zonulin in women was higher than in men. **Conclusion:** We demonstrated that serum calprotectin has a significant increase in active disease and may be used as a biomarker for diagnosing and monitoring IBD patients in routine practice. A significant increase of serum zonulin, which is a biomarker of intestinal epithelial barrier dysfunction associated with decreased serum acetate, referred to as dysbiosis. Each parameter is associated with variables not related to the baseline disease, such as sex.

Keywords: Inflammatory Bowel Disease; Serum Calprotectin; Serum Acetate; Serum Zonulin.

1. Introduction

Inflammatory bowel disease (IBD) is a chronic, recurring inflammation of the gastrointestinal tract. It is divided into 2 types of disorder; Crohn's disease and Ulcerative colitis[1, 2]. The most important difference between the two types is that CD can affect any part of the intestine, though it's also related to the large and

ARTICLE INFO
8 October 2025 | Accepted: 22 December 2025 | Available online: 31 December 2025

CITATION
Bakheet NZ NZ, MAJ AQ. Sex-related differences in serum Calprotectin, Acetate, and Zonulin as Biomarkers for assessment of IBD. *Environment and Social Psychology* 2025; 10(12): 4222. doi:10.59429/esp.v10i12.4222

small intestine (LI and SI). Whilst ulcerative colitis (UC) refers to frequent inflammation of the LI, especially the rectum[3].

Clinically, however, the two diseases are indistinguishable in terms of symptoms, including abdominal pain, fever, constipation, or diarrhea. However, bloody stools are more common in Ulcerative colitis, while Crohn's disease is often associated with weight loss[4]. All ages may be affected, as well as some factors, like genetic, antibiotic exposure, intestinal microbiota, environmental, and both innate and adaptive immunity, may contribute to the development of these diseases[5]. As disease activity continues or treatment effectiveness is monitored, over the years, the biomarkers were identified[5]. The importance of early diagnosis of the disease, as delayed diagnosis of inflammatory bowel disease may lead to many negative consequences, including increased bowel damage and fibrosis, an increased risk of colorectal cancer, and a reduced quality of life. Serum calprotectin (CP) has recently been reported as a promising biomarker in monitoring IBD patients[6]. CP is a protein that binds Ca^{+} and zinc, and plays an important role in innate immunity and inflammatory cell recruitment[7]. Calprotectin is a marker of neutrophil activation and has been reported to be elevated in the blood and stool of patients with active inflammatory bowel disease[8]. The activation of immune cells, such as neutrophils, monocytes, and endothelial cells, produces or releases Calprotectin[9], representing about 40% to 60% of the proteins in the neutrophil cytosol. Calprotectin is a relatively stable protein released by damaged neutrophils into the bloodstream[10].

Dietary fibers are complex carbohydrates, which serve as substrates for anaerobic fermentation by bacteria in the colon[11]. This fermentation process dissociation fiber into simpler compounds, involving short-chain fatty acids. The primary short-chain fatty acids (SCFAs) produced in the intestine are acetate, propionate, and butyrate, which are present in a molar ratio of approximately 60:20:20[12]. Acetate is typically the most abundant SCFA, after that propionate and then butyrate. The moment that is produced, the short-chain fatty acids are absorbed by colonic epithelial cells, which are the cells lining the colon[13]. There is a complex interplay between immune responses, gut microbes, and the integrity of the intestinal epithelial barrier. Occurrence is due to the complex relationship between SCFAs and IBD[13, 14]. This allows harmful materials to penetrate the intestinal lining and trigger immune responses. As a result, inflammation weakens the integrity of the intestinal epithelial barrier. SCFAs contribute to enhancing mucus production and strengthening the tight junctions among epithelial cells, thus maintaining this barrier [15, 1].

Zonulin is a complex protein found in tight junctions (TJs). It is also considered an indicator of increased intestinal permeability [16, 17], by modulating the permeability of the tight junctions between cells of the gastrointestinal wall [18]. It is an important biomarker used to assess impaired intestinal barrier function[19], as its dysfunction leads to increased permeability of the small intestine epithelium. It can be measured in blood and stool samples[16, 20]. Furthermore, short-chain fatty acids are involved in tissue repair processes within the intestine. They promote the proliferation and differentiation of epithelial cells, which aids in the healing of damaged tissue resulting from inflammation in inflammatory bowel disease[13]. It has previously been noted that individuals with IBD may experience alterations in their gut SCFA levels as a result of disturbances in composition of the gut microbiota and decreased dietary fiber fermentation. This disturbance may participate to the impaired immune response and impaired intestinal barrier function that appear in inflammatory bowel disease[21]. It is significant to show that the proofs support the beneficial impacts of SCFAs in reducing inflammation for maintaining intestinal health. Research is ongoing into intestinal microbes, SCFAs, and their role in different GIT diseases, involving inflammatory bowel disease, and more studies are necessary to better elucidate the mechanisms and potential therapeutic applications[11,12] [22,23].

The incidence of IBD is growing, and the disease is accompanied by distinctive presents characteristics of socioeconomic variables in the local population, compared with their counterparts in other countries[24]. A declaration of factors affecting the spread of inflammatory bowel disease in Iraqi patients is warranted, particularly taking into account the high infection rate of inflammatory bowel disease. Many factors may have a role in inflammatory bowel disease; some of them have been studied, such as genetic factors[25], family history, diagnostic age[26], and smoking[27].

Variable biomarkers were used for the management of IBD, however, one of them is not sufficient to diagnose, distinguish, and follow up on the treatment of the disease. Each biomarker has a useful feature; therefore, we should consider their features and use appropriate biomarkers that enable noninvasive and smooth management of IBD. The present study was designed in attempt to compare the use of biomarkers such as calprotectin and zonulin, or the activity of intestinal bacteria in the formation of SCFAs as an indicator of disease progression, as it is affected by several factors such as, gender and psychological state, which also affects patients' emotional state for example the female have higher mean perceived stress, anxiety, and depression scores compared to male. In addition to several basic structures and another new approach to understanding disease progression in this study.

2. Patients and Methods

The current study was conducted at the Gastroenterology and Hepatology Specialized Hospital, located in Najaf, Iraq, lasting at March until October 2024. The patients aged 25-55 years with an IBD diagnosis are based on both clinical and endoscopic features. A total of 96 samples were included in the analysis. Of these, 48 healthy people (G1; men 24 and G2; women 24) and 48 patients diagnosed with IBD disease (G3; men 24 and G4; women 24). The study adhered to the protocols outlined by the Ethics Committee of the College of Medicine at Jabir Ibn Hayyan University for Medical & Pharmaceutical Sciences, Kufa, Iraq, as indicated by approval number 2710, on 15 February, 2024, in accordance with the patient's informed consent and confidentiality.

2.1. Blood Samples

The blood samples from healthy and patient people (5 mL) were collected using syringes and vacuum tubes, sterile to prevent microbial contamination, and allowed to clot for 30 min before centrifugation for 15 min at 3000 rpm. The resulting serum samples were frozen at −20°C or −80°C till the time of analysis of biomarkers. Avoid repeated freeze-thaw cycles.

The serum calprotectin (CALP) was measured using a Human Calprotectin ELISA kit (Melsin Medical Co., Limited, China). The ELISA kit was kept at room temperature before testing, and all procedures were performed at room temperature as shown in **Table 1**. Prepare standard wells and testing samples for addition to the Microelisa strip plate. Added to standard wells (50 µL standard), and added to the sample wells (10 µl sample and 40 µl diluent). No added anything to the blank well. Each well added to (100 µl of HRP-conjugate reagent), and covered with an adhesive strip, and incubated at 37 °C for 60 min. The wells were washed with a wash solution (400 µl). After washing, any remaining wash solution was removed, and the plate was inverted to dry. Next, 50 µl of each chromogen solution A and B were added, mixed gently, incubated at 37 10°C for 15 min, and kept from light. In the final step, each well added (50 µl of stop solution), and the color of the wells changed from blue to yellow. Optical density (OD) values of samples and standards were read at 450 nm within 15 min using a microtiter plate reader. Serum calprotectin concentration was calculated from standards of known concentration and expressed as ng/ml. The same

method (the ELIZA test) was used to assess the Acetate and Zonulin. The Zonulin results were given in ng/mL, and Acetate values were given in pg/ml.

Table 1. Summary of kits and equipment

Diagnostic kits	Supplier	Cat. No.
Human Calprotectin (CALP) ELISA kit	Melsin Medical Co., Limited, China	EKHU-1763
Human serum Acetate ELISA kit	Melsin Medical Co., Limited, China	REF YX-190518H
Human Zonulin ELISA kit	Melsin Medical Co., Limited, China	EKHU-3002

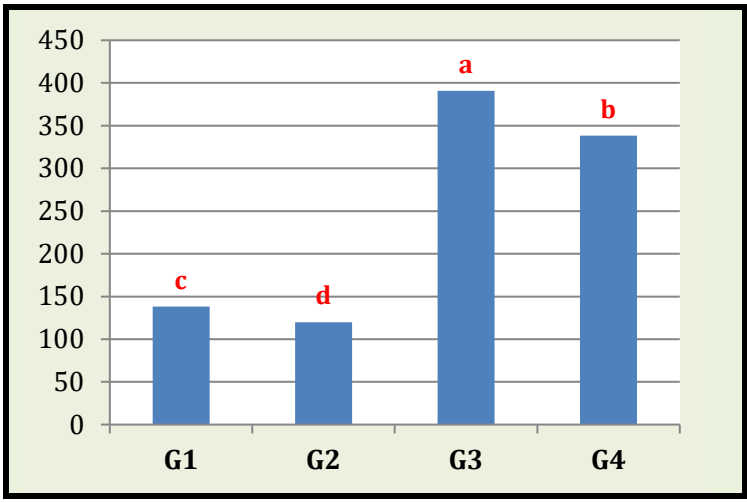
2.2. Statistical Analysis

Results expressed as mean± standard error. Data were analyzed using SAS (version 9.1) [28]. One-way analysis of variance (ANOVA) and post-hoc least significant difference (LSD) tests were performed to assess significant differences between means. Post-hoc tests are an integral part of ANOVA. $P < 0.05$ is considered statistically significant. Integrated biomarker responses analysis used to compare between biomarkers response in both male and female patients.

3. Results

3.1. Serum Calprotectin Concentration ng/ml

The association of serum Calprotectin level ng/ml with IBD is shown in (**Figure 1**). Serum Calprotectin level results were (P<0.05) significantly higher in IBD patients in G3 and G4 (390.87±1.14 and 338.46±1.42) groups compared to controls G1 and G2 (138.19±0.88 and 119.68±0.64) groups. However, according to sex between the IBD groups (G3 and G4), evidence of serum Calprotectin levels being higher (P<0.05) in the male G3 (390.87±1.14) group than the female G4 (338.46±1.42) group.

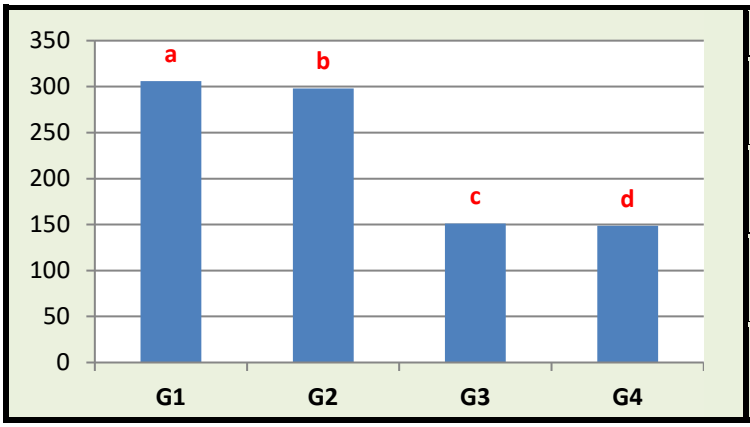


Calprotectin ng/ml	
G1	138.19±0.88
G2	119.68±0.64
G3	390.87±1.14
G4	338.46±1.42

Figure 1. Sex-related differences in serum Calprotectin as a biomarker for assessment of IBD**.** N=24 samples. Mean±SE. **G1 :** Male control group, **G2 :** Female control group, **G3 :** Male patients with IBD group, **G4 :** Female patients with IBD group**.** Small letters denote significant differences between groups (rows). **LSD = 2.98**

3.2. Serum Acetate Concentration Pg/ml

The association of serum Short-Chain Fatty Acids (acetate) level pg/ml with IBD is shown in (**Figure 2**). Serum Acetate level results were (P<0.05) significantly lower in IBD patients in G3 and G4 (151.13±0.66 and 148.51±0.67) groups compared to controls G1 and G2 (306.02±0.76 and 298.12±0.73) groups. However, according to sex between IBD groups (G3 and G4), evidence of serum Acetate level is higher (P<0.05) in the male G3 (151.13±0.66) group than the female G4 (148.51±0.67) group.

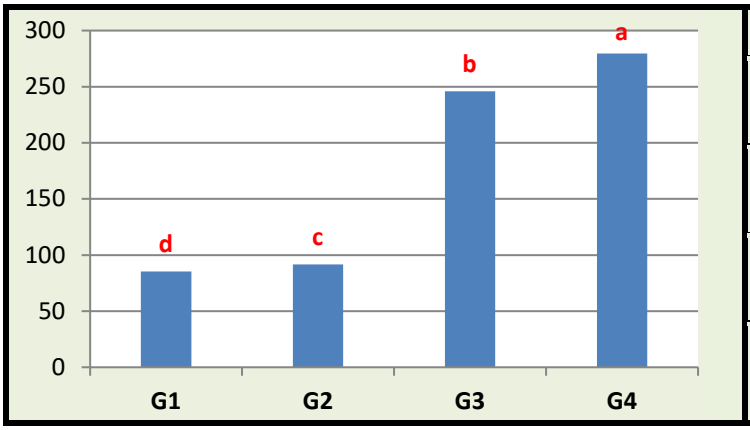


Acetate pg/ml	
G1	306.02±0.76
G2	298.12±0.73
G3	151.13±0.66
G4	148.51±0.67

Figure 2. Sex-related differences in serum Short-Chain Fatty Acids (acetate) level pg/ml as a biomarker for assessment of IBD. N=24 samples. Mean±SE. G1 : Male control group, G2 : Female control group, G3 : Male patients with IBD group, G4 : Female patients with IBD group. Small letter denote significant differences between groups (rows). LSD =1.99

3.3. Serum Zonulin Concentration ng/ml

The association of serum Zonulin-related proteins (ZRP) level ng/ml with IBD showed in (**Figure 3**). The serum ZRP level results were ($P<0.05$) significantly higher in IBD patients in G3 and G4 (245.95±0.68 and 279.69±0.65) groups compared to controls G1 and G2 (85.34±0.61 and 91.54±0.62) groups. However, according to sex between IBD groups (G3 and G4) evidence of serum ZRP level lower ($P<0.05$) significantly in male G3 (245.95±0.68) group less than female G4 (279.69±0.65) group.



Zonulin ng/ml	
G1	85.34±0.61
G2	91.54±0.62
G3	245.95±0.68
G4	279.69±0.65

Figure 3. Sex-related differences in serum zonulin-related proteins (ZRP) level ng/ml as a biomarker for assessment of IBD. N=24 samples. Mean±SE. G1 : Male control group, G2 : Female control group, G3 : Male patients with IBD group, G4 : Female patients with IBD group. Small letter denote significant differences between groups (rows). LSD =1.81

3.4. The integrative biomarker response between Calprotectin (ng/ml), Acetate (pg/ml), and Zonulin (ng/ml)

The integrative biomarker response analysis is illustrated in (**Figure 4**). The results showed the IBR value was highest for Calprotectin (16.88), then Zonulin (8.33), and Acetate had the lowest value (8.33).

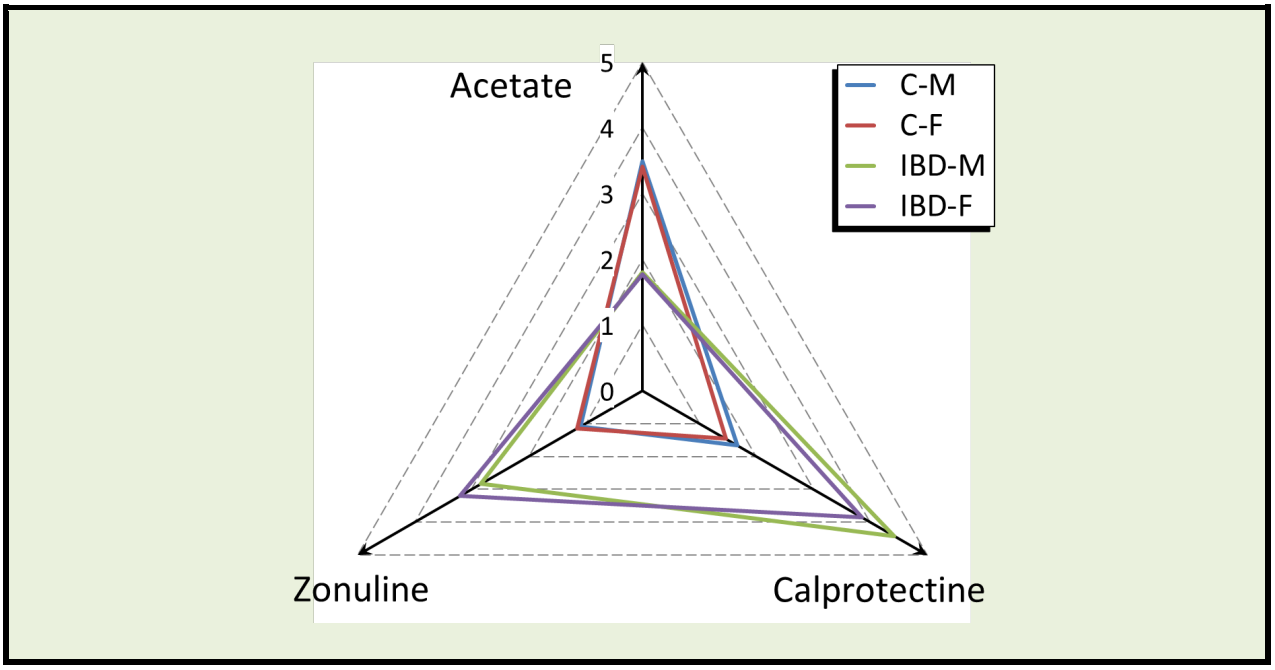


Figure 4. The integrative biomarker response between calprotectin, acetate, and zonulin as Biomarkers for assessment of IBD in both sexes.

4. Discussion

This study aimed to find out which of the used markers gives the best impression of the IBD disease. Initially, the detection of serum calprotectin in IBD is considered a potential instrument for examination and observation of these diseases due to its role as a salutary surrogate biomarker of acute phase activity of GIT diseases and its link with endoscopic signs in patients with ulcerative colitis[29, 30]. In our study, serum calprotectin (sCP) was significantly greater in IBD patients in the G3 and G4 groups than in healthy controls G1 and G2 groups. Several studies agree with our results, in a study[2] of 105 patients with CD and 98 patients with UC who collected blood samples for serum calprotectin levels found that blood sCP concentrations were greater during the active phase of CD and UC compared to healthy people but were more effective in assessing patients with CD than UC[2, 31]. Another study[32], increased a specific pattern (termed CPa9-HNE) of sCP in patients with IBD to measure the activity of neutrophils, demonstrating precision in diagnosing inflammatory bowel disease with severe activity [32]. Kalla et al. demonstrated that sCP strictly correlated with C-Reactive Protein (C-RP) and Fecal Calprotectin (fCP) in a study of 171 (75 without IBD and 96 with IBD) and recorded that sCP strongly correlated with C-RP and fecal calprotectin, and was a good indicator of IBD[33, 34], as well as proved that in a subgroup of 50 patients, sCP was better than fCP in distinguishing IBD from healthy subjects[35]. Furthermore, some authors suggested a positive correlation with disease activity, serum CRP, and platelet count, but not fCP, proposing that sCP was a more representative marker of systemic inflammation than localized intestinal inflammation when contrasted to fCP[7, 2]. Psychological stress appears to precede IBD exacerbation, as evidence suggests that stress can increase the likelihood of relapse in patients with quiescent inflammatory bowel disease (IBD)[36]. Chronic stress and adverse life events are linked to a higher risk of flares, and research indicates that the stress response system, the gut-brain axis (GBA), refers to alterations in the gut microbiota that mediate this link. GBA consists of bidirectional signaling between the gut and the brain (central nervous system). Studies refer to an imbalance in the gut microbiota that is not only associated with depression but can have a causal effect on it through multiple pathways. Gut microbes play a role in the production of neurotransmitters such as serotonin, metabolites such as short-chain fatty acids that influence inflammation and the stress response,

and the hypothalamic-pituitary-adrenal (HPA) axis[37]. The pathogenesis of depression and anxiety is unclear and influenced by external factors, for example, social and environmental factors[38]. Several studies indicate that lifestyle factors such as physical activity, diet, and body weight can influence the development of IBD and play a crucial role in its prevention. Adopting a healthy lifestyle, including regular exercise, a balanced diet, and maintaining a healthy weight, can help reduce the risk of developing the disease and may help manage its symptoms in individuals with the condition[39].

The present study's results were increased serum calprotectin in men more than in women, this agrees with a Park study observed that FC showed a statistically significant difference between males and females[40], while many studies thought there was no difference between sexes, and there was no correlation between serum and fecal calprotectin levels, and other parameters such as gender, age[41, 42], Other than several international studies, reports indicate no significant difference in FC concentration by sex in healthy children under 12 years of age[43]. Many studies have addressed the difference in the pathology and response of males compared to females. This is attributed to several factors, including the difference in psychological state, female showed higher mean perceived stress, anxiety, and depression scores compared to male[44]. Calprotectin as an intestinal permeability biomarker correlated with psychological pathy and depression of IBD patients[45]. Sex hormones such as estrogen and progesterone, in addition to oxytocin, affect intestinal permeability and can thus cause irritable bowel syndrome (IBS). Estrogen has been found to reduce permeability by increasing tight junction protein, while progesterone reduces permeability by increasing occludin secretion. A study of children with IBS found that females had increased intestinal permeability compared to a control group, compared to males, in whom no difference was observed. The degree of hormonal influence on IBS may vary between childhood, adulthood, and old age, suggesting that other factors may be more influential during each stage of life. Furthermore, important paradoxes remain, most notably the relationship of oxytocin to both relationship distress and decreased stress responses. All of this suggests that the influence of sex proteins may vary by age and gender [46]. Research shows that stress increases small intestinal permeability in humans and animals by activating mast cells via corticotropin-releasing hormone (CRH). Both stress and CRH increase permeability, while DSCG inhibits these effects, confirming the role of mast cells in this mechanism. These findings provide new insights into the complex relationship between the central nervous system and the gastrointestinal tract[47].

The intestinal microbiota plays a pivotal role in preserving immune function and gut health. In people with a healthy gut, beneficial bacteria in the colon ferment dietary fiber to make SCFAs such as acetate, propionate, and butyrate, and thus contribute significantly to microbial balance and regulate immune responses[48, 14]. Several studies suggest that patients with IBD often have bacterial dysbalance (called dysbiosis). Bacterial dysbiosis may participate to the inflammatory character of inflammatory bowel disease[49-52], leading to the impaired immune response and impaired gut barrier function visible in inflammatory bowel disease[53, 54]. In the present work, the results showed a decrease in Serum acetate levels pg/ml with inflammatory bowel disease (IBD) were ($P<0.05$) significantly lower in IBD patients in G3 and G4. Our study agrees with Kaczmarczyk et al., in a *pilot study* that demonstrated the acetate levels were lower in the patients with active IBD than in controls[55], as well as reduced other SCFAs such as serum butyrate in patients with IBD[56]. Therefore, SCFAs such as acetate and butyrate have gained interest for their potential beneficial effects on IBD[23]. Deleu *et al*. demonstrated that the administration of acetate might benefit inflammatory diseases such as UC and intestinal barrier integrity[57]. Recent studies have shown that short-chain fatty acids contribute to maintaining this barrier by stimulating mucus output and encouraging the junctions among the epithelial cells[1]. Furthermore, short-chain fatty acids are involved in tissue reform processes inside the intestine[58, 59]. They stimulate the epithelial cells' proliferation and differentiation and

help heal damaged tissue resulting from inflammation in inflammatory bowel disease[56, 13]. Our study shows differences between sexes men are more than women within patient groups. There are no studies that show the serum acetate levels in both sexes with inflammatory bowel disease, except a study on irritable bowel syndrome (IBS) patients found differences in Fecal SCFA were observed to increase in males more than in females[60]. The numbers of fiber-fermenting bacteria that produce SCFAs are typically decreased in the mucosa and feces of patients with inflammatory bowel disease, compared to healthy individuals[13]. In addition, they are an important source of intestinal epithelial cells and are known to enhance intestinal barrier function. Furthermore, we discuss the therapeutic potential of short-chain fatty acids for IBD, either by applying them directly or by stimulating SCFA-producing bacteria through prebiotic or probiotic approaches[56, 13].

Another important consideration is the psychological state of the patients, as it has been proven that there is an increase in acidity in psychiatric patients with schizophrenia due to a greater intestinal disruption[61]. Psychological conditions like anxiety and depression are common in patients with inflammatory bowel disease and can negatively impact their quality of life and disease course[62]. The relationship between depression and inflammation is bipartite, with one feeding into the other, impacting IBD. Inflammation plays a role in causing depression through immune responses, while depression contributes to inflammation through multiple mechanisms, including negative behaviors (e.g., pain and sleep disturbance), depressive symptoms, and negative health behaviors (e.g., poor diet and sedentary lifestyle), affecting the gut microbiome and enhancing intestinal permeability, another pathway that promotes inflammatory responses. Effective treatment of depression and inflammation together promotes recovery and reduces recurrence. The bipartite links between depression, inflammation, and disease suggest that effective depression treatments may have far-reaching impacts on mood, inflammation, and health [63]. Every person with IBD should be mentally screened using simple, clinically feasible tools that can be used to detect psychological problems, as psychological factors play a significant role in disease management due to the complex interplay between the physical and psychological health of patients with IBD. Psychological approaches may be as important, or even more important, than medical treatment, as they rely on behavioral interventions that improve outcomes in part by changing relationships, improving compliance, and preventing recurrence. Antidepressants have been shown to reduce IBD disease activity, recurrence, IBD-related surgery, quality of life, and treatment compliance. A comprehensive management regimen involving gastroenterologists and psychiatrists is proposed as the standard of care[62]. Outcome measures: perceived stress (PSS), multidimensional perceived social support (MSPSS), depressive symptoms (EPDS), happiness (SHS), and others. The perceived stress scale (PSS) is the most widely used psychological instrument for measuring stress perceptions and has adequate reliability. It was a better predictor of the respective outcomes (depressive and somatic symptoms, health service utilization, social anxiety, and smoking cessation maintenance) than life event scores. Compared with the depressive symptoms scale, the perceived stress scale was found to measure a different and independent predictive structure. The Perceived Stress Scale, attached, has been proposed for use in studying the role of nonspecific stress in the etiology of illness and behavioral disorders, and as an outcome measure of experienced stress levels[64]. Developed a self-rated measure of social support, the multidimensional perceived social support scale (MSPSS), which was administered to 275 college students. Three subscales, each addressing a different source of support, were identified and found to have strong factorial validity: family, friends, and significant partner. Furthermore, research has shown that the MSPSS has good internal reliability and test-retest reliability, as well as moderate construct validity. As expected, high levels of perceived social support were associated with lower

levels of depressive and anxiety symptoms, as measured using the Hopkins Symptom Inventory, and gender differences were observed[65].

Zonulin-related protein (ZRP) is a regulator of intestinal permeability, and elevated serum zonulin levels indicate increased intestinal permeability[66]. Increased intestinal permeability has been shown to play a critical role in the pathogenesis of IBDs[67]. In the present study, we evaluated serum ZRP level ng/ml levels in IBD were ($P<0.05$) significantly higher in IBD patients in G3 and G4. I agree with Caviglia et al., who proved higher serum ZRP levels in IBD patients compared to healthy controls[68], Khosainova et al., who demonstrated increased serum zonulin concentrations in patients with UC and CD, associated this with an increase in the functional activity of circulating neutrophils[69]. Under this inflammatory state, intestinal bacterial imbalance may stimulate epithelial cells to produce increased amounts of ZRP into the intestinal lumen/circulation, then leading to impaired function of intestinal barrier, followed by the entry of exogenous antigens into the bloodstream, thereby triggering an excessive immune response that, in turn, leads to further leakage[70]. Unsuitable immune system activation may lead to mucosal inflammation, with increased secretion of proinflammatory cytokines that can impact the epithelium and develop a more leaky barrier[71]. Together, this may demonstrate our finding that serum levels of ZRP were raised in cases of common IBD compared to healthy controls. Circulating serum ZRP is associated with the development of intestinal inflammation, both common and occasional IBD, and has been proposed as a potential indicator of intestinal permeability[72-74]. Our result showed the patients with IBD, zonulin levels were significantly higher among females, this finding is similar to a study by Lacombe et al., who reported that zonulin levels were markedly higher among females when compared to male patients[75], and also similar to a study by Maget et al., researchers have reported that zonulin plays a key role in the two-way communication interface between the brain and the gut. Increased serum zonulin levels, as an indicator of increased intestinal permeability in women, may indicate a state of increased susceptibility to depressive stimuli in the gut inflammation[59], the psychological condition of patients contribute to the serum level of zonulin[76]. The activity of the disease, as it is affected by several factors such as gender, psychological state, and lifestyle[77], also affects patients' emotional state[78].

5. Conclusion

We demonstrated that serum calprotectin has a significant increase in active disease and may be used in biomarkers for diagnosing and monitoring IBD patients in routine practice, A Significant increase of serum zonulin which is a biomarker of intestinal epithelial barrier dysfunction associated with decreased serum acetate referred to as bacterial dysbiosis, and a systemic inflammatory response, thus identifying a group of patients who could benefit from early interventions such as prebiotics, to repair gut microbiome health in the future. Each parameter is associated with variables not related to the baseline disease, such as sex.

Conflict of interest

The authors declare no conflict of interest

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