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Immunological Predictive Value of Interleukin-17 in Ulcerative Colitis Patients in Thi-Qar Province, Iraq

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ORIGINAL STUDY

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Immunological Predictive Value of Interleukin-17 in Ulcerative Colitis Patients in Thi-Qar Province, Iraq

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Abstract

Background: The chronic inflammatory bowel illness known as ulcerative colitis (UC) is characterized by dysregulated mucosal immunity. There is much more to learn about the relationship between interleukin-17 (IL-17), a key mediator in the Th17 pathway, and systemic inflammatory and metabolic indicators.

Objectives: To examine the relationship between inflammatory (CRP), metabolic (FBS, HbA1c), and micronutrient (zinc) indicators and blood levels of IL-17 in individuals with UC, while excluding those with diabetes, autoimmune, hepatic, or renal disorders.

Methods: In a case-control research, 90 participants were matched for age, sex, and BMI: 45 UC patients and 45 healthy controls. Measurements were made of zinc, HbA1c, FBS, CRP, and serum IL-17. Using Pearson correlation and independent t-tests, the data were examined.

Results: IL-17 levels in UC patients were substantially greater than those in controls (63.85 ± 6.53 vs. 28.38 ± 4.94 pg/mL, $p = 0.01$). Moreover, CRP was significantly higher (31.29 ± 5.42 vs. 2.64 ± 0.28 mg/L, $p = 0.01$). IL-17 and CRP showed a high positive association in the UC group ($r = 0.804$, $p < 0.01$). On the other hand, zinc levels in UC patients were considerably lower (55.82 ± 3.32 vs. 89.18 ± 5.36 μg/dL, $p = 0.001$). The groups' FBS and HbA1c levels did not vary significantly from one another.

Conclusion: Increased systemic release of IL-17 along with its robust positive association with CRP suggest a key role of IL-17 in active systemic and mucosal inflammation in UC, whereas low levels of zinc contribute to exaggerated Th17 responses. Importantly, these findings were robust even after excluding the patients who were both autoimmune positive and who had metabolic and systemic autoimmune comorbidities which also increased the reliability of these findings. In UC, zinc status in relation to IL-17 may be a focus for diagnosis and treatment.

Keywords: Ulcerative colitis, IL-17, CRP, Zinc, Th17, Inflammation

1. Introduction

Ulcerative colitis (UC), a chronic idiopathic inflammatory bowel disease (IBD), is characterized by recurring episodes of diarrhea, rectal bleeding, and stomach pain brought on by ongoing inflammation of the colonic mucosa [1]. Although the precise origin of UC is uncertain, it is believed that in genetically susceptible people, a maladaptive immune response to gut microbiota is the primary culprit [2]. One of the immune pathways implicated is the Th17/IL-17 axis, which has emerged as a central orchestrator of chronic mucosal inflammation [3].

The primary source of the proinflammatory cytokine IL-17 is Th17 cells, stimulates epithelial and stromal cells to produce neutrophil-recruiting chemokines and other proinflammatory mediators [4]. In correlation with disease activity and histological severity, elevated IL-17 expression has been seen in the inflammatory colonic mucosa and serum of UC patients [5, 6]. Conversely, IL-17 contributes to both tissue damage and recruitment of neutrophils as it functions with IL-1β, IL-6, and TNF-α to exacerbate epithelial barrier dysfunction [7].

In contrast however, in the experimental models IL-17 has also been proposed to serve the dual

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and context dependent roles in epithelial repair and anti-microbial defense [8]. Clinical evidence further strengthens this paradox as in blocking IL-17 may exacerbate inflammatory bowel disease (IBD) symptoms in individuals, indicating that full abrogation of IL-17 may achieve a pathological dysbalance in the homeostasis of the mucosal environment [9]. The acute-phase reactant C-reactive protein (CRP) is brought on by IL-6 [10], and is one of most common index of systemic inflammation in UC [10]. lastly, the association of IL-17 with CRP levels in human studies suggests an interaction between Th17 driven mucosal inflammation and hepatic acute-phase responses [11].

Food also contributes to the regulation of immunity in UC. Zinc is an essential trace element and is involved in epithelial integrity, antioxidant activity, and T cell function [12]. A dietary zinc deficiency is associated with compromised mucosal healing and increased IL-17 secretion in response to chronic antigen stimulation due to increased Th17 responses [13]. Zinc deficiency may be another contributing factor responsible for the immune imbalance in UC, it is crucial to exclude diabetes mellitus as a confounding factor; therefore metabolic parameters including fasting blood sugar (FBS) and HbA1c are needed. Dysglycemia itself has been demonstrated to have independent effects on immune function and inflammation; however, these indices are typically at comparable levels in well characterized UC cohorts devoid of metabolic comorbidities [14, 15].

Overall, the available evidence highlights IL-17 as an important nexus between adaptive immunity, systemic inflammation, and micronutrient status in UC. Zinc may lend additional pathophysiologic and diagnostic significance to its association with CRP and metabolic markers in a well-characterized cohort of UC patients devoid of autoimmune, hepatic, renal, or diabetic co-morbidities [16].

2. Materials and methods

2.1. Study design and participants

This investigation was carried out as a case-control in Collage of health and medical technology, al-ayen Iraqi University. A total of 90 participants, including 45 patients diagnosed with ulcerative colitis (UC) and 45 healthy people of the same age and sex served as controls, the ages of the participants in this study were between 18 and 65 years, and all participants were non-smokers. The date of sample collection began from March 22, 2025, and ending on July 16, 2025. All UC patients were clinically and histologically confirmed by gastroenterologists at Thi-Qar Teaching Hospital. Patients with diabetes mellitus, autoimmune diseases, hepatic, renal, or malignant conditions were excluded to minimize confounding factors.

2.2. Sample collection and laboratory procedures

Five milliliters of fasting venous blood were extracted from each participant at Thi-Qar Teaching Hospital. Following separation by centrifugation (3000 rpm for 10 minutes), the serum was stored at –20°C until analysis. Standard automated biochemical analyzers were used in the clinical laboratory at Thi-Qar Teaching Hospital to quantify CRP, FBS, and HbA1c. The Bioassay Technology Laboratory provided a quantitative sandwich enzyme-linked immunosorbent test (ELISA) kit (Catalog No. E0980Hu, Bioassay Tech, Shanghai, China) for measuring serum IL-17 levels. Following the manufacturer's instructions, the procedure was carried out. Spectrophotometric measurement of serum zinc levels was performed using a colorimetric technique that included 5-Bromo-2-pyridylazo-5′-sulfonate (5-Br-PAPS). A stable purple complex is produced in an alkaline medium by the combination of zinc with 5-Br-PAPS. The reagent combination included 0.02 mmol/L 5-Br-PAPS, 200 mmol/L bicarbonate buffer (pH 9.8), 170 mmol/L sodium citrate, 4 mmol/L dimethylglyoxime, and 1% detergent. Absorbance at 546 nm was measured after 1.0 mL of the reagent was mixed with 50 μL of serum or standard (200 μg/dL) and incubated for 10 minutes at 25 °C. The following formula was used to determine the zinc concentration (μg/dL):

$$Zinc\,(\mu g/dL) = (Abs.T/Abs.S) \times 200$$

Where Abs.T = absorbance of the test sample, and Abs.S = absorbance of the standard.

2.3. Statistical analysis

The statistical analysis was performed using IBM SPSS software, version [Insert version, such as 25.0]. The data's mean ± standard deviation (SD) was shown. The Independent Student's t-test was used to compare the group means. Pearson's correlation coefficient was utilized to assess the correlations between IL-17 and other observable variables. A p-value of less than 0.05 was considered to be statistically significant.

3. Results

3.1. Demographic characteristics

The study included a total of 90 participants, divided equally into two groups: 45 ulcerative colitis

(UC) patients (G2) and 45 age- and sex-matched healthy controls (G1). As shown in Table 1, there were no statistically significant differences between the two groups in terms of age (G1: 29.76 ± 5.28 years vs. G2: 31.60 ± 6.28 years; p = 0.272) or body mass index (BMI) (G1: 23.56 ± 1.13 kg/m^2 vs. G2: 23.16 ± 1.52 kg/m^2; p = 0.162). The distribution of sexes was comparable, with no significant differences between males and females in either group (p = 1.000).

3.2. Biochemical and inflammatory parameters

Table 2 presents the comparison of the measured biochemical and inflammatory markers between the two study groups. Serum IL-17A levels were significantly higher in UC patients (63.85 ± 6.53 pg/mL) compared to healthy controls (28.38 ± 4.94 pg/mL) with a p-value of 0.01, indicating a robust immune activation in UC (Fig. 1). Similarly, CRP levels were markedly elevated in the UC group (31.29 ± 5.42 mg/L) in contrast to the control group (2.64 ± 0.28 mg/L), also reaching statistical significance (p = 0.01).

In contrast, no statistically significant differences were found in fasting blood sugar (FBS) levels (G1: 98.96 ± 3.25 mg/dL vs. G2: 97.67 ± 3.13 mg/dL; p = 0.481) or in glycated hemoglobin (HbA1c) levels (G1: 5.57 ± 0.10% vs. G2: 5.44 ± 0.09%; p = 0.462), confirming that participants in both groups were metabolically comparable.

A significant reduction in serum zinc levels was observed in the UC group compared to controls (55.82 ± 3.32 μg/dL vs. 89.18 ± 5.37 μg/dL; p = 0.001), suggesting a possible link between zinc deficiency and UC pathophysiology (Fig. 4).

Table 1. The demographic features in the study groups.

Variables	Control (G1) Mean ± SD	patients (G2) Mean ± SD		
Total Number	45	45	T-test	p-value
Age (year)	29.76 ± 5.275	31.60 ± 6.279	1.105	0.272*
BMI (kg/m^2)	23.56 ± 1.131	23.16 ± 1.518	1.409	0.162*
Sex	26.50 ± 3.192	26.50 ± 3.192	0	1
Males = 20				
Females = 33				

p-values < 0.05 are considered statistically significant.

Table 2. Statistical analysis of biomedical parameters levels in the study groups.

Parameters	Control (G1) Mean ± SD	patients (G2) Mean ± SD		
Total Number	45	45	T-test	p-value
IL-17A	28.38 ± 4.94	63.85 ± 6.53	10.77	0.01
CRP	2.640 ± 0.28	31.29 ± 5.42	8.96	0.01
FBS	98.96 ± 3.247	97.67 ± 3.126	6.508	0.481*
HbA1c	5.569 ± 0.097	5.440 ± 0.090	6.418	0.462*
Zinc	89.18 ± 5.365	55.82 ± 3.319	35.47	0.001

p-values < 0.05 are considered statistically significant.

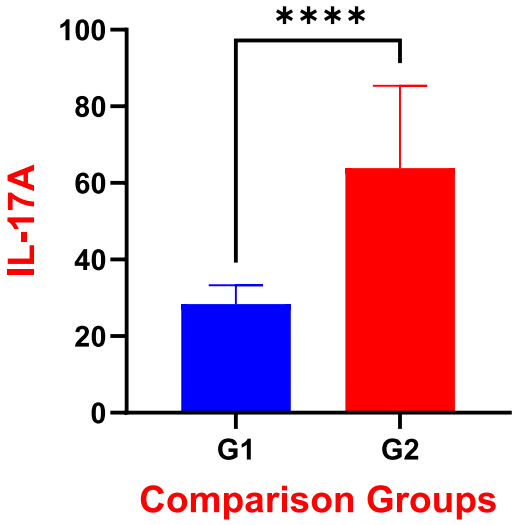

Fig. 1. Shows the comparison of IL-17A levels between the study groups (G1 and G2).

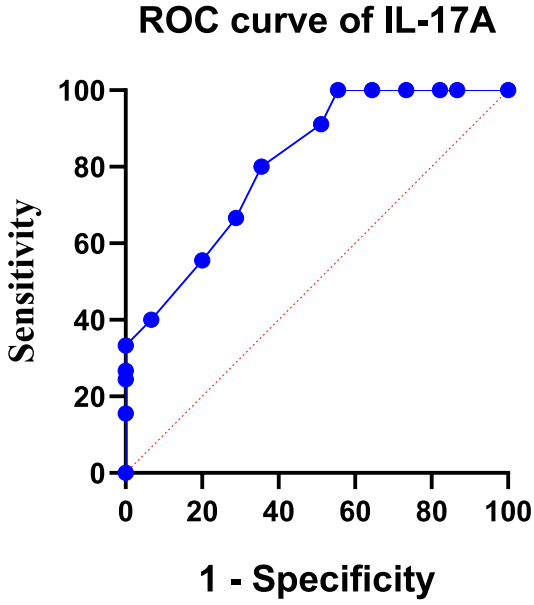

Fig. 2. ROC curve for the IL-17A parameter which can use for diagnosis of Ulcerative colitis patients (G2) against control group (G1).

3.3. Diagnostic value of IL-17A

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic potential of IL-17A in distinguishing UC patients from healthy individuals. As shown in Fig. 2, IL-17A exhibited a strong diagnostic performance, indicating its potential utility as a non-invasive biomarker for UC.

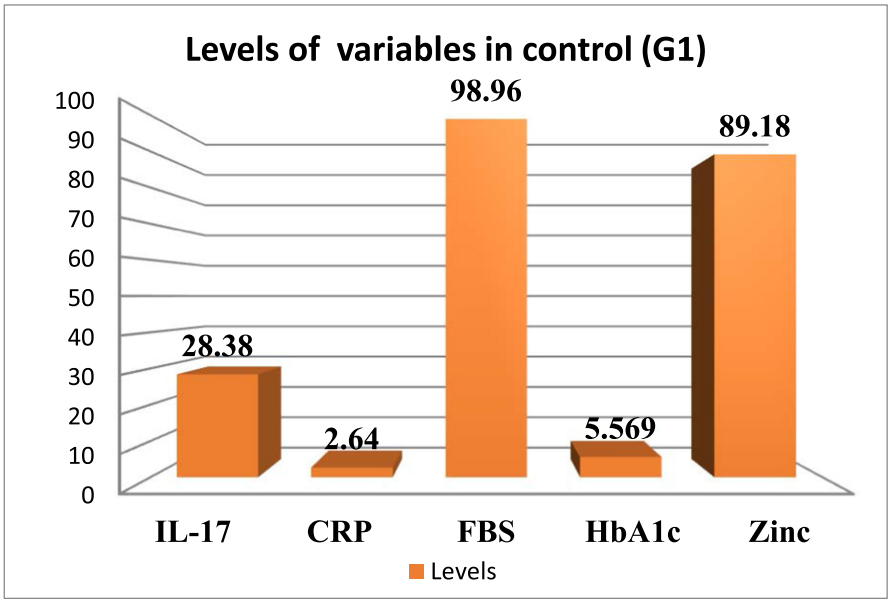

Fig. 3. The levels of IL-17A, CRP, FBS, HbA1c, and Zinc in samples of control (G1).

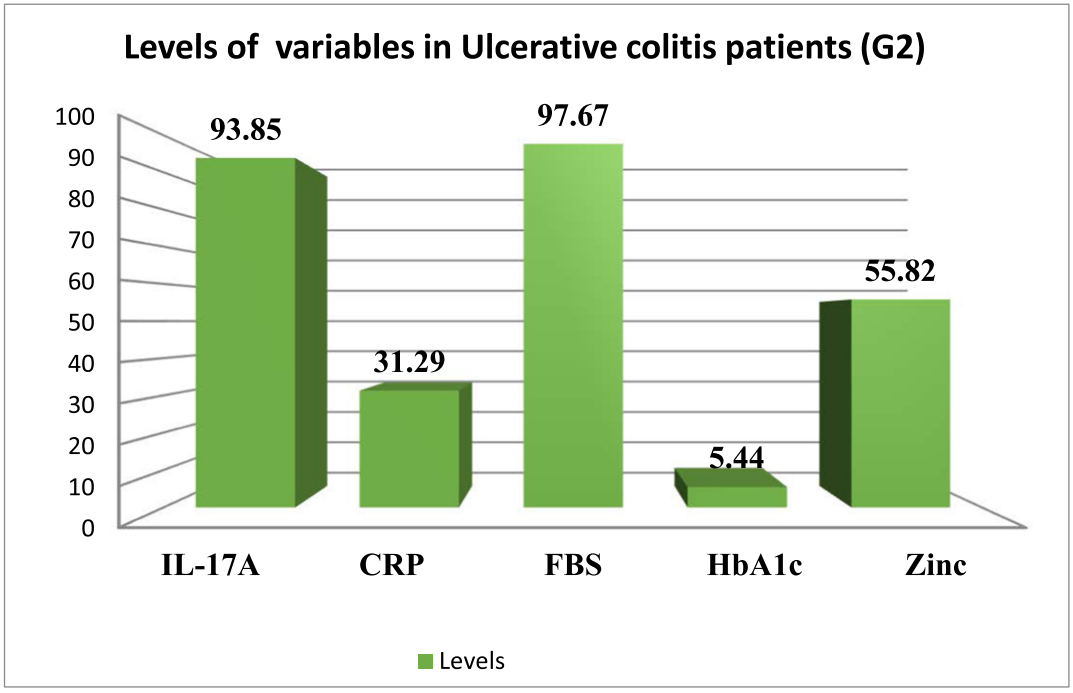

Fig. 4. The levels of IL-17, CRP, FBS, HbA1c, and Zinc in samples of Ulcerative colitis patients (G2).

3.4. Correlation analysis

Tables 3 and 4 present the Pearson correlation matrices for the control (G1) and UC patient groups (G2), respectively.

In the control group (Table 3, Fig. 3), a statistically significant negative correlation was observed between IL-17A and CRP ($r = –0.330$, $p = 0.027$), indicating an inverse relationship under non-inflammatory conditions. No significant correlations were detected between IL-17A and FBS, HbA1c, or zinc in this group.

Conversely, in the UC group (Table 4), a strong and statistically significant positive correlation was found between IL-17A and CRP ($r = 0.804$, $p < 0.01$), reflecting the heightened systemic inflammatory

Table 3. Correlation study of the parameters in the control group (G1).

Correlations				
	IL_17A	CRP	FBS	HbA1c
CRP				
Pearson Correlation	–0.330*			
Sig. (2-tailed)	0.027			
FBS				
Pearson Correlation	0.202	–0.293		
Sig. (2-tailed)	0.183	0.196		
HbA1c				
Pearson Correlation	0.208	–0.152	1.000**	
Sig. (2-tailed)	0.187	0.184	0.001	
Zinc				
Pearson Correlation	0.214	–0.193	–0.054	–0.054
Sig. (2-tailed)	0.157	0.205	0.723	0.723

*. Correlation is significant at the 0.05 level (2-tailed).
**. Correlation is significant at the 0.01 level (2-tailed).

Table 4. Correlation study of the parameters in the Ulcerative colitis patients (G2).

Correlations				
	IL_17A	CRP	FBS	HbA1c
CRP				
Pearson Correlation	0.804**			
Sig. (2-tailed)	0.001			
FBS				
Pearson Correlation	–0.215	–0.186		
Sig. (2-tailed)	0.155	0.222		
HbA1c				
Pearson Correlation	–0.218	–0.185	1.000**	
Sig. (2-tailed)	0.152	0.226	0.000	
Zinc				
Pearson Correlation	0.202	0.104	–0.070	–0.070
Sig. (2-tailed)	0.184	0.495	0.648	0.648

**. Correlation is significant at the 0.01 level (2-tailed).

state associated with active disease. No significant correlations were found between IL-17A and FBS ($r = –0.215$, $p = 0.155$), HbA1c ($r = –0.218$, $p = 0.152$), or zinc ($r = 0.202$, $p = 0.184$). These findings suggest that the elevated IL-17A is more closely linked to inflammation than to metabolic or micronutrient parameters in the UC setting.

4. Discussion

According to the current research, serum IL-17 levels were significantly higher in ulcerative colitis (UC) patients than in healthy controls until the end of October 2023, supporting a key role for UC in the pathophysiology. Significantly elevated IL-17 levels in the patient group (63.85 ± 6.53 vs 28.38 ± 4.94 pg/mL, $p = 0.01$) is consistent with previous reports of the overexpression of IL-17 in the inflamed colonic tissue and in the peripheral circulation of UC patients [17, 18]. This increase corroborates that Th17-driven responses are primary mediators of chronic mucosal inflammation.

Furthermore, the high positive correlation of IL-17 with CRP ($r = 0.804$, $p < 0.01$) in UC patients clearly indicates that IL-17 is not only a marker of adaptive immune activation but also a strong trigger of systemic inflammation. Although CRP is a classical acute-phase reactant dependent on IL-6 and TNF-α, its strong correlation with IL-17 in the present study hint at an indirect role of Th17 cytokines for promoting hepatic acute-phase responses [19, 20]. This result suggests that IL-17 could provide a complementary biomarker to CRP for assessment of disease activity and systemic inflammation in UC.

Remarkably, no more differences were discovered in fasting blood sugar (FBS) and also HbA1c in between individuals and also controls. This finding appears to be related to the selection of patients who did not have diabetes mellitus or metabolic comorbidities, precluding glycemic disturbances as a confounder. On the other hand, past observations suggested that IL-17 does correlate with mucosal immunity in UC better than metabolic regulation [21].

One of important results of this study is that the levels of Zinc in UC patients are significantly lower than in controls. T cell immunity dysregulation and compromised epithelial barrier function have been associated with zinc deficiency. Low zinc availability has been shown to enhance TH17/Treg skewing, with high zinc appropriate for inhibiting Th17 and promoting Tregs [22]. As a result, the low levels of zinc detected in the tissues of our UC cohort may thus be a mechanistic driver of such elevated IL-17 production perpetuating a pathogenic cycle of epithelial barrier breakdown, immune activation and micronutrient depletion [23].

From, our data suggest concurrent roles for IL-17 in UC, overproduction of which drives mucosal and systemic inflammation and thus correlates with traditional inflammatory markers of UC (i.e. CRP); and hyper IL-17 signaling that likely arises from micronutrient deficits, e.g. zinc, which synergistically worsen barrier failure. Importantly, our UC patients had no other relevant comorbidities, such as diabetes, that might confound such associations, nor had the other possible pathophysiological relevant immune, hepatic, or renal comorbidities that might have better characterized incompletely suppressed other intestinal immune alterations to UC pathophysiology.

Future treatment could also involve modulation of the antagonistic IL-17/Th17 axis with nutritional factors (eg, zinc supplementation) to restore mucosal homeostasis. Furthermore, IL-17 is also associated with both protective (mucosal healing) and pathogenic (in the case of chronic over-expression)

functions, indicating that this pathway may be optimally modulated rather than inhibited, with therapeutic benefit [24].

5. Conclusion

According to the research, serum IL-17 levels are much higher in patients with active ulcerative colitis (UC) than in healthy individuals, and a strong positive connection with CRP indicates that IL-17 plays a crucial role in systemic and mucosal inflammation. Illustrating the interplay of micronutrient status and immune dysfunction, the zinc deficiency observed in UC patients might amplify the pathogenicity of IL-17–driven immunity. The lack of significant alterations in FBS and HbA1c consolidates the specificity of these immune alterations to UC independent of metabolic derangements, both as a biomarker of disease activity and a potential therapeutic target. Therefore, restoration of zinc deficiency may expand the armamentarium of therapy for symptom control in UC.

Ethical approval

Al-Ayen University's Institutional Review Board authorized the research, and in compliance with the Declaration of Helsinki, verbal permission was acquired from each participant before any samples were taken.

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