Estimation of IL-23 in ulcerative colitis and Crohn's disease in sample of Iraqi patients with inflammatory bowel disease

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Abstract

Inflammatory bowel disorders (IBD) are a significant cause of disease burden globally. Interleukin 23 (IL 23) is one of many important cytokines that can be studied in this context. The Interleukin- 23 is a critical aspect of the performing of irritation and is intently tied to it. So there are still many unanswered questions about the function every one of them performs in this orchestra in phrases of their pro- and anti-inflammatory elements. In this study, one hundred age- and sex-matched IBD patients had been included in this study. Measurement of serum IL-23 is done by the use of an ELISA kit. Serum IL-23 used to be appreciably extended in IBD sufferers compared with healthy controls (P<0.001). This study indicates that serum IL-23 is higher in IBD patients compared to healthful controls.

***Keywords**: IBD, innate immune response, IL- 23.*

الدور المزدوج لـ IL-23 في التهاب القولون التقرحي ومرض كرون في عينة من المرضى العراقيين المصابين بمرض التهاب الأمعاء

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الخلاصة

تعتبر اضطرابات الأمعاء الالتهابية (IBD) سببًا مهمًا لعبء المرض على مستوى العالم. Interleukin 23 (IL 23 هو واحد من العديد من السيتوكينات المهمة التي يمكن دراستها في هذا السياق. يعتبر Interleukins 23 عنصرًا حاسمًا في أداء الالتهاب وهو مرتبط ارتباطًا وثيقًا به. لذلك ، لا يزال هناك العديد من المخاوف التي لم تتم الإجابة عليها بشأن الدور الذي يلعبه كل منهم في هذه الأوركسترا من حيث الجوانب المؤيدة والمضادة للالتهابات. في دراسة الحالية ، تم إشراك 100 مريض من عمر وجنس مرضى داء الأمعاء الالتهابي متطابقين مع عناصر تحكم صحية في الدراسة الحالية. تم قياس مستوى المصل 23- IL- باستخدام مجموعة ELISA. كان المصل 23 IL- أعلى بشكل ملحوظ في مرضى IBD مقارنة بالضوابط الصحية (P <0.001). بالإضافة إلى ذلك ، يمثل اختبار ROC IL-23in IBD شديد الحساسية والنوعية. ونستخلص من الدراسة : أظهرت الدراسة الحالية ارتفاع مصل 23 IL- في مرضى IBD مقارنة بالضوابط الصحية.

***الكلمات المفتاحية :** مرض التهاب الأمعاء ، الاستجابة المناعية الفطرية ، IL- 23 .*

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Introduction

Multiple cytokines have been linked to the onset and progression of inflammatory bowel disease, according to recent research [1]. Cytokines are known to enhance and maintain inflammatory responses in IBD; therefore, increased concentrations in biological fluids are expected. This also suggests that activation of signaling pathways leads to inflammation and contributes to disease progression [2]. The pathophysiology of IBD has been shown to be primarily mediated by IL23 [3]. Interleukin -IL-23, a member of the IL-12 cytokine family, is a heterodimer composed of two subunits, IL12p40 and IL23p19 [4]. IL-23 is usually produced by means of macrophages and dendritic cells (DCs) and plays a key position in inflammation, which includes activation of Th17 cells, through interacting with the produced IL-23 receptor IL-23R. IL-12R1 unit and dedicated IL-23R unit [5]. Individuals with inflammatory bowel disease (IBD) experience wide variations in illness development and severity, which raises the possibility that different cytokine pathways are to be responsible for the clinical outcomes' variability [6]. The interleukin IL-23 cytokine pathway has been established to play vital function in the development of a range of persistent inflammatory diseases, which include psoriasis, rheumatoid arthritis and multiple sclerosis, and inflammatory bowel disease [7]. Genome-wide affiliation researches have linked IL-23 to IBD threat thru mutations in the IL-23 receptor (IL-23-R) gene that promote activity of the IL-17/IL-23 signaling pathway [8،9]. Given that cytokines are known to beautify and perpetuate inflammatory responses in IBD, higher abundances in organic fluids are predicted [7]. Large quantities of IL-23 are existing in the small intestine and peak in the terminal ileum. When micro- organisms are stimulated, monocytes, macrophages, and dendritic cells launch IL-23, which then engage with their heterodimeric IL-23 receptor (IL-23). 23R) produces inflammatory mediators (IL-17, IL-22, granulocyte-macrophage colony stimulating component (GM-CSF), TNF-) by using activating the JAK-STAT signaling pathway [10].

In research analyzing IL-23 expression in human IBD, lamina propria macrophages from CD patients produced more IL-23, but no longer from UC patients [11-13]. According to recent studies, the CD patient populace who had failed prior anti-TNF remedy responded very well to therapy with certain IL23 inhibitors [14]. Substantial proof from genetic studies has led researchers to conclude that genetic variations in the IL23R protein are related with Cohen's ailment and ulcerative colitis, however might also additionally act as a barrier to the improvement of each disease [15,16].

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Materials and methods

Subjects

During the period from November 2021 till March 2022, the current investigation was carried out at the gastroenterology center in Baghdad, Iraq. Age and gender are among the clinical data. The European Cohn's and Colitis Organizations' (ECCO) diagnostic standards were used to make the patient diagnoses. In this study, 150 people were enrolled; 100 IBD patients (31 males and 19 females), aged 19 to 70, had been clinically diagnosed as having UC; and 27 males and 23 females, aged 20 to 61, were CD patients. In addition, 50 healthy individuals were selected as the control group. Their ages ranged from 20 to 50 and none of them had a history of another inflammatory disease.

Collection of samples

Five milliliters of blood were drawn from each subject via vein puncture with disposable syringes. The blood used to be separated by means of centrifugation at ten thousand rpm for 5 minutes after the blood was once deposited in a gel disposable tube to decide. IL-23 level was detected by using the ELISA kit (My BioSource-USA)

2.3. Statistical analysis

Statistical evaluation was carried out using SPSS Social Sciences Statistics Package (version 20.0 for Windows, SPSS, Chicago, IL, USA). Data are introduced as suggest ± fashionable deviation of quantitative variables. Qualitative relationships have been assessed the usage of the chi-square test. A p-value <0.05 used to be viewed statistically significant. Cutoffs are estimated based on ROC

3. Results

Demographic characteristics of the study population

A total of 150 blood samples were divided into two groups: 100 IBD patients (50 CD and 50 UC) and 50 subjects selected as healthy controls. Table 1 illustrates the baseline traits of the censored sample through age and sex and compares the significance of the censored groups. The outcomes of this table exhibit that at P>0.05, there was no statistically difference between males and female in IBD sufferers and controls. In addition, there used to be no extensive difference between the IBD crew and the manipulate team by using age team in this study (P>0.05).

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Table (1): Initial characteristics of the study group.

Variables		IBD Patients		Control	P-value
		UC	CD		
Age (years)	Range	(19-70)	(20-61)	(20-50)	P=0.843 NS
	Mean ± SD	47.23± 161.11	32.27±4.87	37.17±8.43	
Gender	Male No. (%)	31 (62 %)	27(54%)	25(50%)	P=0.7.51 NS
	Female No (%)	19(38 %)	23 (46 %)	25(50%)	
Total No.		50	50	50	

NS: non -significant

Levels of IL-23 in the studied groups:

Serum IL-23 exhibited a significant decline in the (UC) group (970.28±13.923) in comparison to the CD group (1096,24±23.260) P value =0.005, according to an analysis of the mean value change in serum level in the patients' serum compared to the healthy control group the level increased significantly in the IBD group (997.654± 23.458) compared to the control group (298 .41±24.024). Between the patient groups there were highly statistically significant variations in the mean values of IL-23 (P value = 0.001).

Table (2): IL-23 Serum Levels in Study Group.

IL-23 (Pg/mL)	CD	UC	Control
Mean±SD	1096,24±23.260	970.28±13.923	298 .41±24.024
IBD vs Control	0.001*		
CD vs UC	0.005		
* "Significant difference between two independent means using Student's t-test at the 0.05 level"			

Estimation of cutoff values, sensitivity, specificity and AUROC for IL-23 in IBD patients

In the IBD patient group, the IL-23 cutoff value was 1012.576 pg/mL, the sensitivity was 85.6%, the specificity was 93.5%, the AUCROCs were s0.934 (P value = 0.000) and a 95% confidence interval, as shown in Table 3).

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Table (3): Estimation of breakpoints, sensitivity, specificity and AUROC of miRNA-IL-23 in IBD patients.

Parameters	Cut- off point	Sensitivity (%)	Sepecificity (%)	AURO	P-value	Relative risk	IBD Patients No.(%)	CI
Il-33 pg/ml	1012.576	85.6	93.5	0.934	0.000	PPV	7785.6%	95%
						NPV	2314.4%	

"AUROC: area under receiver operating characteristic, PPV: positive predictive value, NPV: negative predictive value, Sig at P value < 0.05"..

Discussion

Crohen's disease and ulcerative colitis are complex illnesses with their symptoms. Multifaceted pathophysiology, including genetic variation, gut barrier dysfunction, microbiota, and host immune system play role in the diseases. Many questions remain unanswered; Which cytokines are more pronounced than others, and which composition of the microbiota contributes to the development of IBD [12]. In the present study, the serum IL-23 significantly greater increased in IBD patients than that in the control group, whilst the serum IL-23 concentration in CD sufferers was the highest. Similar to the current findings Jefremow & Neurath. Serum IL-23 levels were observed to be almost twice as high in IBD patients as in healthful individuals; CD patients had greater values than UC patients [17]. By looking at a full-size affiliation between IL 23 and nitric oxide stages in the blood of IBD patients, Soufli et al. Further evidence was once provided for a pro-inflammatory effect of IL-23 [18].

Furthermore, colleagues at Atreya and Neurath confirmed that CD sufferers had greater levels of protein and IL-23 p19 mRNA expression in the lamina propria compared with UC sufferers and healthy volunteers (19). On the other hand, in accordance to Zhang et al. Higher degrees of IL 23 p19 mRNA. Anti-TNF non-responders showed upregulation of IL23 p19 and IL23R, suggesting a feasible interaction between IL 23 and TNF-α as well [20]. Kvedaraite et al. It has been proven that the fundamental source of IL 23 in pediatric CD patients is tissue-infiltrating neutrophils [21]. Furthermore, IL-23 superior the activation of intraepithelial lymphocytes (IELs), NK cells and cytotoxicity in IBD patients. Furthermore, IL 23 is able to amplify the manufacturing of IFN-, TNF and IL 17 in IBD [22]. Devayani et al. showed that lamina propria T cells in UC produce IL 17 upon stimulation with IL 23. High serum IL-23 ranges in UC patients have additionally been related with

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sickness severity and lowered Treg/Th 17 mobile ratios [23]. Thus, serum IL-23 levels in patients with ulcerative colitis correlate with disease severity and duration, suggesting that it can be used as a disease diagnostic marker [24]. In a study analyzing IL-23 expression in human IBD, lamina propria macrophages from CD sufferers produced greater IL-23, but now not from UC patients [25]. Studies of co-existing inflammatory ailments such as arthritis and sacroiliitis have shown that sufferers with celiac sickness have higher ranges of IL-23 than those with UC, aiding these findings [26،27]. As stated via Allocca et al., greater IL-23 stages have been solely related with longer ailment duration and severity in UC patients. 2018 [28]. These facts advocate that IL-23 plays a key position in the pathogenesis of IBD, making it an necessary therapeutic target and a potential biomarker of IBD severity and prognosis [27]. Previous studies evaluating IL-23 expression in IBD sufferers categorised sufferers in accordance to "severity of disease," specially the usage of symptom-based disease endeavor scores at a given time point; however, patients can also have severe disease requiring aggressive treatment, even if Their disease signs and symptoms were now not extreme [29،30]. Moderately symptomatic sufferers who are taking excessive doses of corticosteroids, such as B. may additionally be regarded in sufferers with extreme steroid-dependent ulcerative colitis or Crohn's resistant to immunosuppressive therapy [31].

Conclusion

In this study, serum IL-23 levels were elevated in ulcerative colitis and Crohn's disease the patient group compared to the control group

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