Assessment of Serum Levels of YKL40 in Patients with Ulcerative Colitis.

[1]Saif Ali Muttaleb, [2] Estabraq Al-Wasiti, [3] Fadhil A. Abboudi.

1. Wasit University, College of Basic Education, Department of Science, Wasit, Iraq.

2- Al-Nahrain University, College of Medicine, Department of Chemistry and Biochemistry, Baghdad, Iraq.

3-Al-Nahrain University, College of Medicine, Department of Internal Medicine, Baghdad, Iraq.

Email: Smatloob@wasit.edu.iq

Mobile: 00964-7802660970

ABSTRACT:

IBD is a recurring chronic intestinal disease classified into two subtypes: Crohn's disease (CD) and ulcerative colitis (UC). YKL-40 is released by macrophages and neutrophils and is a growth factor for vascular endothelial cells and fibroblasts. Elevated blood concentrations of YKL-40 are detected in individuals with illnesses defined by inflammation or continuing fibrosis. The purpose of this study was to determine the relationship between serum YKL-40 and clinical disease activity in individuals with ulcerative colitis (UC). Identifying the cause of the elevation can be considered one of the most important ways to help the specialist in identifying UC patients prior to endoscopy.

Key Words: Inflammatory bowel disease. YKL-40 · Crohn’s disease. Ulcerative colitis.

INTRODUCTION

IBD is a chronic, recurrent inflammatory bowel disease classified into two subtypes: Crohn's disease (CD) and ulcerative colitis (UC) [1]. CD is an abbreviation for transmural discontinuous inflammation of the intestine, which can affect any portion of the gastrointestinal tract, from the mouth to the perianal area [2]. UC, on the other hand, is a persistent mucosal inflammation affecting the whole colon, from the rectum to the proximal colon [3]. Around 50% of CD patients have ileocolitis, which occurs at a rate of 3.1-20.2 per 100,000. Furthermore, UC is more common than CD, occurring at a rate of 9-20 per 100 000 000[4]. UC is a chronic inflammatory condition that begins in the rectum and extends to the colon .It is a chronic condition that manifests itself through bloody diarrhea, rectal discomfort, and stomach pain. Three and four decades of life are the most prevalent. UC the diagnosis is made by endoscopic, histological, laboratory, serological, and radiographic examinations, which are confirmed by clinical examination and medical history[5].

There are diagnostic criteria for UC: Chronic inflammation of the intestinal mucosa without granulomata, generally affecting the rectum and extending in a continuous pattern to the implicated region or entire colon, with varying degrees of severity [6].

- Chitinase 3-like 1 (YKL-40):-

CHI3L1, also called YKL-40 protein, is a human cartilage glycoprotein-39 (HC-gp-39) generated by the MG-63 human osteosarcoma cell line. It was found as a secreted protein in 1992 by the MG-63 human osteosarcoma cell line. Along with cancer cells, inflammatory and stem cells release YKL-40 [7].

Although the exact biological role of YKL-40 is unknown, it has been shown to operate as a growth factor in fibroblasts, chondrocytes, and synovial cells as well as a chemoattractant for endothelial cells. It accelerates the migration of all of these cells to the same extent as fibroblast-derived basic growth factor.

Additionally, YKL-40 alters the morphology of the vascular endothelium by encouraging the formation of branching tubules, implying that it may stimulate angiogenesis via endothelial migration and endothelial rearrangement. YKL-40 stimulates fibroblast proliferation in synergy with IGF-1 and is efficacious at concentrations equivalent to those of IGF-1 [8].

Prospective studies of patients with IBD are essential to assess if blood YKL-40 readings provide clinically meaningful information regarding disease activity.

Materials and methods

We observed patients with ulcerative colitis in the gastrointestinal tract unit at Al Imamain Alkadhimain Medical City for one year (January 2020 to January 2021).

Approved by the Institutional Review Board of Al-Nahrain University's College of Medicine (approved date: 01/19/2020 and number 130).This research enrolled individuals with ulcerative colitis at the discretion of the attending physician on the endoscopy unit.

The current study included 74 cases with UC and 74 healthy people (as a control group), and the age of all patients averaged between 19 and 64 years of both sexes, while the control group was between 19 and 54 years

old. The number of females is greater than males for the patients, as their percentage was (70.27%), while the percentage of males was (29.73 %), while in the control group their percentage of females was (75.67%) and the males (24.32%).

The sampling process for all people was in a random manner, separating the blood samples immediately without any preservative agent to product serum in its pure form. The serum was used to measure the level of YKL-40 protein concentration by using the ELISA technique.

Statistical Analysis

SPSS was used to conduct the statistical analysis (version 22). Due to the normal distribution of all continuous variables, data was provided as mean ± standard deviation (mean±SD), and all statistical comparisons were performed using the ANOVA test, with a P value of 0.01 considered statistically significant. The relationship between the variables was analyzed using Spearman rank correlation. Two-tailed analyses were conducted, and the descriptive level of significance was set at $p < 0.001$.

RESULTS:-

Patients were divided into three groups according to the severity of the endoscopic findings.

Twenty-seven patients were classified as having moderate endoscopic severity, which included marked erythema, loss of vascular signs, and erosion.

Twenty-four patients were classified as severe endoscopically, which included ulcers. In addition, twenty-three patients from the acute spontaneous bleeding group (Table 1.1) were included as controls, as were seventy-four subjects.

Table (1-1):- classification of grades is according to the degree of endoscopic severity.

Grade	Endoscopic features	no. of patients
2	Moderate: marked erythema, loss of vascular marking, erosions.	27
3	Severe: ulcers.	24
4	Severe: spontaneous bleeding.	23

The estimated levels of serum YKL-40 for UC patients compared to control (1648.14 ± 295.45 vs. 981.78 ± 478.60 pg/ml; $p < 0.001$).

It was highly significantly increased level in three groups of UC patients was observed compared to control (1612.27± 316.39 , 1596.15 ± 292.03 and 1744.49 ±261.06 vs. 981.78 ± 478.60 pg/ml, respectively; $p < 0.001$) which are shown in Table (1.2) and figure (1.1) respectively.

Table (1.2):-The means of YKL-40 values for UC patients.

Groups	YKL-40 pg/ml (Mean ± SD)	P-value
Grade 2 (N = 27)	1612.2± 316.13	P < 0.001**
Grade 3(N = 24)	1596.15 ± 292.03	P < 0.001**
Grade 4 (N = 23)	1744.49 ±261.06	P < 0. 001**
Control (N = 74)	981.78 ± 478.60	P < 0.001**

- **Grade 2: Moderate(marked erythema, loss of vascular marking,erosions) .**
- **Grade 3:Severe(ulcers).**
- **Grade 4: Severe(spontaneous bleeding).**

- ****:- The difference is highly significant at p=0.001 when compared patients group with control group.**

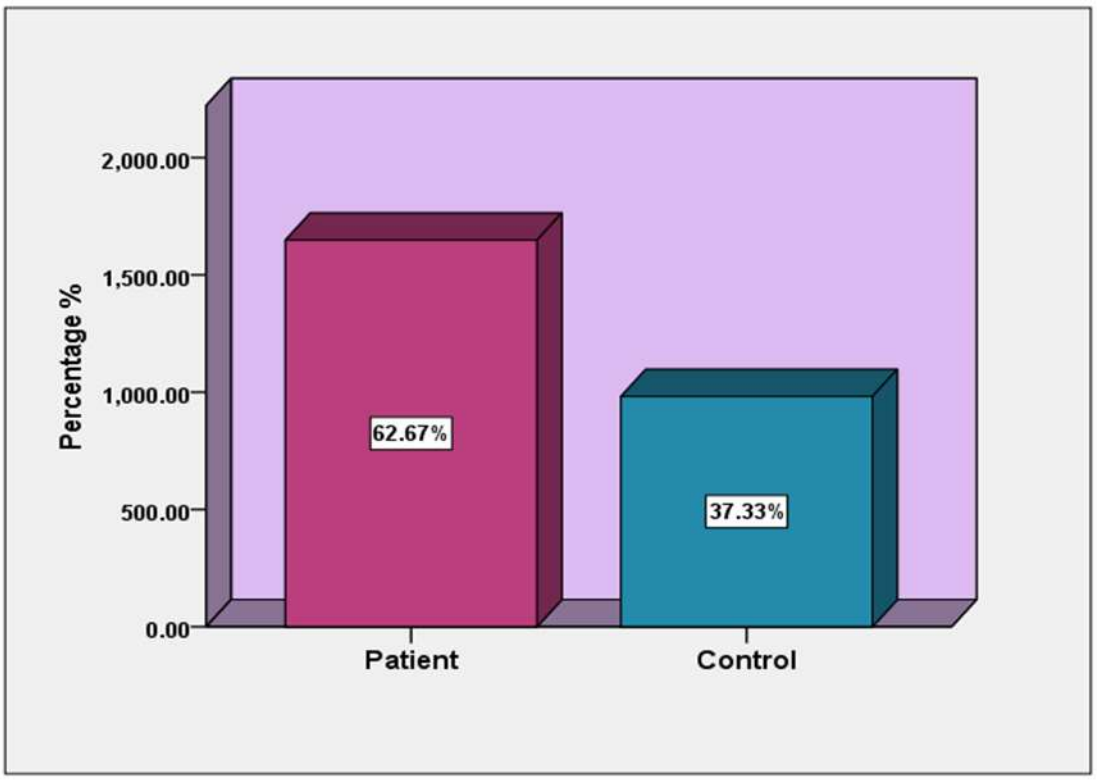

Figure (1.1): Distribution of serum YKL-40 (pg/ml) concentrations for patient and control groups.

Discussion

Despite significant advances in the diagnosis and treatment of UC, the illness remains a significant public health concern in many areas of the world, particularly in developing nations. The primary cause for failure to manage UC is a lack of early diagnosis. While colonoscopy with biopsy is the standard method for diagnosing UC, it is intrusive, inconvenient, and costly. Additionally, there is no very sensitive and specific endoscopic or histological score that accurately predicts UC clinical recurrence. In comparison to serum biomarkers, fecal biomarkers have a higher level of sensitivity and specificity[9].

According to the severity of endoscopy, (grade 2) has the largest percentage, accounting for (36.49) percent of total collected samples, followed by (grade 3) at (32.43) and (grade 4) at (31.08 percent).

Serum YKL-40 levels were significantly higher ($p < 0.001$) in UC patients than in the control group. that is consistent with the findings of other investigations that agreement with several studies such as Mazur et al study conducted in individuals with (IBD) suggests that YKL-40 can be used as a predictive biomarker for disease progression. In addition, it is suggested that inhibition of YKL-40 enzyme activity could be investigated as a potential therapeutic modality for (IBD) [10] .

Serum and fecal YKL-40 levels, which reflect the intensity of inflammation, may be used to monitor disease activity, particularly in (IBD).

In patients with UC, those with higher YKL-40 levels, which dropped as the illness remained inactive, were associated with increased disease activity as evaluated by (SCCAI).

Revealed that both inflammation and endothelial dysfunction are related with the protein YKL-40, which is hypothesized to be involved in tissue remodeling during inflammation and angiogenic processes that control macrophage infiltration, differentiation, and maturation[11].

Ethical approval: Al-Nahrain University, College of Medicine,

The committee approved the study (approval date: 01.19.2020 and approval number: T/B/2/3/130).

Acknowledgements: None.

REFERENCES;-

[1] A. Nishida, R. Inoue, O. Inatomi, S. Bamba, Y. Naito, and A. Andoh, "Gut microbiota in the pathogenesis of inflammatory bowel disease," *Clin. J. Gastroenterol.*, vol. 11, no. 1, pp. 1–10, 2018.

[2] M. Gajendran, P. Loganathan, A. P. Catinella, and J. G. Hashash, "A comprehensive review and update on Crohn's disease," *Disease-a-month*, vol. 64, no. 2, pp. 20–57, 2018.

[3] M. Gajendran *et al.*, "A comprehensive review and update on ulcerative colitis," *Disease-a-month*, vol. 65, no. 12, p. 100851, 2019.

[4] J. Deng, Y. Chen, S. Xu, and F. Pan, "Elevated serum levels of resistin in inflammatory bowel disease: a meta-analysis," *Authorea Prepr.*, 2020.

[5] A. Kornbluth, D. B. Sachar, and P. P. C. of the A. C. of Gastroenterology, "Ulcerative colitis practice guidelines in adults: American college of gastroenterology, practice parameters committee," *Am. J. Gastroenterol.*, vol. 105, no. 3, pp. 501–523, 2010.

[6] K. Conrad, D. Roggenbuck, and M. W. Laass, "Diagnosis and classification of ulcerative colitis," *Autoimmun. Rev.*, vol. 13, no. 4–5, pp. 463–466, 2014.

[7] A. Szymańska-Chabowska, J. Juzwiszyn, B. Jankowska-Polańska, W. Tański, and M. Chabowski, "Chitinase 3-Like 1, Nestin, and

Testin Proteins as Novel Biomarkers of Potential Clinical Use in Colorectal Cancer: A Review," *Heal. Med.*, pp. 1–8, 2020.

[8] A. D. Recklies, C. White, and H. Ling, "The chitinase 3-like protein human cartilage glycoprotein 39 (HC-gp39) stimulates proliferation of human connective-tissue cells and activates both extracellular signal-regulated kinase-and protein kinase B-mediated signalling pathways," *Biochem. J.*, vol. 365, no. 1, pp. 119–126, 2002.

[9] C. Ge, Y. Lu, H. Shen, and L. Zhu, "Monitoring of intestinal inflammation and prediction of recurrence in ulcerative colitis," *Scand. J. Gastroenterol.*, pp. 1–12, 2022.

[10] M. Mazur, A. Zielińska, M. M. Grzybowski, J. Olczak, and J. Fichna, "Chitinases and Chitinase-Like Proteins as Therapeutic Targets in Inflammatory Diseases, with a Special Focus on Inflammatory Bowel Diseases," *Int. J. Mol. Sci.*, vol. 22, no. 13, p. 6966, 2021.

[11] S. M. Hanafy, A. M. Hamed, A. A. Elfallah, and M. A. Elsharkawy, "Assessment of Serum Levels of YKL40 in Men with Varicocele," *Benha J. Appl. Sci.*, vol. 6, no. 5, pp. 275–280, 2021.