Gastroenterology

Evaluation of Serum Amyloid (A) Level in Ulcerative Colitis as a New Predictor of Disease Activity

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ABSTRACT

Background: in a genetically predisposed host, ulcerative colitis (UC) is a kind of inflammatory bowel disease (IBD), marked by an unregulated immune response produced by the gut microbiota.

Aim of the work: To determine the level of serum amyloid A as a novel predictor of ulcerative colitis disease activity

Patients and Methods: this is a prospective study that will take place at Al-Azhar University Hospitals (Al-Hussein and Bab-Elsheria). Patients were categorized into three groups: Group I: twenty-five patients confirmed with ulcerative colitis during remission state. Group II: twenty-five patients confirmed with ulcerative colitis during exacerbation state (activity state). Group III: Included twenty-five healthy volunteers. Serum amyloid A measurement done during remission and activity.

Result: High sensitive predictive value of Serum amyloid (A) level was in mild diseases, and the most specific predictive value was in severe diseases. Moderate ulcerative colitis was the most common in the active ulcerative colitis group.

Conclusion: For UC diagnosis and management, the level of SAA in the blood can be used as a potentially accurate laboratory biomarker, as well as disease activity and prognosis assessment.

Keywords: *Ulcerative colitis; Serum amyloid A (SAA); Predictor; Activity.*

INTRODUCTION

Inflammatory bowel disease (IBD) is a big health problem all over the world that is becoming more common.[1] Inflammatory bowel illnesses such as Crohn's disease (CD) and ulcerative colitis (UC) are relapsing and are two of the most common types.

UC is far more prevalent than the CD. This ratio increased in some areas reached around 15:1 in northeastern Poland, with an increase in the total number of people diagnosed with IBD recorded.[2] In addition, UC is far more common in Egypt than CD, as evidenced by 15-years research in which the ratio of individuals diagnosed with UC to patients diagnosed with CD was roughly 6:1.[3] Endoscopy and mucosal biopsy for histopathology are the best ways to diagnose UC. Laboratory tests and imaging examinations can also help to narrow down the diagnosis.[4] Several studies have employed laboratory markers, including C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) to quantify with a sensitivity and specificity of 50 to 60%, can detect UC activity. Other markers are more specific and sensitive, such as fecal calprotectin and lactoferrin..[5] Multiple inflammatory processes cause the acute phase reactant serum amyloid A protein (SAA) to be released., the liver is considered the primary source of SAA. It is considered a type of apolipoprotein associated with HDL in plasma. During acute inflammation, the concentration of SAA rises quickly, reaching 1000 times the usual amount in 5 to 6 hours[6]. Furthermore, SAA has a link to clinical activity in UC, but no research has been done to see if it is linked to endoscopic findings.[7] our study aimed to assess the serum amyloid A in ulcerative colitis as a novel predictor of the activity of the disease.

PATIENTS AND METHODS

It was a prospective study that took place at two Al-Azhar university hospitals (Al-Hussein and Bab-ElSheria). The study was designed to analyze the utility of serum amyloid A as a predictor for the activity in ulcerative colitis (UC). Patients with UC were included in the study besides healthy volunteers to assess the serum amyloid (A) and its relation to disease activity. Serum amyloid A done during remission and activity. We divide the patients into three groups:

Group I: twenty-five patients confirmed and well-known cases of ulcerative colitis by colonoscopy and histopathological examination during remission state,

Group II: twenty-five patients confirmed cases of ulcerative colitis by colonoscopy and histopathological examination, during exacerbation state (activity state). Group III: Included twenty-five healthy volunteers. We exclude the patients who received new medicines between colonoscopy and those who had a concomitant autoimmune illness, such as collagen diseases, individuals who had infections, such as the common cold and colonic malignancy.

We subjected the selected patients to the following: - Clear written consent. Clinical assessment including Full history tacking (including name, age, sex, smoking habit, alcohol, education level, residential area (urban/rural) gastrointestinal discomfort, nausea, loss of weight, distension, constipation, tenesmus, diarrhea, mucus passing, vomiting, fever, and IBD in the family).

A local abdominal examination is part of the overall checkup. Laboratory investigations: Renal function tests, (CRP), and (ESR), Complete Blood Count (CBC), Alanine transferase (ALT), Aspartate transferase (AST), serum albumin, total bilirubin, direct bilirubin, and prothrombin time are examples of routine laboratory examinations, We measure CRP, and SAA values at the same time. SAA was determined using an ELISA kit.

Radiological examinations, including abdominal ultrasound, will be carried out to rule out the presence of any related diseases or problems. Colonoscopy will be conducted; we took multiple biopsies after intubating the terminal ileum.

We researched by Al-Azhar University's ethical board.

Analytical statistics

The (SPSS) version 15.0 was used to analyze the data. (Quantitative and qualitative data).

The tests that will be carried out are as follows: When comparing non-parametric data, the Chi-square test was utilized. When comparing more than two means, The analysis of variance (ANOVA) is employed in this study. The post hoc test is used to make numerous comparisons between variables.

RESULTS

		Group I (25)	Group II (25)	Group III (25)	P–Value
Age	Mean (SD)	35.6 (6.5)	32.9 (5.6)	33.9 (4.5)	> 0.05[1]
Sex	N (%)				
Female		15 (60)	16 (64)	12 (48)	
Male		10 (40)	9 (36)	13 (52)	
Residential Area	N (%)				>0.05[2]
Urban		15 (60)	13 (52)	10 (40)	
Rural		10 (40)	12 (48)	15 (60)	
Smoking	N (%)	8 (32)	7 (28)	2 (8)	
Family history of inflammatory bowel diseases N (%)		1 (4)	1 (4)	0	

1: ANOVA | 2: Chi-square
N: Number

Table 1: shows no difference among included groups regarding demographic characteristics, smoking, or family history.

Clinical presentation	Group I (25)		Group II (25)		Group III (25)		P – Value
	N	%	N	%	N	%	
Abdominal pain	5	20	20	80	2	8	
Weight Loss (> 10Kg)	3	12	5	60	0	0	
Rectal Bleeding	0	0	9	36	0	0	
Diarrhea	5	20	10	40	0	0	
Nausea	3	12	25	100	1	4	<0.05[2]
Tenesmus	4	16	25	100	0	0	
Abdominal distension	5	20	20	80	1	4	
Passage of Mucus	1	4	10	40	0	0	
Vomiting	2	8	19	76	0	0	

2: Chi-square
Table 2: demonstrates a significant difference in clinical presentation across the groups studied.

Active Ulcerative Colitis	Number	(%)
Mild	7	28
Moderate	16	64
Severe	2	8

Table 3: shows moderate ulcerative colitis was the most common in the active ulcerative colitis group.

	Mild (7)	Moderate (16)	Severe (2)	Remission (25)	P – Value
CRP Mean (SD)	7.5 ± (1.2)	12.6± (2.4)	32± (6.9)	1.1± (1.5)	
SAA Mean (SD)	7.6± (1.2)	12.6± (2.4)	25± (5.9)	2.3± (1.2)	
ESR Mean (SD)	37± (5)	39± (8)	47± (10)	17± (11)	<0.01[3]
Hb Mean (SD)	10.7± (1.3)	9.4± (0.9)	9.1± (1.2)	10.8± (1.7)	

3: Kruskal-Wallis test.
Hb: Hemoglobin | CRP: C - reactive protein; SAA: Serum Amyloid A; and ESR: Erythrocyte.Sedimentation.Rate.

Table 4: shows a highly statistical difference among different categories of ulcerative colitis regarding serum inflammatory markers.
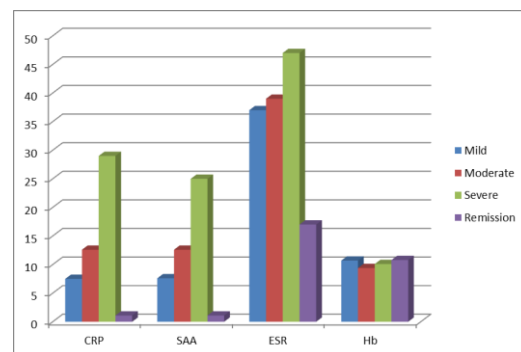

Fig. 1: Illustrates laboratory investigations of different categories of ulcerative colitis.

SAA	Sensitivity	Specificity
Remission	72%	68%
Mild	83.33%	66.67%
Moderate	75%	75%
Severe	80%	80%

Table 5: shows that the most sensitive predictive value was in mild diseases, and the most specific predictive value was in severe diseases.
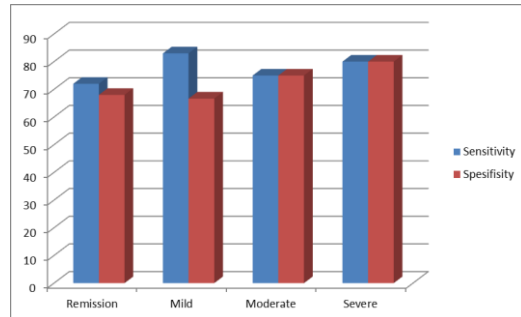

Fig. 2: Illustrates SAA predictive values of different categories of ulcerative colitis.

DISCUSSION

The results of this investigation revealed that there was no distinction in the attitudes of the participant's demographic features. Also, there was no statistical difference among included groups regarding smoking or family history. To our knowledge, this is one of the few studies that have looked into the serum amyloid (A) level in ulcerative colitis as a predictor of disease activity, however, there were very limited reports were found in the literature suggesting the role of SAA in ulcerative colitis and other inflammatory bowel diseases.

This study aimed to see if serum amyloid A in ulcerative colitis patients is a stronger biomarker for predicting activity and clinical remission. There is a study that has a goal to see if serum amyloid A in ulcerative colitis patients is a biomarker for predicting mucosal repair. The study included 108 ulcerative colitis patients. [7]

There is another study that wanted to find a combination of inflammatory markers to predict the endoscopic activity of the disease. Sixty-four patients with Crohn's disease (CD) and fifty-four patients with ulcerative colitis (UC) were found to have inflammatory bowel disease (IBD), and twenty healthy people as controls, inflammatory biomarker concentrations in the blood (including SAA) were measured. [8] Furthermore, there is another study related to this topic, The goal of this study was to see if there was a link between SAA, inflammatory cytokines, in Crohn's disease patients, as well as mucosal inflammation and if this measure could be beneficial in individuals with active disease but no increased C-reactive protein (CRP). There were ninety-four patients in all, and the females were thirty-five (37.2%).

At the time; the samples were taken, the cohort's average age was 38 years (SD: 16), and six patients (6.4 percent) were smokers. They divide the cases

into two groups, mucosal healing, and non-mucosal healing groups, with no significant differences in demographic characteristics. Also, that there was a statistical difference among included groups regarding smoking. [9]

In addition; Ishihara et al., [10] The study's purpose was to see if there was a link between SAA and Crohn's disease-related endoscopic activity of the disease. A total of 55 CD patients were included in the study. [10]

In terms of clinical presentation among the included groups, our findings demonstrated was a substantial difference in clinical presentation among the groups. Diarrhea, stomach discomfort, rectal pain, bloody stool, fever, weight loss, and malnutrition are the most common symptoms of UC. Swelling of the rectum lining and a constant feeling at the rectum site are common symptoms of proctitis colitis. Extensive colitis causes cramping, significant bleeding, and colon dilatation, which depending on the area and severity of the ailment, the treatment will differ. [11]

The findings of this study revealed was a significant disparity in sentiments among the groups tested. There was no statistical difference among active and remission groups regarding diseases characteristics. This is in line with the findings of Okba et al., [12]

Inactive UC patients and controls showed significantly greater WBC, absolute neutrophilic count, absolute monocytic count, NLRs, CRP, and ESR than active UC patients. UC is dormant. Patients and controls performed worse than active UC patients. LMRs and absolute lymphocyte count were both found to be considerably lower. NLRs were on average higher in the three research groups (active UC: 2.630.43 versus inactive UC: 1.640.25 versus controls: 1.440.19; p 0.0001). In the three studied groups, the average LMRs were (active UC: 2.250.51 versus inactive UC: 3.580.76 versus controls: 3.640.49; p 0.0001). [12]

Furthermore, our findings were backed up by Zhang et al., [13] They discovered that patients of UC had lower levels of hemoglobin, albumin, and total protein than normal people (p0.001). Severe UC patients had lower hemoglobin, albumin, and total protein levels than mild-to-moderate UC patients (p0.001). [13]

The present results revealed that there was a statistical difference among included groups regarding levels of CRP, ESR, and SAA. (p<0.05). We also found that SAA, CRP, ESR, and Hb had a highly statistical difference among different categories of ulcerative colitis. As the study by Wakai et al., [7] enrolled one group in their investigation. The relationship between SAA, CRP, and endoscopic findings was studied. Our findings are backed up by the data. They discovered a low association between CRP and endoscopic however, there is SAA and MES (r = 0.614, p = 5.44 1022), as well as ayo score (MES) (r = 0.352, p = 3.38 107), had a significant connection. The ratio of normal CRP to SAA is highest at MES 0, and it gradually falls as MES increases. In SAA (p 0.05), the declining trend in the MES relationship was significant statistically but not in CRP. CRP, SAA,

and MES levels were also measured in people who were not in remission in clinical practice (CAI > 5).CRP and SAA were be shown to be substantially associated with MES, with SAA being the stronger relationship. In clinical remission patients alone, the link between CRP and clinical remission was greater. The study agrees with our findings. Bourgonje et al., [8] reported a statistically substantial distinction between the studied groups regarding levels of CRP and SAA (p<0.05). [8]

Furthermore, the study by Yarur et al., [9] In terms of CRP and SAA levels, there was a statistically substantial distinction between the tested groups (p0.001). [9] Hu et al.,[14] The levels of SAA were considerably higher in the active group than the inactive group. In agreement with the present results Xia & An et al., [15] The serum CRP and ESR levels in the control group were considerably less than different grades of UC groups, according to the study.[15]

As regard serum amyloid A predictive values of different categories of ulcerative colitis, we found that the highest sensitive predictive value was in mild diseases (Sensitivity and Specificity 83.33% and 66.67% respectively), and the most specific predictive value was in severe diseases (Sensitivity and Specificity 80% and 80% respectively).To our knowledge, this is the first study to disclose SAA's ability to predict the severity of ulcerative colitis; prior research had only shown SAA's ability to predict the presence of ulcerative colitis. The study by Wakai et al., [7] In the ROC research, the SAA had an area under the ROC curve of 0.807, indicating that it was more predictive than the CRP, This had a 0.701 area under the ROC curve. When the ROC curves for SAA and CRP for mucosal inflammation were compared, SAA outperformed CRP by a wide margin (p 0.01).

and SAA sensitivity, specificity, PPV, NPV, and accuracy in clinical remission patients with appropriate mucosal inflammatory threshold values can differentiate inflammation of the mucosa from the healing of the mucosa. In distinguishing mucosal inflammation from mucosal healing. Their findings suggest that SAA, rather than CRP, could be a better predictor of mucosal repair in clinical remission patients.[7]

As well our results were supported by Bourgonje et al., [8] (serum amyloid A (SAA), Eotaxin-1, IL-6, IL-8, IL-17A, and TNF-) are Six inflammatory biomarkers that surpassed standard measurements in predicting IBD CRP, fecal calprotectin, and HBI/SCCAI scores indicate disease activity. SAA, IL-6, IL-8, and Eotaxin-1 were the greatest combination of predictive inflammatory biomarkers, with an AuROC of 0.84 (95 percent CI: 0.73–0.94, P = 0.0001), predicting substantially better (P = 0.002) than the CRP level in the blood, which had an AuROC of 0.57 (95 percent CI: 0.43–0.72, P = 0.32).

CONCLUSION

For UC diagnosis; the level of SAA in the blood can be used as a potentially accurate laboratory biomarker to assess disease activity and prognosis as well as illness diagnosis and treatment.

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