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ORIGINAL ARTICLE

Leucine Rich Glycoprotein as a biomarker In Ulcerative Colitis Disease

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ABSTRACT

Background: Crohn's disease (CD) and ulcerative colitis (UC) are examples of inflammatory bowel diseases (IBDs), which are chronic gastrointestinal tract illnesses with no known cause. In UC, there is a correlation between leucine-rich alpha-2 glycoprotein (LRG) and clinical disease activity. The purpose of this study was to evaluate the relationship between UC patients' LRG serum levels and their illness activity and severity.**Method:** We performed this prospective cohort study on 36 Ulcerative colitis patients. C-Reactive Protein (CRP), serum urea, creatinine, total bilirubinand fecal calprotectin were assessed. Serum LRG levels were measured by using double antibody sandwich enzyme-linked immunosorbent assay (ELISA).**Results:** The best cutoff of baseline LRG for diagnosing severe UC in comparison to mild and moderate cases was ≤67.4µg/ml with area under curve 0.913 with sensitivity 91.7%, specificity 87.5%, positive predictive value 78.6%, negative predictive value 95.5% and overall accuracy 91.7% (p=0.002). A statistically significant positive correlation was revealed between baseline LRG and Mayo score (p<0.001). A significant difference was found between mild, moderate &severe disease groups with baseline LRG (p<0.001). On comparing each two groups with one way ANOVAand Mann Whitney test, the difference was significant between mild and both moderate and severe disease (significantly lower in mild group with p values of 0.013, and <0.001 respectively).**Conclusions:**Leucine-rich glycoprotein could be a reliable serum biomarker for the assessment of clinical disease activity in patients with IBD. It can be an alternative to CRP and fecal calprotectin for the assessment of ulcerative colitis disease.
Keywords: Leucine Rich Glycoprotein, biomarker, Inflammatory Bowel Disease

INTRODUCTION

Crohn's disease (CD) and ulcerative colitis (UC) are examples of inflammatory bowel diseases (IBDs), which are chronic gastrointestinal tract illnesses with no known cause. Fatigue, anemia, weight loss, and diarrhea with blood are the most common symptoms of inflammatory bowel disease [1]. The symptoms can appear slowly at first, with non-bloody diarrhea and poor weight growth. Extraintestinal symptoms impact more than one-third of people with IBD [2,3].

The "gold standard" methods for identifying and measuring intestinal inflammation are still endoscopic inspection and histological analysis of biopsy materials; however, these procedures are

expensive, intrusive, and patients dislike having to undergo repeated tests[4].

It is necessary to have a trustworthy surrogate marker that may mimic intestinal inflammation and act as an alternative to endoscopy. In most cases, blood-based biomarkers offer a non-invasive way to estimate the inflammatory burden in IBD [5]. Less blood-based indicators are still regularly used in clinical settings, and only a small number have received thorough validation in IBD [6].

C-reactive protein (CRP) is one potential indication. The degree of pathogenic activity that induces CRP generation determines its clinical level [7]. Even with active disease, some people do not experience elevated CRP levels. Consequently, more sensitive biomarkers are required [6].

Leucine-rich alpha-2 glycoprotein (LRG) is a 50 kDa glycoprotein that was first discovered to be an inflammatory biomarker for immune-mediated illnesses like IBD and rheumatoid arthritis [8]. LRG comprises repeating sequences with a leucine-rich pattern.

Other inflammatory disorders like Still's disease, Kawasaki disease, juvenile idiopathic arthritis, psoriasis, appendicitis, malignant diseases like gastric cancer and colorectal cancer, heart failure, diabetes, and obesity have all been linked to elevated LRG levels, according to subsequent investigations. It is primarily produced by intestinal epithelial cells, neutrophils, macrophages, and hepatocytes in response to interleukin-1β (IL-1β), IL-6, IL-22, and tumor necrosis factor-α (TNFα) [8,9]. It is a biomarker, though, and it is independent of IL-6. Additionally, LRG is produced in serum by cytokine-stimulated neutrophils and epithelium in intestinal epithelial cells of IBD patients. Put differently, LRG is a better indicator of intestinal inflammation than CRP [10].

As a proxy marker of endoscopic inflammation, serum LRG level associated favorably with clinical disease activity in UC and aided in the detection of endoscopic mucosal healing [5].

Therefore, the purpose of this study was to ascertain the relationship between the LRG serum level and the activity and severity of the disease in UC patients.

METHODS

At the Clinical Pathology and Internal Medicine Departments, Faculty of Medicine, Zagazig University, we conducted this prospective cohort study on 36 patients with ulcerative colitis. The patients had their biological treatment from March 2023 until February 2024 and subjected to follow up for six months.

All subjects were told about the operation and medical research before providing their written informed consent. The Helsinki Declaration, which is the World Medical Association's code of ethics for human research, was followed during the study. The Institutional Review Board gave their clearance before this study could be completed. (IRB) (#ZU-IRB#10650).

Individuals over the age of eighteen, regardless of gender, who had lower gastrointestinal symptoms and were scheduled for a colonoscopy and had been identified with inflammatory bowel illnesses using a combination of endoscopic, stool, biochemical, clinical, and

histological examinations were included [11].

Exclusions from the study included patients under the age of 18, those with acute infections, other inflammatory disorders, chronic conditions like chronic renal failure, congestive heart failure, thyroid disorders, cancer, and other autoimmune diseases, patients receiving steroid therapy or non-steroidal anti-inflammatory drug therapy, and pregnant patients.

In addition to a thorough history collection, patients had a broad and methodical clinical examination.

Laboratory investigations

Venipuncture was used to take blood samples for each patient's CBC, ESR, CRP, urea, creatinine, total bilirubin, ALT, and AST tests. Three milliliters of blood were collected in a BD Vacutainer ® ESR tube, and two milliliters in a ® A plastic serum tube, a BD vacutainer, and two milliliters of blood in an EDTA tube (Becton, Dickinson and Company, NJ) were used. ELISA was used to measure the LRG level after the serum was separated and kept frozen at –80°C. Also, samples of stool were taken for measurement of fecal calprotectin.

Fully automatic cell counter (XN 1000 Sysmex, Germany) for a full blood count. An automatic erythrocyte sedimentation rate (ESR) analyzer called Vision B was used to find the ESR. It was made by Shenzhen YHLO Biotech Co., Ltd. in China. The immunoturbidimetry test for C-Reactive Protein (CRP) was done on a Cobas 6000 with a c501 module from Roche Diagnostics in Mannheim, Germany. These tests (serum urea, creatinine, total bilirubin, ALT, and AST) were done on using the Roche 8000, c702 module. Fecal calprotectin was done by quantitative fluorescence Immunoassay (FIA) on ichroma® by Boditech Med Inc. in Korea (CatLog No. CFPC-83). It could measure between 10 and 1000 mg/kg, and the standard value was less than or equal to 50 mg/kg of feces. The test took 10 minutes, had a performance CV of less than 10%, and needed 10 mg of feces as a sample.

Special investigation

Serum LRG levels were measured by using double antibody sandwich enzyme-linked immunosorbent assay (ELISA) **(DL-develop Co, China) CAT:DLR-LRG1-HU**, following the directions from the maker. A standard curve was used to figure out the LRG values. It was thought that the findings meant µg/ml.

Colonoscopy was done by two top experts and an OLYMPUS colonoscope (model/CV-190, serial NO 7336784), as long as there were no reasons not to. Hematoxylin and eosin (H&E) staining was used for the histopathological study, which was enough to make the diagnosis [12].

Scores of Disease activity

The Mayo Score for ulcerative colitis disease activity measures how bad the disease is and can be used to keep an eye on patients while they are on treatment. Scores run from 0 to 12, with higher scores showing worse disease. For example, remission cases got scores of 0 to 1, mild disease got scores of 2 to 4, moderate disease got scores of 5 to 6, and severe cases got scores of 7 to 12 [13].

STATISTICAL ANALYSIS

IBM's SPSS 27.0 (IBM, 2020) was used to look at the data statistically. To show the

qualitative statistics, frequencies and relative percentages were used. A Shapiro-Wilk test was used to find the difference between the parametric factors. Means plus or minus standard deviations were used to show data that could be measured. We used an independent T test for normally distributed data to find the difference between the two groups' quantitative variables, and a Mann Whitney test for not normally distributed data. The ANOVA F-test was used to find the difference between more than two groups of normally distributed quantitative factors. Pairwise comparison and Bonferroni were used to find differences between each two groups when the differences were big. The ROC curve was used to find the best cutoff value for a certain quantitative measure in diagnosing a health problem. To find out which way the two continuous variables were linked and how strong the link was, the Person correlation coefficient was used. The paired sample t test was used to look at how a certain measure changed between two points in time.

RESULTS

This study included 36 patients with ulcerative colitis with age range from 19 to 60 years with mean age 32.9 ± 10.9, Male represented 47.2% and 50% came from rural areas (Table 1).

Statistically significant differences were revealed in total bilirubin and Mayo score between the three activity groups of the UC patient'sgroups (p=0.04, p=0.043 respectively). On pairwise comparison, the difference of total bilirubin was significant between newly diagnosed and patients with relapse (p=0.014), and difference of Mayo score was significant between remission and relapse (p=0.017) (Table 2).

Statistically significant differences were found between severity of UC with each of lymphocytic count, CRP, fecal calprotectin and Mayo score (p=0.005, p=0.004, p=0.027, and p<0.001 respectively), on pairwise comparison, the differences were significant between mild and severe patients (p<0.001, p<0.001, p=0.008, p=0.001 respectively) as the median of the Myo score were 3,7 and 8 for mild, moderate and sever UC cases respectively (Table 3).

The best cutoff of CRP in diagnosis of severe ulcerative colitis in comparison to mild and moderate cases was ≥18.5 mg/L with area under curve 0.8 with sensitivity 83.3%, specificity 66.7%, positive predictive value 55.6%, negative predictive value 88.9% and overall accuracy 72.2% (p=0.004). The best cutoff of fecal calprotectin in diagnosis of severe ulcerative colitis in comparison to mild and moderate cases was ≥396 µg/g with area under curve 0.7 with sensitivity 75%, specificity 66.7%, positive predictive value 52.9%, negative predictive value 84.2% and overall accuracy 69.4% (p=0.036). The best cutoff of baseline LRG in diagnosis of sever ulcerative colitis in comparison to mild and moderate cases was ≤67.4 µg/ml with area under curve 0.913 with sensitivity 91.7%, specificity 87.5%, positive predictive value 78.6%, negative predictive value 95.5% and overall accuracy 91.7% (p=0.002) (Table 4, Figure A).

A statistically significant negative correlation was found between baseline LRG and lymphocytes (p=0.01), while a statistically significant positive correlation was revealed

between baseline LRG and Mayo score (p<0.001) (Table 5).

A statistically non-significant relation was found between activity of UC and baseline LRG, LRG after 6 months of treatment or percent change in LRG in comparison of the three groups together. Within newly diagnosed patients and those on relapse, paired t test showed there was significant decrease in LRG (p=0.003) while those with remission, there was a non-significant decrease in LRG.A statistically significant relation was found between the three severity groups of UC and baseline LRG (p<0.001). On comparing each two groups with paired t test, the difference was significant between mild and both moderate and severe disease (significantly lower in mild group with p values of 0.013, and <0.001 respectively) (Table 6).

Figure 1: (A): ROC curve showing performance of CRP and Fecal calprotectin in detection of ulcerative colitis severity, (B): ROC curve showing performance of baseline LRG in detection of ulcerative colitis severity.

Table (1): Demographic data of all patients:

	Ulcerative Colitis	
	N=36	%
Gender: Male Female	 17 19	 47.2% 52.8%
Age (year) [Mean ± SD] Range	 32.9 ± 10.9 19 – 60	
Geographic: Rural Urban	 18 18	 50% 50%

Table (2) Clinical and laboratory data of UC patients according to disease activity:

	Newly diagnosed	Remission	Relapse	χ^2	p
	N=13 (%)	**N=3 (%)**	**N=20 (%)**		
Gender Female Male	 7 (53.8%) 6 (46.7%)	 1 (33.3%) 2 (66.7%)	 9 (45%) 11 (55%)	0.163	0.687
Residence Rural Urban	 7 (53.8%) 6 (46.7%)	 3 (100%) 0 (0%)	 8 (40%) 12 (60%)	0.768	0.381
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	F	P
Age (year)	28.4 ± 5.7	38.3 ± 7.4	35.1 ± 13.0	2.002	0.151
WBCs (x10^3/uL)	8.0 ± 2.3	8.6 ± 2.6	8.7 ± 2.6	0.291	0.75
Neutrophil (x10^3/uL)	4.9 ± 2.3	4.9 ± 1.5	5.9 ± 2.2	0.977	0.387

	Newly diagnosed	Remission	Relapse	χ^2	p
Lymphocytes (x10^3/uL)	2.5 ± 0.8	2.8 ± 1.4	2.2 ± 0.8	0.812	0.452
Hemoglobin (g/dl)	11.3 ± 1.9	12.4 ± 1.8	11.2 ± 2.0	0.518	0.601
BUN (mg/dl)	18.2 ± 7.9	24.1 ± 5.4	16.9 ± 7.4	1.212	0.31
ALT (U/L)	14.3 ± 7.0	6.0 ± 6.0	13.1 ± 4.8	0.398	0.675
AST (U/L)	17.9 ± 7.2	23.2 ± 9.8	18.1 ± 5.1	0.944	0.399
LRG (µg/ml)	82.7 ± 19	60.9 ± 3.1	75.3 ± 18.5	1.903	0.165
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	KW	P
Creatinine (mg/dl)	0.7(0.5 – 0.7)	1(0.6 – 1.0)	0.7(0.5 – 0.9)	1.354	0.508
Platelet (x10^3/uL)	275(256 – 277)	235(230.5 – 332.5)	322.5(267.5 – 393)	2.96	0.228
T. bilirubin (mg/dl)	0.27(0.2 – 0.3)	0.5(0.4 – 0.6)	0.6(0.4 – 0.7)	6.46	**0.04***
Pairwise	P_1 0.148	P_2 0.932	**P_3 0.014***		
CRP (mg/L)	24.7(15.4–42.2)	6.3(6.1–7.8)	18.1(11.9 – 27.1)	5.507	0.064
ESR (mm.)	26(17 – 36)	26(18 – 30.5)	29(13 – 42)	0.3	0.861
Calprotectin (µg/g)	334(290 – 553)	309(307.5-310)	438.5(232 – 678.5)	1.604	0.448
Mayo score	7(3 – 7)	3(2 – 3.5)	7(6 – 8)	6.277	0.043*
Pairwise	P_1 0.106	**P_2 0.017***	P_3 0.209		

χ^2Chi square for trend test F One way ANOVA test KW Kruskal Wallis test *p<0.05 is statistically significant p1 difference between new cases and remission cases p2 difference between remission cases and relapse p3 difference between new cases and relapse cases of UC

Table (3): Clinical and laboratory data of UC patients according to disease severity:

	Mild	Moderate	Severe	χ^2	p
	N=12 (%)	**N=12 (%)**	**N=12 (%)**		
Gender Female Male	 6 (50%) 6 (50%)	 6 (50%) 6 (50%)	 5 (41.7%) 7 (58.3%)	0.163	0.687
Residence Rural Urban	 6 (50%) 6 (50%)	 5 (41.7%) 7 (58.3%)	 7 (58.3%) 5 (41.7%)	0.162	0.687
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	F	P
WBCs (x10^3/uL)	8.4 ± 1.7	8.7 ± 2.6	8.2 ± 2.9	0.114	0.867
Neutrophil (x10^3/uL)	4.8 ± 1.2	5.8 ± 2.2	5.9 ± 2.9	0.869	0.429
Lymphocytes (x10^3/uL)	2.9 ± 0.8	2.3 ± 0.9	1.8 ± 0.5	6.232	**0.005***
Bonferroni	P_1 0.133	P_2 0.497	**P_3 0.004***		

	Mild	Moderate	Severe	χ^2	p
Hemoglobin (g/dl)	12.1 ± 1.2	11.3 ± 2.1	10.6 ± 2.2	1.883	0.168
BUN (mg/dl)	17.0 ± 6.3	20.2 ± 9.6	16.5 ± 6.4	0.837	0.442
Creatinine (mg/dl)	0.7 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.411	0.667
LRG (µg/ml)	60.9 ± 7.6	78.9 ± 18.3	90.4 ± 15.1	12.9	**<0.001****
Bonferroni	**P_1 0.013***	P_2 0.173	**P_3<0.001****		
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**KW**	**P**
Age (year)	30(22.25 – 38)	34(31 – 41.5)	26.5(23 – 38.5)	2.798	0.247
Platelet (x10^3/uL)	277(229 – 343)	285.5(267 – 372)	288.5(259 – 395.3)	0.448	0.799
T. bilirubin (mg/dl)	0.4(0.2 – 0.6)	0.5(0.2 – 0.8)	0.5(0.3 – 0.8)	1.683	0.431
ALT (U/L)	11(8.3 – 15.5)	15.5(11.3 – 16.8)	13(10 – 20)	2.578	0.276
AST (U/L)	15.5(12.8 – 20.2)	18.2(13.8 – 21.5)	17.9(16.2 – 23.3)	1.427	0.49
CRP (mg/L)	9.7(5.3–20.9)	16.2(12.3–24.5)	37.1(20.0 – 69.0)	10.929	**0.004***
Pairwise	P_1 0.121	P_2 0.079	**P_3<0.001****		
ESR (mm.)	27.5(17.8 – 37.3)	24.5(12 – 38.8)	27.5(14.8 – 44.5)	0.558	0.756
Calprotectin (µg/g)	310(245 – 350.3)	439.5(245.5-689.3)	566(350.5 – 777.5)	7.213	**0.027***
Pairwise	P_1 0.094	P_2 0.328	**P_3 0.008***		
Mayo	3(2 – 4)	7(6 – 7.8)	8(7.3 – 9)	27.804	**<0.001****
Pairwise	**P_1<0.001****	**P_2 0.046***	**P_3 0.001****		

χ^2Chi square for trend test F One way ANOVA test KW Kruskal Wallis test *p<0.05 is statistically significant p1 difference between new cases and remission cases p2 difference between remission cases and relapse p3 difference between new cases and relapse cases of UC

Table (4): Performance of CRP, Fecal Calprotectin and LRG to detect severity of Ulcerative colitis:

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	p
CRP (mg/L)	≥18.5	0.802	83.3%	66.7%	55.6%	88.9%	72.2%	0.004*
Calprotectin (µg/g)	≥396	0.717	75%	66.7%	52.9%	84.2%	69.4%	0.036*
LRG (µg/ml)	≤61.4	0.855	80%	81.8%	66.7%	90%	81.3%	0.027*

Table (5): Correlation between baseline LRG and the studied parameters among ulcerative colitis group:

	R	P
Age (year)	-0.278	0.101
WBCs	-0.128	0.455
Neutrophil	0.097	0.574
Lymphocyte	**-0.424**	**0.01***
Hemoglobin	-0.187	0.274
Platelet	-0.041	0.81
CRP	0.113	0.512
ESR	-0.177	0.302
BUN	0.024	0.809
Creatinine	-0.077	0.655

	R	P
Total bilirubin	-0.118	0.492
ALT	0.191	0.265
AST	0.079	0.648
Calprotectin	0.243	0.153
LRG after 6 months	0.139	0.419
Mayo score	**0.679**	**<0.001****

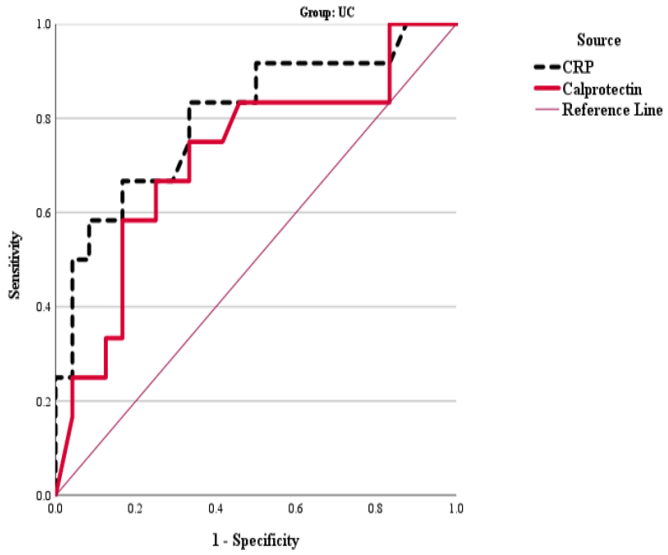
r Pearson correlation coefficient *p<0.05 is statistically significant

Table (6): Level of LRG before and after 6 months of treatment according to disease activity and severity:

UC patients activity					
	Newly diagnosed (n=13)	**Remission (n=3)**	**Relapse (n=20)**	**F**	**p**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Baseline LRG (µg/ml)	82.7 ± 19	60.9 ± 3.1	75.3 ± 18.5	1.903	0.165
After 6 months of treatment (µg/ml)	45.6 ± 25.2	42.8 ± 26.6	36.4 ± 17.4	0.771	0.471
p¥	0.003*	0.321	<0.001**		
	Median (IQR)	**Median (IQR)**	**Median (IQR)**	**KW**	**p**
% Change	47.9(19.5–72.1)	11.5(7.2–44.99)	56.3(32.6 – 64.5)	1.049	0.576
UC patients severity					
	Newly diagnosed (n=13)	**Remission (n=3)**	**Relapse (n=20)**	**F**	**p**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Baseline LRG (µg/ml)	60.9 ± 7.6	78.9 ± 18.3	90.4 ± 15.1	12.9	**<0.001****
Bonferroni	**P_1 0.013***	P_2 0.173	**P_3<0.001****		
After 6 months of treatment (µg/ml)	41.0 ± 23.9	44.9 ± 21.9	34.8 ± 17.4	0.7	0.5
p¥	0.005*	<0.001**	<0.001***		
	Median (IQR)	**Median (IQR)**	**Median(IQR)**	**KW**	**p**
% change	30.7(4.9 –56.1)	48.5(25.6–64.4)	61.8(46.9 – 73.9)	4.6	0.099

For UC patients disease activity: IQR interquartile range F One way ANOVA test KW Kruskal Wallis test paired sample t test

For UC patients disease severity: IQR interquartile range F One way ANOVA test KW Kruskal Wallis test *p<0.05 is statistically significant p1 difference between mild and moderate p2 difference between moderate and severe p3 difference between mild and severe UC ¥ paired sample t test ,*difference between newly diagnosed and remission,**difference between remission and relapse and ***difference between newly diagnosed and relapse UC.



DISCUSSION

Serum LRG has been described as a useful biomarker to measure how active the disease is in people with UC, and histological analysis of colons that had been surgically removed showed that LRG is expressed in epithelial cells within inflamed lesions [14].

A protein called blood C-reactive protein (CRP) is often used to predict how active inflammatory diseases, like IBD, will be. However, CRP levels are not always high in people who have active IBD. These days, fecal calprotectin is often used as a reliable measure for UC mucosal healing. In UC, however, there is only a good to poor link between fecal calprotectin and clinical symptoms. So, different biomarkers are needed to find the best way to treat inflammatory diseases because they make it easy and accurate to track how the disease is progressing during treatment [8].

There were 36 people with ulcerative colitis in our study. UC was founded to be more common in women, but there wasn't a statistically significant difference between the groups as looked at based on gender. It is known that the recurrence rates of IBD in men and women are about the same (about 1:1.2 in UC), but there isn't a lot of information about how the disease is different in men and women [15].

Mak et al. [16], on the other hand, found that the risk ratio of UC in men compared to women was 2.4:1. Some groups of people found that women were more likely than men to get UC, while others didn't find any difference between the sexes at all. A review of population-based studies on UC cases found that the age at which UC started was different for men and women. In fact, the risk of getting UC is about the same for men and women until age 45. After this age, women had a 13% to 32% smaller chance of being diagnosed with UC than men [17].

This study founded that there was a statistically significant link between the activity of UC and total bilirubin there was a big difference between newly identified cases and patients who were going through a relapse when they were compared pairwise. In contrast to our study, it was found that UC patients have much lower amounts of bilirubin in their blood than healthy controls. There is a negative relationship between bilirubin levels and the severity of the disease and levels of inflammatory markers in UC patients. It was found that even when CRP levels were low, blood bilirubin levels

dropped in people with active UC compared to those who were in remission [18].

There is also a statistically significant link between the severity of UC and the lymphocytic count, CRP, calprotectin, and Mayo score when looking at the relationship between the seriousness of UC and background and lab data of patients.

Like what we found, Horiuchi et al. [9] showed that the results of comparing each number of the partial Mayo score and CRP in people whose colonoscopies were normal and people who had active UC were the same. People who have active UC have much higher amounts of the partial Mayo score and CRP than people whose colonoscopies were normal.

This study discovered that a limit level of ≥18.5 mg/L of CRP had an 83.3% sensitivity, a 66.7% specificity, a 55.6% positive predictive value, an 88.9% negative predictive value, and an overall 72.2% accuracy for finding severe UC. The results we got today make it clear that a calprotectin level of 396 µg/g or higher in feces is the best way to diagnose serious ulcerative colitis. This level has a sensitivity of 75%, a specificity of 66.7%, a positive predictive value (PPV) of 52.9%, a negative predictive value (NPV) of 84.2%, and an overall accuracy of 69.4%.

Regarding the CRP cut-off of ≥12 mg/L, it had an 85% PPV, a sensitivity of 95%, and an accuracy of 82%. The suggested CRP ≥12 mg/L cut-off is a broad, sensitive, and useful choice to ESR for figuring out how bad UC is [19].

These results agreed with those of Horiuchi et al. [9], who said it is hard to tell if someone has ongoing UC without a colonoscopy and histology. 48% of the time, CRP wasn't very sensitive. The data show that the CRP level could not be used to tell if someone had active UC. However, it has been said that the amount of calprotectin in feces shows how inflamed the gastrointestinal system is. It has been said that the amount of calprotectin in feces is a good indicator of what is happening in the UC through endoscopy and histology.

Regarding Faecal calprotectin Suttichaimongkol et al.[20] showed that there were strong links between the Mayo score and other clinical factors. A calprotectin cutoff of 60 µg/g in feces has a sensitivity of 78% and a specificity of 97%, which means it can identify clinical remission.

D'Amico et al. [21] It was thought that feces calprotectin cut-off levels that showed disease activity in the body's tissues ranged from 72 to 250 µg/g and those that showed histologic resolution were between 40.5 and 200 µg/g. All of the studies that had high PPV, on the other hand, had low NPV, and the studies that had high NPV did not have enough PPV. There is a clear link between feces calprotectin levels and the histological state of UC patients, even though no feces calprotectin cut-off has been found yet that meets the needs of high PPV and NPV.

On the contrast, the diagnostic efficiency of Faecal calprotectin to predict mucosal inflammation in UC was found with sensitivity 93%, specificity 71%, PPV 91%, and NPV 81% using a cut-off 50 µg/g. [22].

The level of baseline LRG in mild cases of UC were 60.9 ± 7.6 and were 78.9 ± 18.3, 90.4 ± 15.1 µg/ml in moderate and severe cases respectively. After 6 months of treatment the levels of LRG were 41.0 ± 23.9, 44.9 ± 21.9 and 34.8 ± 17.4 in mild, moderate and severe cases respectively, within each group, there is significant decrease in LRG.

In order to tell the difference between severe UC and mild or moderate cases, the best estimate for baseline LRG was ≤67.4 µg/ml with area under curve 0.913 with sensitivity 91.7%, specificity 87.5%, PPV 78.6%, NPV 95.5% and overall accuracy 91.7% (p=0.002)

This was in accordance with Yoshimura et al. [8] who said that the AUC for LRG was 0.732 in the study of people with UC. The cutoff number for LRG is used to find clinical remission. (39.8µg/mL) had a sensitivity of 71.1% and a specificity of 67.9%. Yoshida et al. [23] said that the AUC for LRG in people with UC was 0.874. For LRG values, a good AUC was shown. There was a 16.3 µg/ml cut-off for LRG. Based on the work of Horiuchi et al. [9], LRG was able to find real cases of UC 96% of the time and 97% of the time. Based on these findings, LRG may be a useful and non-invasive serum biomarker for sorting people in a primary care setting who are thought to have UC. LRG may have clinical promise in the future to help find people with active UC more quickly.

Matsumoto & Mashima [24] found that LRG levels were linked to higher scores on the Ulcerative Colitis Endoscopic Index of Severity for all kinds of the disease. That level of LRG was needed for mucosal healing, and it worked 72% of the time and 66% of the time. The average delta value of LRG in people who had a return of UC was 5 µg/ml before and after the relapse.

Nakamura et al. [25] looked into ways to tell how UC patients will do in the future. They found that amounts of LRG were much higher during the clinically active phase than during the remission phase. LRG is not a reliable way to predict clinical relapse on its own, but it can help find people who are not likely to relapse when combined serum albumin or fecal immunochemical tests are used.

This study found that there was a statistically significant link between the intensity of UC and the LRG at the start of the study. There was a big difference between the two groups when it came to mild, moderate, and serious disease. Following up, there was a notable drop in LRG in all four groups.

Like what we found, Shimoyama et al. [26] showed that LRG had a strong connection with the seriousness of UC in both the clinic and the endoscope. When used to test for UC in a clinical setting, LRG was much more accurate than CRP. There was a big difference between how accurate LRG and CRP were in the endoscopic assessment of UC. However, fecal calprotectin was much less accurate.

Our findings agreed with those of Hayashi et al. [27], who found that LRG was a better measure for predicting endoscopic activity than CRP, leukocyte, neutrophil, platelet, or albumin. Also, there was a link between the serum LRG levels and the endoscopic action. Unlikely, Yasutomi et al. [28] showed that in UC patients, both fecal markers (calprotectin and FIT) were linked to endoscopic activity and were better at predicting mucosal healing than LRG.

Our latest results made it clear that there was a statistically significant link between the UC group's baseline LRG and their Mayo score. Yoshimura et al. [8] agreed with our findings; they said that LRG levels were strongly linked to CRP and blood albumin levels in UC. There is a statistical link between the LRG levels and the partial Mayo score. This suggested that LRG is a good way to measure how active the disease is in UC.

In line with what we found, Horiuchi et al. [9] compared the diagnostic accuracy of LRG for finding active UC to that of the partial Mayo score and CRP by looking at the ROC curves. The AUC for LRG was a lot bigger than those for the partial Mayo score and CRP. Findings like these show that LRG levels were better at detecting ongoing UC, even in people whose CRP levels were normal.

One of the good things about the study is that it is one of the most up-to-date ones to look into LRG levels in the blood and how

they relate to the seriousness and activity of the disease in UC patients. They were very picky about the cases they looked at, and their samples were carefully collected and kept.

Some problems with this study are that it only looked at 36 people, which is a small sample size, and it was only done in one center. To make our results more general, we need more studies with bigger samples and more than one center. Also, there haven't been enough similar studies done before to give us more information.

CONCLUSION

A blood biomarker called leucine-rich glycoprotein might be a good way to figure out how active the disease is in people with IBD. As a substitute to CRP and fecal calprotectin, it can be used to test for ulcerative colitis.

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