

DOI:10.38173/RST.2020.20.2.11:121-127

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Section: MEDICAL SCIENCES

Issue: 2(20)/2020

Received: 14 September 2020	Revised: 29 September 2020
Accepted: 3 October 2020	Available Online: 15 November 2020

Paper available online [HERE](#)

INFLAMMATORY BOWEL DISEASE AND SEROLOGIC MARKERS OF INFLAMMATION

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ABSTRACT:

INFLAMMATORY BOWEL DISEASES, CROHN DISEASE AND ULCERATIVE COLITIS, CAUSE CHRONIC INFLAMMATION OF THE DIGESTIVE TRACT, TRIGGERED BY A COMPLEX INTERACTION OF ENVIRONMENTAL FACTORS, IMMUNE, BACTERIAL, GENETIC FACTORS. MANY MARKERS HAVE BEEN STUDIED AS INDICATORS OF INTESTINAL INFLAMMATION. SERUM C - REACTIVE PROTEIN, ERYTHROCYTE SEDIMENTATION RATE, LEUKOCYTES, SERUM LYSOZYME ARE NON-INVASIVE, EASY TO REPRODUCE AND ACCESSIBLE BIOMARKERS OF INFLAMMATION IN IBD. THIS ARTICLE AIMS TO HIGHLIGHT THEIR ROLE IN EXPRESSING THE INTESTINAL INFLAMMATION, IN ESTABLISHING THE DEGREE OF DISEASE ACTIVITY, IN MONITORING THE DISEASE, IN PREDICTING RELAPSES AND IN MONITORING THE THERAPEUTIC RESPONSE.

KEYWORDS: INFLAMMATORY BOWEL DISEASE, C-REACTIVE PROTEIN, ERYTHROCYTE, SEDIMENTATION RATE, LEUKOCYTES, SERUM LYSOZYME

INTRODUCTION

Inflammatory bowel diseases, Crohn Disease (CD) and Ulcerative Colitis (UC), cause chronic inflammation of the digestive tract. With unknown etiology, they are triggered by a complex interaction between environmental, immune, bacterial, genetic factors. IBD evolves with periods of remission and exacerbation⁷.

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⁷ Gheorghe L., Gheorghe C. *Vademecum in gastroenterologie*. Editura Nemira. Bucuresti. 2002; Bamias G. et al New Concepts in the Pathophysiology of Inflammatory Bowel Disease. *Annals of Internal*

The incidence and prevalence of IBD are increasing. IBD has become a real health problem, which involve high costs, so they are closely studied for a good understanding of pathophysiology⁸

IBD diagnosis include clinical, laboratory, endoscopic, histopatologic and imaging findings, and some of them are invasive and not accepted by all patients⁹.

Numerous laboratory markers have been studied in IBD for their role in diagnosing the disease, determining the severity of the disease, establishing the differential diagnosis, monitoring the therapeutic effect and evaluating the risk of complications.

We performed a study that included 63 patients with IBD and control, analysed CRP, ESR, leukocytes, lysozyme, and made multiple correlations.

In this article we present our observations on inflammatory markers in IBD.

Biomarkers are laboratory tests, that must be characterised by sensitivity and specificity, low or none invasiveness, easy to perform, reproductibility and inexpensiveness.

Some of the most common markers used to demonstrate inflammation in IBD, and analysed in this paper, are CRP, ESR, leukocytes, serum lysozyme¹⁰

They are a non-invasive way to demonstrate inflammation¹¹.

MAIN TEXT

Our study included 63 patients admitted in Fundeni Clinical Institute - Gastroenterology Clinic: IBD group A ,with 36 patients with CD and UC, and control group B, with 27 patients without IBD.

All patients agreed to participate in the study and signed the informed consent.

For the study, we collected blood samples from patients, and analysed CRP, ESR, leukocytes and serum lysozyme.

Measurement of serum lysozyme was realised using turbidimetric method, based on lysozyme lytic activity on *Micrococcus lysodeikticus* cells¹².

To determine the enzymatic activity of lysozyme, we measured the decrease in absorbance at 450nm, and correlated with a calibration curve.

⁸ Yulan Y. et al. The epidemiology and risk factors of inflammatory bowel disease. *International Journal of Clinical and Experimental Medicine*. 8(12):22529-22542.2015; Feldman M. et al. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: pathophysiology, diagnosis, management. 10th Edition*. Saunders/Elsevier. 2016;

⁹The role of endoscopy in inflammatory bowel disease. *Guideline-American society for gastrointestinal endoscopy*. 2015;81:1101–1121

¹⁰ Barnes E. et al. New Biomarkers for Diagnosing Inflammatory Bowel Disease and Assessing Treatment Outcomes. *Inflammatory Bowel Diseases*. 22(12):2956-2965. Dec. 2016; Rogler G et al. Clinical Utility of Biomarkers in IBD. *Current Gastroenterology Reports*. 2015 Jul;17(7):26;

¹¹ Radziejewska C et al. Properties and application of egg white lysozyme and its modified preparations - a review [2008]. *Food and agriculture organisation of the united nations*. Vol. 58. Issue 1. pages 5-10;

¹² Nugent F. et al. Serum lysozyme in inflammatory bowel disease. *Gastroenterology* Vol. 70:1014-1016, 1976;

In the study we analysed leukocytes in both groups. In group A it is observed that 36% of patients have leukocytosis, 64% of patients have normal leukocyte levels (Figure 1). In group B it is observed that 99% of patients have a normal level of leukocytes, only one patient having a mild leukocytosis (Figure 2). Patients with IBD have a higher level of leukocytes compared to the control group (Figure 3)

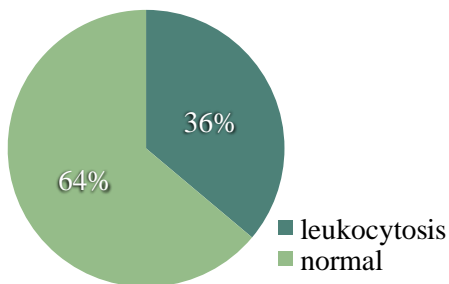


Figure 1. Percentage distribution group A

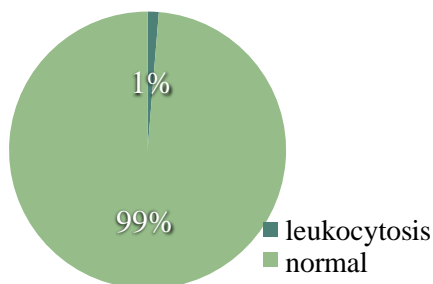


Figure 2. Percentage distribution group B

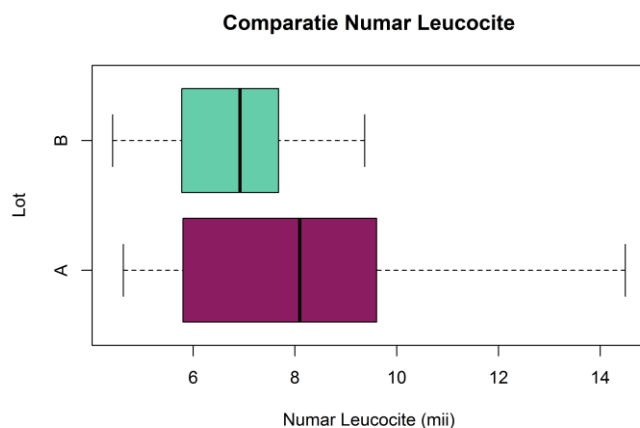


Figure 3. Comparison leukocytes

From a percentage point of view, leukocytosis in patients with CD was in proportion of 48%, and in patients with UC of 20%. In Figure 4 it is presented the leukocyte histogram in group A and B.

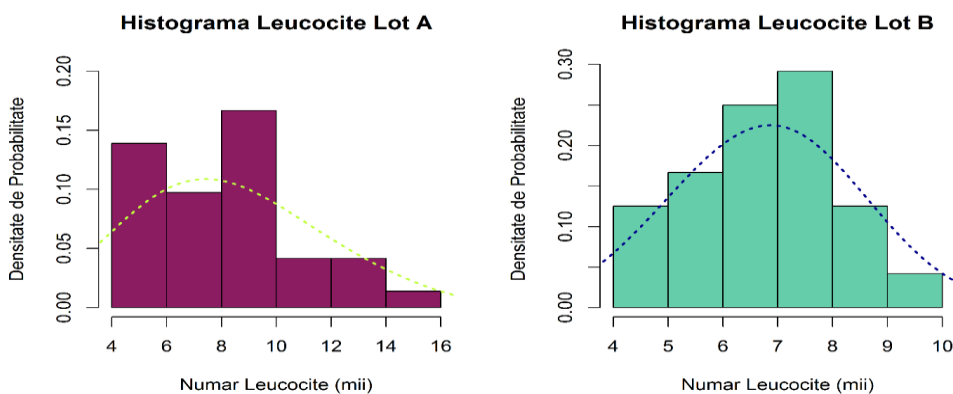


Figure 4. Leukocytes histogram in group A and B

We correlated leukocytes with serum lysozyme and no associations of statistical significance were observed ($p > 0.05$).

In Table 1 the Pearson r index (p value) of leukocytes, of -0.06 and the linear regression coefficient of -0.49 are highlighted.

Dependent variable	r Pearson (p value)	Linear regression coefficient(p value)	IC95% Coeficent
Leucocite	-0.06 (0.6862)	-0.49 (0.6860)	-2.86 la 1.88

Table 1. Leukocyte - lysozyme correlation

In Table 2 we present the values of lysozyme, higher in group A ,with IBD patients, vs. group B.

In the obtained data, it is observed that serum lysozyme has higher values in patients with BC, than in those with UC(Table 3, Figure 5).

Lysozyme	Group A	Group B	Lysozyme	CD (N = 21)	UC (N = 15)
Mean ± D.S	1.36 ± 0.38	1.17 ± 0.37	Medie ± D.S	1.41 ± 0.46	1.28 ± 0.24
Mediana (IQR)	1.31 (0.36)	1.09 (0.35)	Mediana (IQR)	1.34 (0.46)	1.29 (0.33)
Min la Max	0.78 la 2.73	0.12 la 2.15	Min la Max	0.78 la 2.73	0.83 la 1.83
Skewness	1.29	0.24			

Table 2. Serum lysozyme in study groups

Table 3. Lysozyme and CD/UC

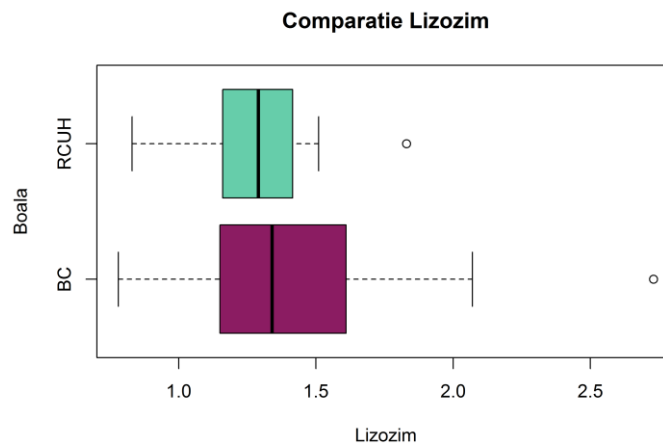


Figure 5. Comparison lysozyme in CD vs. UC

The performed analyses, according to the Montreal Classification, show that in pancolonic UC, the lysozyme has the highest value, followed by the colonic and rectal UC (Figure 6).

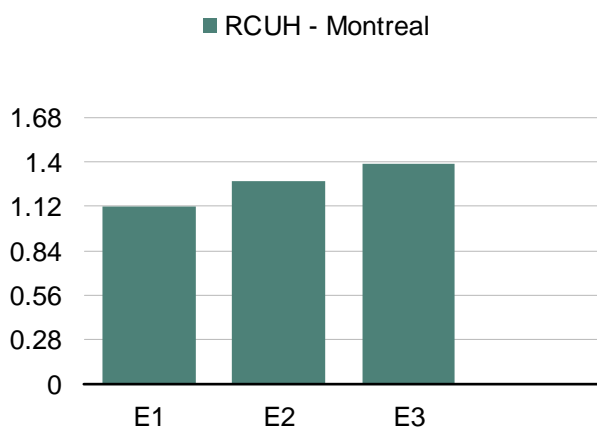


Figure 6. Lysozyme in UC - Montreal Classification

We correlated serum lysozyme and CRP in IBD group, and we observed that mean value for CRP for CD patients was 21,6, and for UC patients was 9,29 . CRP and serum lysozyme are directly proportional, but no statistical correlation was identified (Figure 7).

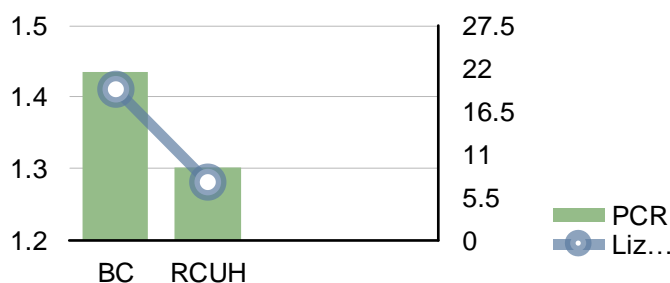


Figure 7. Relationship between serum lysozyme and CRP

We observe a relationship between ESR and serum lysozyme, with statistical value, observed in Table 4.

Dependent variable	r Pearson (p value)	Linear regression coefficient (p value)	IC95% Coefficient
VSH	0.46 (0.0386)	29.51 (0.0386)	3.58 la 55.43

Table 4. Relationship between ESR and serum lysozyme

CONCLUSION

CRP, ESR are among the best studied noninvasive biomarkers of inflammation in IBD. They are extremely valuable, accurate and inexpensive measures of intestinal inflammation, and provide informations to the clinician so that the patient receives the best treatment strategy.

The data obtained in our study show that patients with IBD have higher values of serum lysozyme, than the control group, and are in accordance with the literature. Also CD patients have higher values of lysozyme than UC patients.

Patients with IBD, compared to the control group, have leukocytosis.

We observed a direct proportionality relationship between ESR, CRP and serum lysozyme, therefore patients with elevated ESR and CRP values also have elevated serum lysozyme values. This highlights the role of lysozyme in inflammatory processes.

Serum lysozyme showed increased activity in patients with CD and UC, and correlates with parameters showing the disease, prone to complications.

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