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Evaluation of diagnostic accuracy of C-Reactive protein as a biomarker of spontaneous bacterial peritonitis in patients having decompensated chronic liver disease.

Kapeel Raja[1], Rizwan Saeed Kiyani[2], Sadia Rehman[3], Abdul Rashid[4], Sanjay Kumar[5], Anila Bibi[6]

1. MBBS, FCPS (Gastroentrology) Assistant Professor Gastroenterology Pir Abdul Qadir Shah Jilani Institute of Medical Sciences Gambat.
2. MBBS, FCPS (Gastroentrology) Senior Registrar Gastroenterology Poonch Medical College Rawalakot Azad Kashmir.
3. MBBS, M.Phil (Biochemistry) Assistant Professor Biochemistry Bahria University Medical and Dental College.
4. MBBS, FCPS (Internal Medicine) Assistant Professor Medicine Ghulam Mohammad Mahar Medical College Sukhur.
5. MBBS, FCPS (Gastroentrology) Senior Registrar Medicine and Allied Bahria University Medical and Dental College.
6. MBBS, M.Phil (Biochemistry) Senior Lecturer Biochemistry Jinnah Sindh Medical University, Karachi Pakistan.

Correspondence Address:
Dr. Sadia Rehman
Department of Biochemistry
Bahria University Medical and Dental College.
dr.sadia89@hotmail.com

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ABSTRACT… Objective: The objective of this study was to evaluate the diagnostic accuracy of C Reactive Protein (CRP) in diagnosing spontaneous bacterial peritonitis (SBP) in patients with decompensated chronic liver disease. **Study Design:** Cross Sectional study. **Setting:** Department of Medicine Sheikh Khalifa Bin Zayed Hospital Rawalakot Azad Kashmir. **Period:** Feb 2018 to Dec 2018. **Material & Methods:** One hundred subjects with decompensated liver disease were recruited in this study after fulfilling inclusion criteria. The patients' medical record number, age and gender was recorded upon admission. Baseline investigations including complete blood count, urine examination and chest X ray were done. Abdominal ultrasound was performed for detecting the presence of ascitic fluid. SBP was diagnosed if > 250 mm^3 neutrophils are detected in the ascitic fluid. Serum CRP was detected and reported in mg/L. **Results:** SBP was detected in 32.8% of the patients having decompensated chronic liver disease. CRP levels were > 29.5mg/L in 36% of the patients while in 64% patients the CRP levels were < 29.5mg/L. The sensitivity of CRP for the diagnosis of SBP was calculated as 83.61% while the specificity was calculated as 87.2%. A positive predictive value was estimated as 76.12% and a negative predictive value was 91.59% while the diagnostic accuracy was calculated as 86.02% from the given data. **Conclusion:** CRP is a reliable diagnostic biomarker for spontaneous bacterial peritonitis in subjects having complications of chronic liver disease.

Key words: CRP, Chronic Liver Disease, SBP.

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INTRODUCTION

Ascitic fluid infection (AFI) is the most commonly occurring complication in patients having decompensated liver disease.[1] AFI acts as a trigger for the development of other complications of cirrhotic liver disease which include variceal bleeding, hepatic encephalopathy and hepatorenal syndrome. AFI is of two type's culture-negative neutrocytic ascites (CNNA) and spontaneous bacterial peritonitis.[2] The in-hospital mortality rate is much higher in SBP patients than those with culture-negative neutrocytic ascites. Prompt detection and early initiation of antibiotic therapy are crucial for the better outcome of treatment in patients with SBP.[3] Early stage of SBP is difficult to detect. Culture examination of ascitic fluid takes 24-48 hours which causes a delay in the diagnosis and initiation of treatment.[4] Hence, for the early diagnosis of SBP the evaluation of clinical and laboratory parameters are of great clinical importance. SBP is an ascitic fluid infection without any surgically treatable intra-abdominal cause. SBP is diagnosed by a positive bacterial culture of the ascitic fluid and an elevated ascitic fluid polymorphonuclear leukocyte (PMN) count (≥250 cells/mm3).[5] Elevated ascitic fluid PMN count is enough to make a preliminary diagnosis of SBP and put the patient on antibiotic therapy.[6] If the paracentesis is performed after initiation of the antibiotic therapy, then the culture mostly gives negative result.[7]

An accurate diagnosis of cause is essential for successful treatment of ascites. Liver cirrhosis is the cause of approximately 80 percent of the cases of ascities in the United States. The patients

having ascities due to liver disorder usually give a good response to sodium restriction and diuretics.[8]

C-Reactive protein is an acute phase inflammatory protein present in the serum.[9] CRP is produced by liver and vascular endothelial cells.[10] Elevated levels of CRP indicates the ongoing inflammatory process, and the absence of a high CRP level indicates the exclusion of infection or inflammation. CRP may also be used as an assessment biomarker of inflammatory changes in response to treatment.[11,12]

Traditionally, suspected intra-peritoneal bacterial infections in patients with decompensated chronic liver disease were evaluated by evaluation of the ascitic fluid. Neutrophils count was taken as > 250 cells/mm3 as the gold standard for the diagnosis of SBP.[13]

For immediate diagnosis of the presence of ascitic fluid infections in decompensated liver disease patients, reliable biomarkers are necessary. The biomarkers like CRP and pro-calcitonin are helpful in the diagnosis of SBP.[14] Diagnosis at an early stage and early initiation of treatment are essential for good prognosis of SBP. The first stage of the disease is difficult to determine in cases of bacterial infection.[15,16] Hence the evaluation of these biomarkers is of great clinical importance.

We planned this study to evaluate the role CRP in the detection of SBP in patients having decompensated chronic liver disease. This study will help the gastroenterologists in the identification of early diagnostic biomarkers of this disease and hence improve the treatment outcome of these patients.

MATERIAL & METHODS

This study was a cross sectional study which was conducted from 01-02-2018 to 20-12-2018 at Department of Medicine Sheikh Khalifa Bin Zayed Hospital Rawalakot Azad Kashmir.

With the help of WHO calculator a sample size of 186 subjects was calculated.

Consecutive Non probability sampling technique was used. Inclusion criteria was adult patients (age >18 to <75 years) presenting with decompensated chronic liver disease. Exclusion criteria was Decompensated chronic liver disease patients with absence of ascites as determined by an abdominal ultrasound and evidence of infection from other sources as evident by urine and stool routine examination, chest x-ray or obvious source of skin infection.

This study was approved by the ethical review board (PMC-RKT/520/2019). Confidentiality of the patients was ensured. SPSS (version 21) was used to enter and analyze the data. Mean ± standard deviation (SD) of the quantitative variables were calculated. For qualitative variables frequencies and percentages were calculated.

The objective of the present research was to determine the diagnostic accuracy of CRP for evaluation of SBP in patients with decompensated chronic liver disease keeping asicitic fluid neutrophilic count more than 250/mm^3 as a gold standard.

RESULTS

In this regard we collected data from one hundred and eighty six (186) patients having decompensated chronic liver disease. The minimum age was found as 21 years and maximum age was 75 years with mean + standard deviation 43.36 + 13.68 years. The minimum neutrophil count in ascitic fluid was found as 45 /mm^3 and maximum neutrophil count was 255/mm^3 with mean + standard deviation 794.60 + 1032.53 /mm^3. The minimum CRP level was found as 5 mg/L and maximum CRP level was 160 mg/L with mean + standard deviation 52.42 + 60.66 mg/L. There were 104 (55.59%) male patients and 82 (44.41%) female patients. Spontaneous bacterial peritonitis was present in 61 (32.8%) patients of decompensated chronic liver disease and 125 (67.2%) patients were without spontaneous bacterial peritonitis. There were 67 (36%) patients in which CRP levels was greater than 29.5mg/L and there were 119 (64%) patients in which CRP levels was less than 29.5mg/L.

For evaluation of diagnostic accuracy of CRP in SBP in patients with chronic liver disease, we calculated sensitivity, specificity, positive predictive value and negative predictive value. The sensitivity was calculated as 83.61%, specificity was calculated as 87.2%, positive predictive value was 76.12%, negative predictive value was 91.59% and diagnostic accuracy was observed from the collected data as 86.02%.

Sensitivity, specificity, Positive predictive value (PPV) and Negative prediction value (NPV) were calculated according to the following Table-I.

	SBP Present	SBP Absent
CRP levels ≥ 29.5mg/L	a (TP)	b (FP)
CRP levels <29.5mg/L	c (FN)	d (TN)

Table-I. Diagnostic accuracy of CRP for evaluation of SBP.

CRP: C-reactive protein; SBP: Spontaneous Bacterial Peritonitis

TP: True positive
TN: True negative
FP: False positive
FN: False negative
Sensitivity: a/a+c x 100
Specificity: d/b+d x 100
PPV: b/a+b x 100
NPV: d/c+d x 100
DA: a+d / a+b+c+d x 100

	Minimum	Maximum	Mean	Std. Deviation
Age	20	75	43.36	13.68
Neutrophil Count in ascitic fluid	45	2550	794.60	1032.53
CRP Level	5	160	52.42	60.66

Table-II. Descriptive statistics.

	Frequency	Percentage
Yes	67	36%
No	119	64%
Total	186	100.0

Table-III. Frequency and percentage of CRP Level > 29.5mg/L.

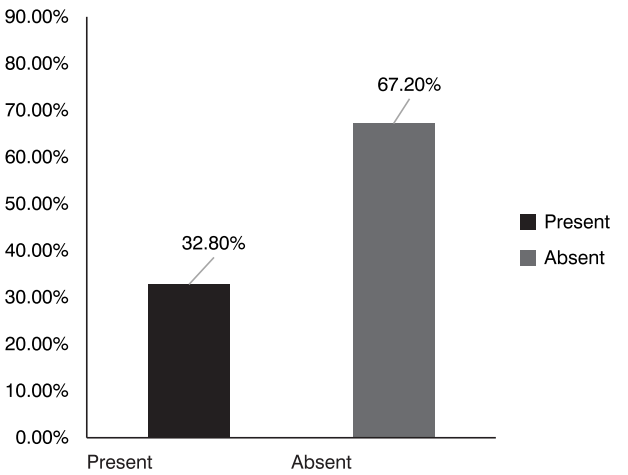

Figure-1. Bar Chart of presence of SBP.

		Spontaneous Bacterial Peritonitis		Total
		Present	Absent	
CRP Level > 29.5mg/L	Yes	51	16	67
	No	10	109	119
Total		61	125	186

Table-IV. 2x2 table of CRP Levels > 29.5mg/L and SBP.

Sensitivity: $\frac{a}{a+c} \times 100 = 83.61\%$

Specificity: $\frac{d}{d+b} \times 100 = 87.2\%$

Positive Predictive Value: $\frac{a}{a+b} \times 100 = 76.12\%$

Negative Predictive Value: $\frac{d}{d+c} \times 100 = 91.59\ \%$

Diagnostic Accuracy: $\frac{a+d}{a+b+c+d} \times 100 = 86.02\%$

DISCUSSION

We collected data from one hundred and eighty six patient having decompensated chronic liver disease. In 186 patients, the age of the patients was between 20 years and 75 years. There were 55.59% male and 44.41% female subjects suffering from chronic liver disease. The minimum neutrophil count found in the ascitic fluid was found as 45 /mm^3 and the maximum neutrophil count was 2550/mm^3 with mean + standard deviation 794.60 + 1032.53 /mm^3. The minimum level of CRP in our study subjects was found as 5 mg/L and the maximum level was 160 mg/L with mean + standard deviation 52.42 + 60.66 mg/L.

Deutsch et al[17] in their article have discussed the characteristics of bacterial infections in cirrhotic liver disease patients and the role of CRP. Their results are similar to the findings of our study. In our study SBP was detected among 32.8% subjects of decompensated chronic liver disease while 67.2% of the study subjects were without SBP. In 36% subjects CRP level was found to be >29.5mg/L and in 64% subjects CRP level was < 29.5mg/L.

According to our study the sensitivity of CRP in diagnosing SBP was calculated as 83.61% while the specificity of CRP was calculated as 87.2%. The positive predictive value was 76.12% while the negative predictive value was 91.59%. The diagnostic accuracy of CRP as calculated from the collected data was 86.02%. Ashour et al[18] and Khedher et al[19] in their studies have also shown that CRP is a good diagnostic and prognostic biomarker in cases of SBP in cirrhotic liver disease.

Lazzarotto et al[20] showed that CRP level of ≥ 29.5mg/L is 81% accurate for diagnosis of SBP in patients presenting with acute decompensated chronic liver disease with a sensitivity and specificity of 82%. The results from our study and those from previous studies shown that CRP has a good diagnostic and prognostic accuracy in detecting SBP in patients suffering from chronic liver disease.

CONCLUSION

A CRP level of ≥ 29.5mg/L gave 86.02% accuracy for the diagnosis of spontaneous bacterial peritonitis in patients presenting with decompensated chronic liver disease. So CRP is reliable for the diagnosis of bacterial infections in ascitic patients having chronic liver disease.

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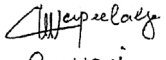
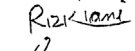
AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Kapeel Raja	Main researcher.	
2	Rizwan Saeed Kiyani	Data collection and final approval.	
3	Sadia Rehman	Literature review and write up.	
4	Abdul Rashid	Data analysis.	
5	Sanjay Kumar	Drafting of work.	
6	Anila Bibi	Data collection.