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Original Research Article

Evaluation of C Reactive Protein Levels in Spontaneous Bacterial Peritonitis in Patients with Decompensated Chronic Liver Disease

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Abstract

The objective of the study was to determine the diagnostic accuracy of CRP for evaluation of spontaneous bacterial peritonitis in patients with decompensated chronic liver disease keeping ascitic fluid neutrophilic count more than 250/mm^3 as a gold standard. This cross section validation study was conducted from 01-02-2014 to 20-12-2014 at Department of Medicine Shifa International Hospital, Islamabad, Pakistan. One hundred and eighty six cases were included in this study after fulfilling the inclusion criteria. Patients' medical record number (MR), age and gender were recorded upon admission. Baseline investigations including complete blood count, urine RE and chest X-ray were done. An abdominal ultrasound was done to confirm the presence of ascites. Diagnostic abdominal paracentesis was done with 24 gauge needle. A diagnosis of spontaneous bacterial peritonitis was made and documented if>250 mm^3 neutrophils are found in 1scetic fluid. A serum sample was drawn for CRP and the results were reported in mg/L. The minimum neutrophil count in 1scetic fluid was found as 45/mm^3 and maximum neutrophil count in 1scetic fluid was 2550/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. Spontaneous bacterial peritonitis was present in 32.8% patients of decompensated chronic liver disease and 67.2% patients were without spontaneous bacterial peritonitis. There were 36% patients in which CRP levels was greater than 29.5mg/L and there were 64% patients in which CRP levels was less than 29.5mg/L. 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%.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 bacterial infection in subjects admitted due to complications of chronic liver disease.

Keywords: Chronic Liver Disease, CRP Level, Spontaneous Bacterial Peritonitis

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is defined as an 1scetic fluid infection without an evident intra-abdominal surgically-treatable source; it primarily occurs in patients with advanced cirrhosis (Abbas et al., 2007). The diagnosis is established by a positive 1scetic fluid bacterial culture and an elevated 1scetic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3). An elevated 1scetic fluid absolute polymorphonuclear leukocyte (PMN) count (≥250 cells/mm^3) is adequate to make a presumptive diagnosis

of SBP and to start empiric therapy (Alam et al., 2005). Too often the paracentesis is performed after antibiotics are initiated and/or inadequate culture technique is used. In these situations, culture is regularly negative (Bosetti et al., 2002).

Successful treatment of ascites depends upon an accurate diagnosis of its cause. (Campello et al., 2002).The most common cause in the United States is cirrhosis, which accounts for approximately 80 percent of cases (Bell et al., 2008). Ascites is the most common complication of cirrhosis (Thomson et al., 2008). Such patients usually respond to diuretics and sodium restriction in contrast to those with some other causes of ascites (such as peritoneal carcinomatosis) in whom sodium restriction and diuretics usually cause intravascular volume depletion without loss of 2scetic fluid (Ribes et al., 2008).

CRP - an acute phase serum protein – is a surrogate for the pro-inflammatory interleukin IL-6 (Sagnelli et al., 2005; Simonato et al., 2008). It is a member of pentraxin family of proteins and is synthesized by liver.(Raza et al., 2007) CRP is also produced by cells in the vascular wall such as endothelial cells, smooth muscle cells, and also by adipose tissue.(Campello et al., 2002; Donato et al., 2006). A significant rise in CRP indicates clinically relevant inflammation, and in contrast, the absence of a high CRP helps in exclusion of infection/inflammation (Lonati et al., 2008; Liao et al., 2011). Sequential CRP may provide a more accurate assessment of inflammatory changes in response to treatment. CRP is very helpful in assigning a non-inflammatory cause to a markedly abnormal ESR. As for instance, in a patient with a monoclonal protein without any evidence of infection, ESR may be high (in 100) but CRP will be normal (Fleming et al., 2008; Guadagnino et al., 1997).

CRP rises rapidly reaching a peak in 2 days during an acute phase reaction. CRP decreases rapidly with the resolution of the acute phase response (with a half-life of 18 hours). High CRP level does not have diagnostic specificity as a large number of clinical conditions increase CRP (Jepsen et al., 2008; Mumtaz et al., 2010). CRP more than 10 mg/L indicates clinically significant inflammation. Therefore, monitoring CRP levels may provide useful information on the diseases activity such as flare up of rheumatoid arthritis and giant cell arteritis (Raza et al., 2007). Decompensated chronic liver disease is a common complaint among patients presenting to the emergency department. One of the most important complications of decompensated chronic liver disease is spontaneous bacterial peritonitis, which is common and associated with a high risk of morbidity and mortality (Mühlberger et al., 2009).

Traditionally, ascitic fluid evaluation has been used for evaluating suspected intra-peritoneal bacterial infection in patients with decompensated chronic liver disease. By considering a neutrophils count > 250 cells/mm3 determined by the manual method as the “gold standard” for the SBP diagnosis, the automated blood cell count had a sensitivity of 100% and a specificity of 97.7%, whereas positive and negative predictive values were 94.1% and 100%, respectively (Ribes et al., 2008; Sagnelli et al., 2005)

Simple and reliable laboratory parameters are necessary for immediate diagnosis of infections in decompensated chronic liver disease patients. Recently, serum inflammatory biomarkers such as CRP and pro-calcitonin (PCT) have been shown to improve clinician accuracy for the diagnosis of spontaneous bacterial peritonitis with important prognostic and therapeutic implications (Simonato et al., 2008).

Early diagnosis and prompt initiation of antibiotic therapy have been considered to be crucial for the treatment of SBP (Lonati et al., 2008). However, it is difficult to determine the early stage of SBP in the detection of bacterial infection. Ascitic fluid culture examination is time consuming (24-48h) which delays the diagnosis and treatment. Therefore, the identification of clinical and laboratory parameters for the early diagnosis of SBP would be of special interest.

To aim of this study was to determine the diagnostic accuracy of CRP for evaluation of spontaneous bacterial peritonitis in patients with decompensated chronic liver disease keeping ascitic fluid neutrophilic count more than 250/mm^3 as a gold standard. This study will help gastroenterologists in early detection and prevention of spontaneous bacterial peritonitis in patients suffering from chronic liver disease and hence improve the morbidity and mortality of these patients.

MATERIALS AND METHODS

It was a cross-sectional validation study and was conducted in the Department of Accident and Emergency and the Department of Gastroenterology, Shifa International Hospital, Islamabad from 01-02-2014 to 20-12-2014.

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

Reference study

Mumtaz et al. (2010) precipitating factors and the outcome of hepatic encephalopathy in liver cirrhosis. J Coll Physicians Surg Pak 2010; 20:514.

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.

Ethical permission for the present study was taken from ethical review board. Data which were obtained during the study was kept confidential.

SPSS (version 21) was used to enter and analyze the data. Mean ± standard deviation (SD) was calculated for quantitative variable like age and CRP levels. Frequencies and percentages were calculated for qualitative variables like gender, presence or absence of spontaneous bacterial peritonitis (on the basis of ascitic fluid findings).

RESULTS

We collected data from 186 patients having decompensated chronic liver disease. The minimum age was found as 20 years and maximum age was 75 years having 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 in ascitic fluid was 2550/mm^3 with mean±SD794.60±1032.53 /mm^3. The minimum CRP level was found as 5 mg/L and maximum CRP level was 160 mg/L with mean±SD52.42±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 (Table 3)

For the sake of diagnostic accuracy of CRP for evaluation of spontaneous bacterial peritonitis in patients with decompensated 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.

DISCUSSION

We collected data from one hundred and eighty six patients having decompensated chronic liver disease. From 186 patients, the minimum age was found as 20 years and maximum age was 75 years having mean±SD 43.36 ± 13.68 years. The minimum neutrophil count in ascitic fluid was found as 45 /mm^3 and maximum neutrophil count in ascitic fluid was 2550/mm^3 with mean±SD 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 +SD 52.42 + 60.66 mg/L. Danish FA, et al. (2010) expressed that the final sustained virological response rates attained in the patients are relatively low, successful antiviral therapy is potentially lifesaving which explains the need to go for it. In their article, the pros and cons of antiviral therapy in decompensated liver cirrhosis are reviewed with special emphasis on how to avoid antiviral dose reductions/withdrawals secondary to the development of hematologic side effects by using hematopoietic growth factors. In the present research, there were 55.59% male patients and 44.41% female patients. Spontaneous bacterial peritonitis was present in 32.8% patients of decompensated chronic liver disease and 67.2% patients were without spontaneous bacterial peritonitis. There were 36% patients in which CRP levels was greater than 29.5mg/L and there were 64% patients in which CRP levels was less than 29.5mg/L. Significantly higher median CRP levels were observed among infected patients ($p < 0.001$). The AUROC of CRP for the diagnosis of infection were 0.835 ± 0.052 and 0.860 ± 0.047, respectively ($p= 0.273$). CRP levels > 29.5 exhibited sensitivity of 82% and specificity of 81% for the diagnosis of bacterial infection. Similarly, PCT levels > 1.10 showed sensitivity of 67% and specificity of 90%. Significantly higher levels of CRP ($P = 0.026$) and PCT ($P = 0.001$) were observed among those who died within three months after admission. It was concluded that CRP and PCT were reliable markers of bacterial infection in subjects admitted due to complications of liver cirrhosis and higher levels of these tests are related to short-term mortality in those patients. These findings are similar to the findings of Lazzarotto et al. (2013).

For the sake of diagnostic accuracy of CRP for evaluation of spontaneous bacterial peritonitis in patients with decompensated 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%.

Lazzarotto et al. (2013) showed that CRP level of ≥ 29.5mg/L is 81% accurate for diagnosis of spontaneous bacterial peritonitis in patients presenting with acute decompensated chronic liver disease. The corresponding sensitivity and specificity are 82% and 81% respectively. A CRP level of < 29.5mg/L has a negative predictive value was 92% for ruling out spontaneous bacterial peritonitis. This data was calculated assuming a spontaneous bacterial peritonitis prevalence of 41.7 %.In contrast to this Papp et al., (2011) demonstrated that the accuracy of CRP for identifying patients with infection decreased in advanced liver disease. In a case-control study (n=30 infected vs. 30 non infected patients), despite the increased basal CRP concentrations in patients with advanced liver dysfunction, the more severe

Table 1. Diagnostic Accuracy of CRP for Evaluation of SBP

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

CRP: C-reactive protein; SBP: Spontaneous Bacterial Peritonitis; TP: True positive; TN: True negative; FP: False positive; FN: False negatives
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

Table 2. Demographic and descriptive variables

	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

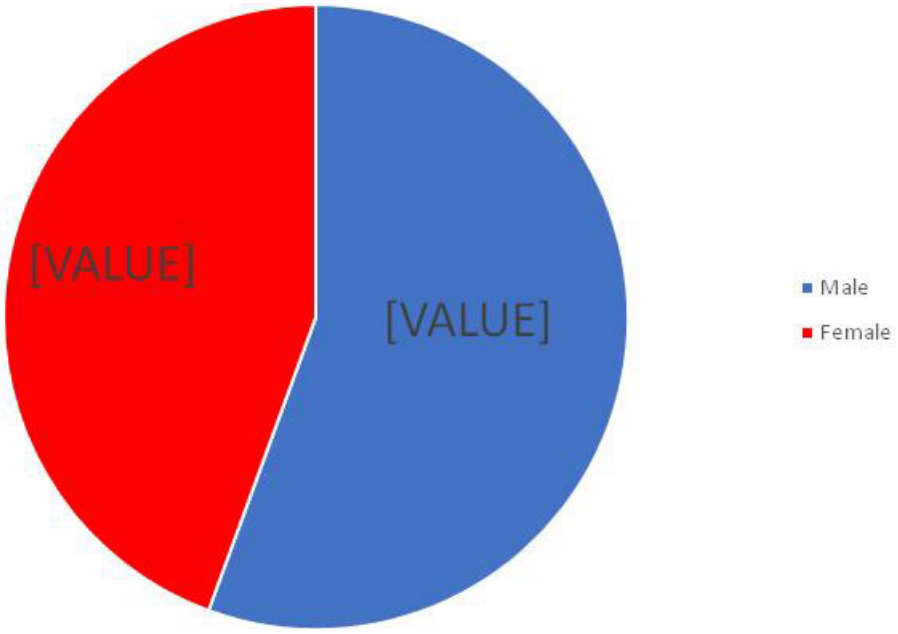

Figure 1. Pie Chart of Gender

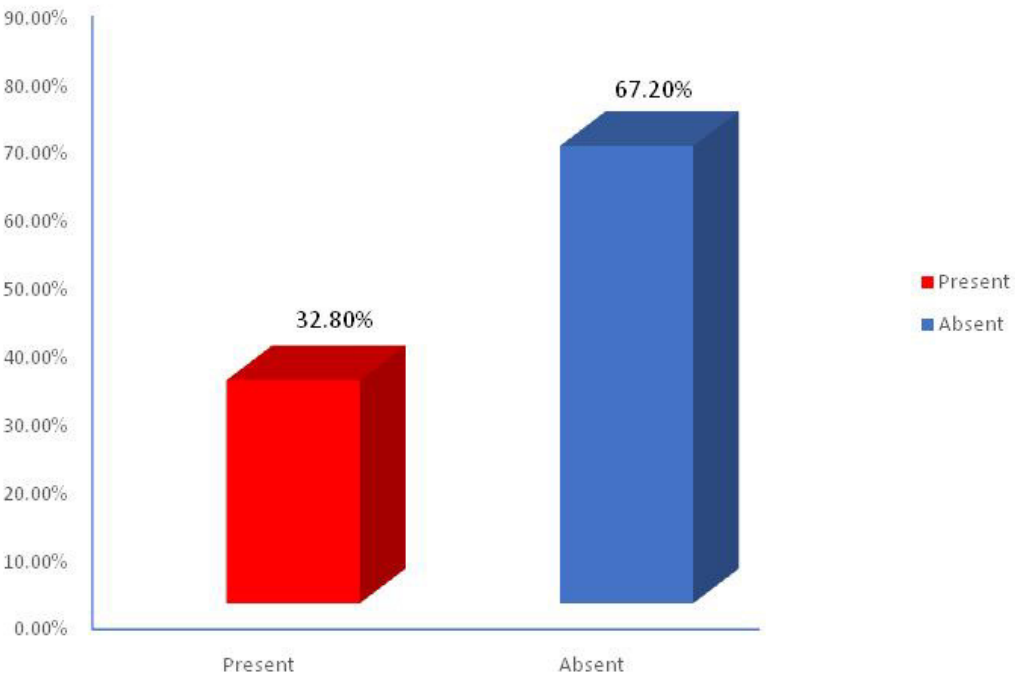

Figure 2. Bar Chart of Presence of SBP

Table 3. Frequency and Percentage of CRP Level ≥ 29.5mg/L

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

Table 4. 2x2 table of CRP Levels ≥ 29.5mg/L and SBP

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

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

the underlying liver dysfunction, the lower the CRP response to bacteremia (Park et al., 2005).

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 bacterial infection in subjects admitted due to complications of chronic liver disease.

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