

*Research Article***Validity of c-reactive protein and procalcitonin in prediction of bacterial infection in patients with liver cirrhosis****Enas M. Kamal, Mohamed A. Abd EL-Hakeem, Amr M. El Sayed, and Marwa Mostafa Ahmed**

Department of Tropical, Faculty of medicine, Minia University.

**Abstract**

**Introduction:** Cirrhosis is the end-stage of most liver diseases. Patients with cirrhosis are at high risk of developing bacterial infections, sepsis and sepsis-related death<sup>(1)</sup>. **Aim of the study:** Our aim is to evaluate the role of CRP and procalcitonin as a diagnostic tool for detection bacterial infection in a hospitalized patients with cirrhosis. **Patients & Methods:** This study was conducted in Tropical medicine department -Minia University Hospitals, from May to October 2018. 90 patients were included in the analysis. Forty two patients presented clinically with infection (Group 1), while 48 patients clinically non infectious (Group 2). **Results:** Ninety consecutive hospitalized patients with liver cirrhosis of different etiologies were included in the study. Forty two patients (61.9% male, age 61.8±11.2 years) had documented bacterial infection at admission or during the first 3 days of admission (Group 1) and 48(66.7% male, age 58.9±8.2 years) were hospitalized for other reasons (Group 2). **Conclusion:** CRP and procalcitonin are good inflammatory markers; CRP is more sensitive than procalcitonin in detection bacterial infection but both are specific in detection bacterial infection in patients with advanced chronic liver disease.

**Keywords:** c-reactive protein, procalcitonin, bacterial infection**Introduction**

Cirrhosis is the end-stage of most liver diseases. Patients with cirrhosis are at high risk of developing bacterial infections, sepsis and sepsis-related death<sup>(2)</sup>. There is evidence that about one third of cirrhotic patients present with infection at hospital admission or develop infection during hospitalization<sup>(3)</sup>. However, the diagnosis of bacterial infection in cirrhotic is often difficult, since these patients usually present with signs of unspecific clinical deterioration and not the classical clinical characteristics of systemic inflammation, such as fever and raised white blood cell (WBC) count. Therefore the diagnosis of bacterial infection and sepsis in patients with cirrhosis remains challenging<sup>(4)</sup>.

C-reactive protein (CRP) is an acute-phase protein that serves as an early marker of inflammation or infection. The protein is synthesized in the liver and is normally found at concentrations of less than 10 mg/L in the blood. During infectious or inflammatory disease states, CRP levels rise rapidly within

the first 6 to 8 hours and peak at levels of up to 350–400 mg/L after 48 hours<sup>(5)</sup>.

Procalcitonin (PCT) is the prehormone of calcitonin, which is normally secreted by the C cells of the thyroid in response to hypercalcemia; under these normal conditions, negligible serum PCT concentrations are detected<sup>(6)</sup>. It is believed that PCT is produced by the liver and peripheral blood mononuclear cells, modulated by lipopolysaccharides and sepsis-related cytokines<sup>(7)</sup>.

**Aim of the study**

Our aim is to evaluate the role of CRP and procalcitonin as a diagnostic tool for detection bacterial infection in a hospitalized patients with cirrhosis.

**Patients & Methods**

This study was conducted in Tropical medicine department - Minia University Hospitals, from May to October 2018. A total of 200 consecutive cirrhotic patients who admitted to our department were included in this study.

One hundred ten patients were excluded from our analysis because they had either incomplete medical records, variceal bleeding at the time of admission, evidence of hepatocellular carcinoma or other solid tumors, were already being treated with antibiotics, or had non-cirrhotic portal hypertension; thus, 90 patients were included in the further analysis. Forty two patients presented clinically with infection (Group 1), while 48 patients clinically non infectious (Group 2).

**Inclusion criteria**

- Body temperature >/38 C
- New onset encephalopathy or worsening of pre onset encephalopathy by at least one grade according to West Heaven criteria.
- New onset ascites or hydrothorax or worsening of preexisting ascites or hydrothorax patient with past history of spontaneous bacterial peritonitis or with clinical manifestation suggestive of spontaneous bacterial peritonitis or documented to have spontaneous bacterial peritonitis by ascetic fluid analysis.
- Respiratory tract symptoms (cough, dyspnea, or tachypnea)
- Urinary tract symptoms (loin pain, dysuria, polyuria)
- Clinical evidence of pyodermatitis (cellulitis)

- Upper gastro intestinal bleeding (esophageal or gastric varices or portal hypertensive gastropathy)
- White blood cell count >/ 10,000 cumm
- Increase in creatinine by 50 % from the baseline or increase in bilirubin by 3 mg/dl from baseline

**Results**

Ninty consecutive hospitalized patients with liver cirrhosis of different etiologies were included in the study. Forty two patients (61.9% male, age 61.8±11.2years) had documented bacterial infection at admission or during the first 3 days of admission (Group 1) and 48(66.7% male, age 58.9±8.2 years) were hospitalized for other reasons (Group 2).

Blood culture was positive in 100% of patients in group 1, while positive in 6.3% of patients in group 2 (p=<0.001\*).

The mean CRP value in patients with bacterial infection was 21.1±23.2 mg/L, compared to 3.5±2.5mg/L in patients without bacterial infection (P<0.001) table 5 and figure 2. Also the mean procalcitonin level in patients with bacterial infection was335.3±88.9 compared to 295.1±63.2mg/L in patients without bacterial infection (P<0.017\*)

**Table: blood culture, CRP, procalcitonin in group 1 and group 2**

		Clinical Infection		P value
		Group 1	Group 2	
		N=42	N=48	
<b>Blood culture</b>	- Ve	0(0%)	45(93.8%)	<b>&lt;0.001*</b>
	+Ve	42(100%)	3(6.3%)	
<b>CRP</b>	<i>Range</i>	(1-135)	(.6-13.1)	<b>&lt;0.001*</b>
	<i>Mean ± SD</i>	21.1±23.2	3.5±2.5	
	<i>Median</i>	13.8	3.3	
<b>Procalcitonin</b>	<i>Range</i>	(241-491)	(191-491)	<b>0.017*</b>
	<i>Mean ± SD</i>	335.3±88.9	295.1±63.2	

## Discussion

Bacterial infections in patients with cirrhosis represent a major cause of hospitalization and a common reason for clinical deterioration or death. Immediate treatment initiation is required, but clear clinical and laboratory data supporting the diagnosis are lacking. Our study aimed to evaluate the characteristics of these patients to set a clinical context that could help improve clinicians' skills in detecting early bacterial infection in patients with liver CIRRHOSIS<sup>(8)</sup>.

Early detection of infection in these patients still remains a major challenge. Even though early institution of antimicrobial therapy may significantly reduce the morbidity and mortality, empirical treatment for all suspected patients is fraught with huge risk of antimicrobial resistance. Identification of a reliable marker which can identify the subjects with infection, early in the course will be extremely valuable in these patients<sup>(9)</sup>.

We performed study of collected data from 90 consecutive hospitalized cirrhotic patients. We compared clinical and laboratory parameters with obvious clinical infection (group 1) and without clinical infection (group 2). Regarding CRP The mean CRP in patients group 1 was  $21.1 \pm 23.2$  mg/L higher than group 2 ( $3.5 \pm 2$  mg/L) significantly.

Regarding **Procalcitonin** the mean value in patients with infection group 1 was ( $335.3 \pm 88.9$  pg/ml) significantly higher than without infection ( $295.1 \pm 63.2$  pg/mL) in group 2. Melanie Deutsch et al., 2017 who studied the role of CRP in detection of bacterial infection in liver cirrhosis) found that (The mean of WBC count was higher in group 1 clinical infection ( $7567.8 \pm 4241.5$  SD) than in group 2 clinical non infection ( $6121 \pm 2518$ ) and The mean CRP value in patients with cirrhosis and infection was  $34 \pm 38.8$  mg/L, compared to  $5.7 \pm 7.3$  mg/L in the group of patients who had cirrhosis without infection<sup>(10)</sup>.

## Conclusion

Patients with advanced chronic liver disease with higher meld score and child score especially B and C more are liable to have bacterial infection

CRP and procalcitonin are good inflammatory markers; CRP is more sensitive than procalcitonin in detection bacterial infection but both are specific in detection bacterial infection in patients with advanced chronic liver disease

Procalcitonin is more specific than CRP in patients with Chronic liver disease with higher meld score.

## Recommendation

CRP and Procalcitonin should be a routine investigations for patients with liver cirrhosis for early detection of bacterial infections and early administration of proper antibiotic to decrease mortality in patients with liver cirrhosis as infection is the most common cause of mortality.

## References

1. Borzio M, Salerno F, Piantoni L, et al., Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. *Dig Liver Dis* 2001; 33:41-48.
2. Borzio M, Salerno F, Piantoni L, et al., Bacterial infection in patients with advanced cirrhosis: a multicentre prospective study. *Dig Liver Dis* 2001; 33:41-48.
3. Fernández J, Navasa M, Gómez J, et al., Bacterial infections in cirrhosis: epidemiological changes with invasive procedures and norfloxacin prophylaxis. *Hepatology* 2002;35:140-148.
4. Pieri G, Agarwal B, Burroughs AK. C-reactive protein and bacterial infection in cirrhosis. *Ann Gastroenterol* 2014;27:113-120.
5. Kolb-Bachofen V. A review on the biological properties of C-reactive protein. *Immunobiology*. 1991;183:133-45.
6. Whicher J, Bienvenu J, Monneret G. Procalcitonin as an acute phase marker, *Ann Clin Biochem*, 2001, vol. 38 (pg. 483-93)
7. Nijsten MW, Olinga P, The TH, et al., Procalcitonin behaves as a fast responding acute phase protein in vivo and in vitro, *Crit Care Med*, 2000, vol. 28 (pg. 458-61)
8. Cervoni JP, Thévenot T, Weil D, et al., C-reactive protein predicts short-term mortality in patients with cirrhosis. *J Hepatol* 2012;56:1299-1304.

9. Papp M, Vitalis Z, Altorjay I, et al., Acute phase proteins in the diagnosis and prediction of cirrhosis associated bacterial infections. *Liver Int* 2012;32:603-611.
10. Melanie Deutsch, Spilios Manolakopoulos, Ioannis Andreadis, Markos Giannaris,

George Kontos, Hariklia Kranidioti, Maria Pirounaki, John Koskinas. Bacterial infections in patients with liver cirrhosis: clinical characteristics and the role of C-reactive protein. *Annals of Gastroenterology* (2017) 30, 1-7