



## A CROSS-SECTIONAL STUDY ON BACTEREMIA AS A RISK FACTOR FOR VARICEAL UPPER GASTROINTESTINAL TRACT BLEEDING IN CIRRHOTIC PATIENTS

Murad Baig<sup>1</sup>, Mashhood Sulaman<sup>2</sup>, Muhammad Muizz Hassan<sup>3\*</sup>, Ahmed Aftab<sup>4</sup>, Akashnath Kivalur Ganeshanath<sup>5</sup>, Muhammad Munawar<sup>6</sup>, Saifullah Syed<sup>7</sup>, Kamel J. K. Walwil<sup>8</sup>, Jumana Abdelrahman Diab<sup>9</sup>, Hosam Alazazzi<sup>10</sup>

<sup>1</sup>Paediatrics Department, Shaukat Khanum Hospital, Lahore - Pakistan

<sup>2</sup>House Officer, CDA Hospital, Islamabad - Pakistan

<sup>3\*</sup>Senior House Officer, General Medicine Department, University of Limerick Hospitals Group. Limerick - Ireland

<sup>4</sup>Medical Officer, DHQ Hospital, Bagh - AJK

<sup>5</sup>Royal College of Surgeons Ireland- Medical University of Bahrain

<sup>6</sup>Department of Internal Medicine, CMH, Kharianm - Pakistan

<sup>7</sup>Royal College of Surgeons in Ireland, Dublin - Ireland

<sup>8,9,10</sup>Royal College of Surgeons in Ireland - Bahrain

**\*Corresponding Author:** Muhammad Muizz Hassan

\*Senior House Officer, General Medicine Department, University of Limerick Hospitals Group. Limerick – Ireland. Email: muizz\_hassan@hotmail.com

### Abstract

**Background and Aim:** Rupture and bleeding from gastroesophageal reflux veins (GEVs) represent major complications for individuals with chronic liver disease (CLD), often leading to high mortality. The present study aimed to evaluate the bacteremia as a risk factor in cirrhotic patients suffering from variceal upper gastrointestinal tract bleeding.

**Patients and Methods:** This cross-sectional study investigated 88 cirrhotic patients in the Department of Internal Medicine, Tertiary Care Hospital, Lahore from January 2022 to April 2024. Patients aged 20 to 60 years of either gender with liver cirrhosis disease were included. All the patients were grouped into three groups; Group-I (first attack), Group-II (recurrent attack), and Group-III (control or no history of variceal bleeding). Eligible patients underwent history taking, complete physical examination, and laboratory investigations. Upper GI endoscopy, pro-calcitonin level measurement in blood, and blood culture were done. Data analysis was done using SPSS version 26.

**Results:** The overall mean age was  $52.8 \pm 8.62$  years. Out of 88 patients, there were 54 (61.4%) male and 34 (38.6%) female. Patient's distribution in groups were as follows; Group-I 32 (36.4%), Group-II 32 (36.4%), and Group-III 24 (27.2%). The incidence of positive blood culture such as Escherichia coli, Staphylococcus aureus, and Klebsiella in Group-I, Group-II, and Group-III was 15 (46.9%), 20 (62.5%), and 6 (25%), respectively whereas the rate of positive Procalcitonin (ng/ml) was 14 (43.8%), 19 (59.4%), and 5 (20.8%) respectively. The highest percentage of positive blood cultures was observed in Group-II, followed by Group-I, and a control group and, Patients with recurrent venous

hemorrhage showed statistically higher PCT values compared with first-time venous hemorrhage and the control group.

**Conclusion:** The present study observed that bacteremia and elevated procalcitonin levels are risk factors in patients with cirrhosis. Procalcitonin may serve as a surrogate biomarker for variceal bleeding and bacteremia.

**Keywords:** Cirrhosis, Bacteremia, Variceal Bleeding, Risk factor

## INTRODUCTION

Upper gastrointestinal bleeding in patients with gastrointestinal ulcers presents a frequent and serious complication with intra-abdominal hemorrhage with significant morbidity and mortality [1, 2]. Several recent studies have shown that prophylactic antibiotic therapy reduces viral infections, rebleeding, and in-hospital mortality in hemorrhagic ulcers on the bladder or abscess of the rectum among patients [3, 4]. Portal hypertension leads to gastroesophageal varices (GEVs), which are treated as porto-systemic collaterals. Rupture and hemorrhage from these aneurysms are significant complications, and the mortality rate is high [5]. Each type of active variceal bleeding is associated with a mortality rate of 30% [6]. GEV hemorrhage ranks third in the list of causes of upper gastrointestinal bleeding, after pelvic and gastrointestinal ulcers. It is a gastrointestinal bleeding in 50%–60% of patients with gastroenteritis [7, 8]. Studies show that nearly half of patients with liver disease have GEVs at the time of diagnosis, with the highest prevalence in those with advanced liver disease with early prognostic GEVs and seeing when primary prophylaxis is used has the potential to prevent early variceal bleeding, thereby reducing mortality, morbidity and associated health care costs [9].

Liver disease contributes to increased rates of medical visits, hospitalizations, healthcare costs, morbidity, and mortality [10]. The severity of cirrhosis significantly related to the possibility of portal hypertension with varices and symptoms [11]. Bacterial infections are common in patients with upper gastrointestinal bleeding (UGIB) ulcers. Procalcitonin is an excellent marker for viral infections due to its ability to provide early diagnosis, disease progression and prognosis, and aid in treatment decisions. Compared with other conventional markers for applications such as C-reactive protein (CRP), Indicates diagnostic accuracy. This increased accuracy can significantly improve the accuracy of clinical assessments and guide appropriate treatment strategies [12]. Bacteremia is associated with liver disease along with gastrointestinal (GI) bleeding like complications as reported in an earlier study [13].

## METHODOLOGY

This cross-sectional study investigated 88 cirrhotic patients in the Department of Internal Medicine, Tertiary Care Hospital, Lahore from January 2022 to April 2024. Patients aged 20 to 60 years of either gender with liver cirrhosis disease were included. All the patients were grouped into three groups; Group-I (first attack), Group-II (recurrent attack), and Group-III (control or no history of variceal bleeding). Patients presented with bacterial infections were excluded. Additionally, individuals taking antibiotics before admission and non-variceal causes of gastrointestinal bleeding were excluded. Eligible patients underwent history taking, complete physical examination, and laboratory investigations. Upper GI endoscopy, pro-calcitonin level measurement in blood, and blood culture were done. Age, body mass index (BMI), gender, smoking, fasting blood glucose (FBG), hemoglobin A1C (HbA1C) level, complete blood count (CBC), total bilirubin, serum albumin, serum creatinine, C-reactive Protein (CRP) levels, and analysis of ascites fluid samples were different parameters measured.

Data analysis was done using SPSS version 26. Categorical variables were expressed using frequencies and percentages, whereas numerical variables were presented as mean value  $\pm$  standard deviation (SD). Chi-square test was used for comparative analysis and comparative statistics. A p-value of  $\leq 0.05$  was considered statistically significant for all statistical tests.

## RESULTS

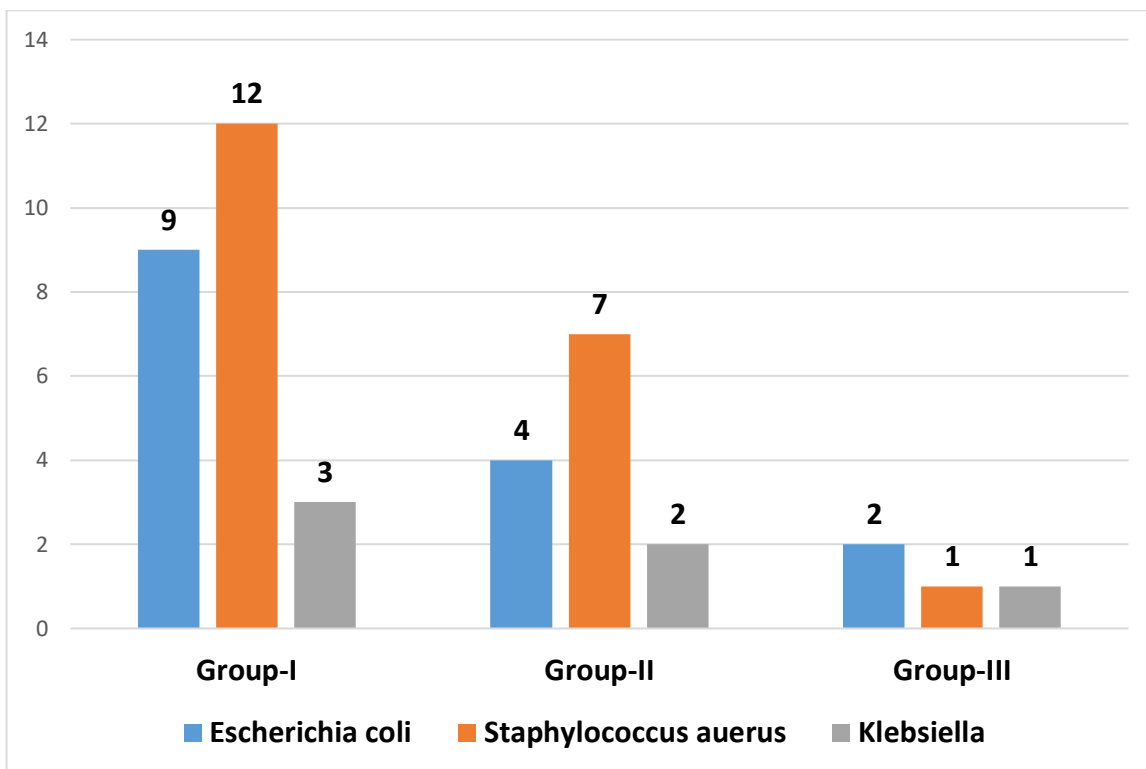
The overall mean age was  $52.8 \pm 8.62$  years. Out of 88 patients, there were 54 (61.4%) male and 34 (38.6%) female. Patient's distribution in groups were as follows; Group-I 32 (36.4%), Group-II 32 (36.4%), and Group-III 24 (27.2%). The incidence of positive blood culture such as Escherichia coli, Staphylococcus auerus, and Klebsiella in Group-I, Group-II, and Group-III was 15 (46.9%), 20 (62.5%), and 6 (25%), respectively whereas the rate of positive Procalcitonin (ng/ml) was 14 (43.8%), 19 (59.4%), and 5 (20.8%) respectively. The highest percentage of positive blood cultures was observed in Group-II, followed by Group-I, and a control group and, Patients with recurrent venous hemorrhage showed statistically higher PCT values compared with first-time venous hemorrhage and the control group. The baseline details of patients is shown in Table-I. Laboratory analysis of patients are presented in Table-II. Incidence of positive blood culture is depicted in Figure-1. Figure-II illustrate the incidence of positive procalcitonin.

**Table-I** baseline details of patients (N=88)

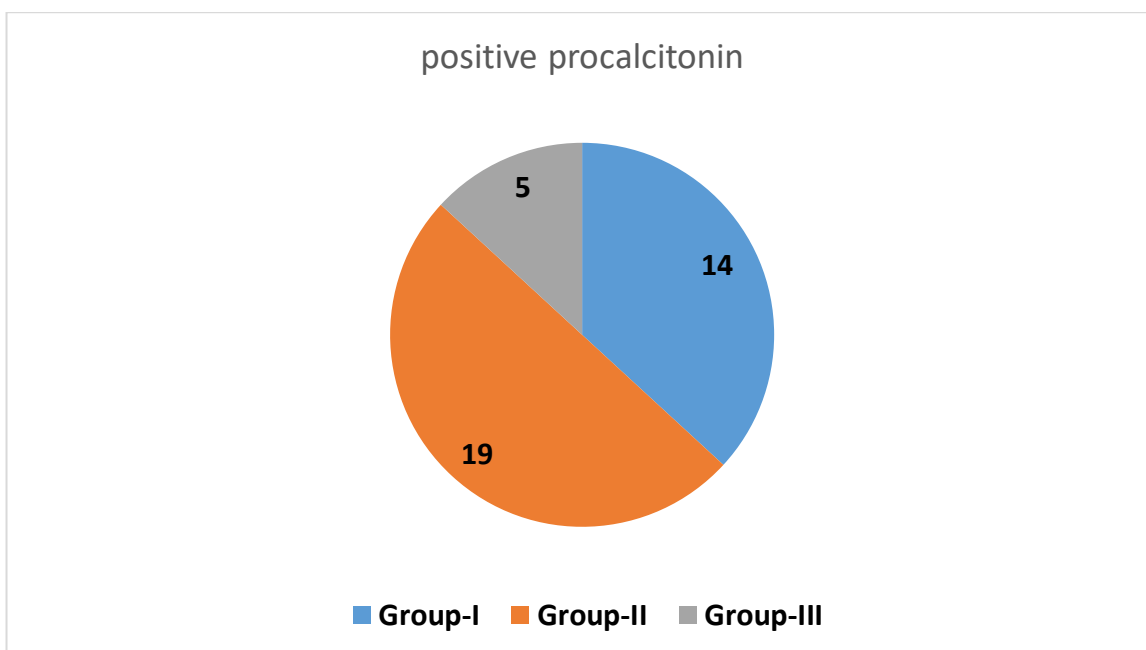
Parameters	Group-I (N=32)	Group-II (N=32)	Group-III (N=24)	P-value
Age (years)	53.2 $\pm$ 9.14	52.1 $\pm$ 8.94	53.1 $\pm$ 7.78	0.89
<b>Age Groups</b>				0.98
20-30	3 (9.4%)	4 (12.5%)	2 (8.3%)	
31-40	5 (15.6%)	6 (18.8%)	3 (12.5%)	
41-50	7 (21.9%)	8 (25%)	4 (16.7%)	
51-60	17 (53.1%)	14 (43.8%)	15 (62.5%)	
<b>Gender</b>				0.69
Male	22 (68.8%)	19 (59.4%)	13 (54.2%)	
Female	10 (31.2%)	13 (40.6%)	11 (45.8%)	
<b>Hepatic encephalopathy (HE)</b>				0.25
Yes	4 (12.5%)	8 (25%)	3 (12.5%)	
No	28 (87.5%)	24 (75%)	21 (87.5%)	
<b>Ascites</b>				0.0079
Yes	23 (71.9%)	27 (84.4%)	13 (54.2%)	
No	9 (28.1%)	5 (15.6%)	11 (45.8%)	
<b>Virology</b>				0.39
Positive	29 (90.6%)	29 (90.6%)	19 (79.2%)	
Negative	3 (9.4%)	3 (9.4)	5 (20.8%)	

**Table-II** Comparison of Laboratory analysis in groups (N=88)

Lab. Parameters	Group-I (N=32)	Group-II (N=32)	Group-III (N=24)	P-value
Procalcitonin (ng/ml)	0.281 (0.11-2.9)	1.89 (0.09-2.89)	0.21 (0.10-2.20)	0.022
WBC ( $\times 103/\text{mm}^3$ )	9.6 (3.1 – 11.7)	8.9 (1.5 – 13.8)	9.5 (4.1-11.8)	0.628
Platelet ( $\times 103/\text{mm}^3$ )	109.10 $\pm$ 38.6	85.21 $\pm$ 30.61	114.6 $\pm$ 22.8	0.001
Hemoglobin (g/dl)	8.63 $\pm$ 1.89	8.42 $\pm$ 1.61	10.64 $\pm$ 1.10	<0.001
Creatinine (mg/dl)	0.97 (0.40-1.5)	0.97 (0.22-2.6)	0.78 (0.45-4.1)	0.276
Albumin (g/dL)	2.7 $\pm$ 0.41	2.65 $\pm$ 0.59	2.99 $\pm$ 0.45	0.05
Total bilirubin (mg/dl)	1.25 (0.2-4.1)	1.41 (0.57-34.8)	1.21 (0.49-29.8)	0.5



**Figure-1** Incidence of Positive blood culture



**Figure-2** Incidence of positive procalcitonin

## DISCUSSION

The present study mainly focused associated bacteremia as a risk factor in cirrhotic patients causing variceal upper gastrointestinal tract bleeding and reported bacteremia and elevated procalcitonin levels are risk factors in patients with cirrhosis. Cirrhotic patients usually suffer from bacterial infection. Patients with ulcerative colitis have a high incidence of bacterial infections due to their compromised immune system and overproduction of pro-inflammatory cytokines, which makes them susceptible to infection. Procalcitonin (PCT) is a biomarker for infection, sepsis, and septic shock [14]. Bacterial infection are more prevalent, but the incidence of other infections such as pneumonia, urinary tract infection (UTI), and spontaneous bacterial infection (SBP) was significantly higher in

group a encountered mortality compared with the non-mortal group may act as an exacerbating factor. One possibility is that viral infections triggers excessive inflammatory responses, causing cardiovascular and endocrine dysfunction [15].

Patients with cirrhosis are susceptible to a variety of infections due to a compromised immune system and activation of pro-inflammatory cytokines. This vulnerability extends to spontaneous infections, hospital-acquired infections and infectious diseases, which are rarely caused. In addition, patients frequently have intestinal bacterial translocation imbalances, especially those exacerbated by upper gastrointestinal bleeding (UGIB), which impair intestinal barrier function and local immune protection causing Gram-negative enteric bacilli, anaerobes, and *Enterococcus* spp [16, 17].

Chronically ill patients were found to be increased risk of bleeding. This finding is consistent with the results of a study in Pakistan [18]. Furthermore, studies have shown that low platelet count is significantly associated with an increased risk of thrombosis. Earlier studies have shown similar adverse effects as having low platelet counts in gastrointestinal ulcers (GEVs), all suggesting a higher risk as bleeding into the stomach [19].

Hemoglobin level was found to be a reliable predictor of variceal and infectious bleeding. Similarly, albumin levels emerged as another valuable predictor of variceal and infectious bleeding. Elevated hemoglobin and albumin levels were associated with decreased bleeding risk. Likewise, another study reported bleeding in patients after endoscopic variceal ligation (EVL) and their hemoglobin levels were significantly reduced [20].

Bacteremia was found to increase the risk of variceal bleeding premature by 2.65-fold compared with non-infectious patients, and the recurrence risk in infected patients increased 4.71 times [21]. Our findings showed that *Escherichia coli* (*E. coli*) was the most prevalent pathogen in patients with positive blood cultures, in both bleeding and nonbleeding groups, followed by *Staphylococcus aureus* (*Staph. aureus*), where *Klebsiella* was most prevalent. These findings resembled with an earlier studies, who noted that gram-negative bacteria, such as *E. coli coli*, *Klebsiella* spp., and *Enterobacter* spp., are the main causative bacteria [22, 23]. Moreover, Lee et al. found a high frequency of viral infections in patients with varicose bleeding [24].

## CONCLUSION

Increased level of procalcitonin and bacteremia are the major risk factors for cirrhotic patients. Procalcitonin may serve as a surrogate biomarker for variceal bleeding and bacteremia.

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