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ORIGINAL ARTICLE

Prophylactic antibiotic use for variceal bleeding in Child Class A cirrhosis; Scope for risk adaptive strategy

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ABSTRACT

Background: Acute variceal bleeding is one of the serious complications in patients with liver cirrhosis, significantly contributing to morbidity in this population. The current recommendations encourage universal antibiotic prophylaxis. However, its benefit in low-risk patients, especially those in early stage of cirrhosis, is still not well understood. The aim of this study was to evaluate the necessity of antibiotic prophylaxis in patients with compensated, Child-Pugh Class A cirrhosis.

Methods: A study with a quasi-experimental design was carried out in Medical Unit 1 of Jinnah Hospital Lahore. This study involved 120 patients with early-stage cirrhosis (Child-Pugh A) who experienced acute variceal bleed. Patients with ascites, WBC >12×10^3/µL, Child-Pugh B/C, hepatic encephalopathy, SBP, or hepatorenal syndrome were excluded. Two groups were formed from the study participants. Group A received intravenous ceftriaxone 1 gram daily, while Group B received a placebo. Outcomes included infection, hepatic encephalopathy, and mortality. Infection Probability Score (IPS) was calculated and predictive accuracy was evaluated using ROC curve analysis. Data analysis was carried out using SPSS v20.

Results: Mean age was 57.4 ± 12.1 years; 58.3% were male. Baseline characteristics did not differ significantly between the groups. No significant difference was found in encephalopathy (2.5%), ascites (5%), transfusion (16.7%), fever (6.7%), or mortality (4.2%) between groups (p > 0.05). IPS was substantially elevated in patients who died (12.6 ± 3.4) versus survivors (8.2 ± 1.1), p < 0.001. IPS showed strong predictive value for mortality (AUC = 0.877). IPS >10 predicted mortality with 80% sensitivity, 93.9% specificity, and 99.1% NPV.

Conclusion: Antibiotics for primary prophylaxis in Child Class A cirrhosis experiencing variceal bleed is not necessary and a risk adaptive strategy should be adopted. IPS may serve as a valuable tool in evaluating mortality risk associated with variceal bleeding.

Keywords: Acute Variceal Bleeding, Child Class A Cirrhosis, Prophylactic Antibiotic, Risk Adaptive Strategy

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Introduction

Variceal bleeding is one of the chief causes of bleeding from the upper gastrointestinal tract, accounting for upto 30% of the cases (1). Gastrointestinal bleeding associated with cirrhosis is primarily due to the development of gastroesophageal varices (65%–70%), followed by fundal varices (10%–15%) and rarely due to gastropathy associated with portal hypertension (2). The occurrence of

esophageal varices correlates with the Child-Turcotte-Pugh (CTP) class: 42% in CTP A, 71% in CTP B, and 76% in CTP C (3).

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Mortality due to acute variceal bleed is around 15–20% as per western literature, but it rises to 30-40% in CTP C patients and is relatively less in patients with CTP A cirrhosis (4). However, deaths linked to bleeding from gastroesophageal varices is found to be much less in our region, primarily because there is lesser proportion of individuals with cirrhosis secondary to alcohol intake than cirrhosis due to viral hepatitis (5). Over the past few decades, mortality and complications after upper gastrointestinal bleed has significantly declined due to improvement in hemodynamic resuscitation techniques. The hemostatic methods employed to control bleeding these days include endoscopic variceal ligation, endoscopic injection of cyanoacrylate tissue adhesives, use of argon plasma coagulation (APC) and advancements in the medicines available for management of liver cirrhosis (6,7,8).

Cirrhosis is the result of persistent liver damage, identified on histopathology by fibrous septa bridging vascular structures and the development of regenerative nodules, which destroy the lobular arrangement. This disturbance causes impedance within the hepatic circulation, raised portal pressure and formation of varices which are at risk of rupture and bleeding. Among major factors contributing to mortality and morbidity related to acute variceal bleeding is higher risk of infections (9, 10). Presence of blood in gastrointestinal system creates favorable environment for bacterial overgrowth and this may lead to bacteria spreading into the lymphatic structures in the mesentery, circulation, and ascitic fluid, resulting in sepsis and spontaneous bacterial peritonitis (11). Conditions favoring this translocation include excessive bacterial colonization of the intestines, increased intestinal wall permeability, and diminished immune response in cirrhosis, all precipitated by variceal bleeding (12).

Infections are tied to a heightened probability of early rebleeding and elevated death rates (3). These patients have impaired liver filtration, reduced Opsonization in ascitic fluid, increased gut permeability, and deficiencies in immune components like C3, C4, and monocyte HLA-DR expression. Alcoholic cirrhosis further weakens immunity by impairing neutrophil function (13). During variceal bleeding, the most common bacterial isolates are aerobic, gram-negative rods, particularly Escherichia coli, Enterococcus, Klebsiella, and Pseudomona (14). Bacteremia, ascitic fluid infection, urinary and lower respiratory tract infections are frequently encountered (11, 14). Therefore, prophylactic antibiotic is recommended in individuals admitted with variceal bleed (9, 15).

As per recommendations, Intravenous ceftriaxone 1 gram once daily should be advised for patients with late stage cirrhosis presenting with variceal bleed and a history of quinolone use for prophylaxis or in regions with high resistance rates (16). Antibiotics should be chosen based on local resistance data and hospital antibiotic policies (7).Repeated use of antibiotics for prophylactic and therapeutic purposes has resulted in emergence of multi-drug

antibiotic resistance (2). There has been growing number of Clostridium difficile infection during prolonged hospitalization resulting in higher in-hospital mortality (17). Therefore, requirement for the use of antibiotics should regularly be reassessed and carefully reviewed for efficacy, cost effectiveness and potential for contribution to rising trends of antibiotic resistance (6, 11, 18).

While antibiotic prophylaxis is broadly recommended by major gastrointestinal societies for acute variceal bleeding, the Baveno VII consensus points out that a lower incidence of infectious complications and death is observed in individuals with CTP A cirrhosis. Thus, further research is necessary to evaluate whether empirical administration of antibiotics for infection prevention is justified across all cases of variceal bleeding, or if a selective approach based on disease stage and individual risk is more appropriate (7). There are few studies suggesting that Child-Pugh class A cirrhotic with variceal bleed have a minimal risk of microbial infection, and the benefit of use of antibiotics for infection prevention is unclear (5,19). This research is designed to assess the impact of parenteral antibiotics for primary prophylaxis of infection in Child Class A cirrhosis patients with acute bleeding from varices.

Methods

We carried out a quasi-experimental study with an intent to assess the need for antibiotic use in prophylaxis of infections in cirrhotic individuals in Child Pugh A category admitted with upper gastrointestinal bleeding. The study was conducted in Medical Unit 1 of Jinnah Hospital Lahore from July to September 2025 vide letter number 3324620. Ethical approval was taken from the Ethical Committee and confidentiality of data was maintained.

Sample size of 120 was determined with the OpenEpi calculator, based on a 95% two-sided level of significance, margin of error 5% and confidence level 80% (20). 623 patients were assessed for suitability to be involved in the research and 120 were finally enrolled after a thorough screening with 60 patients in each group. Male and female adult subjects presenting with Cirrhosis CTP grade A and active bleeding from varices were selected for study. Patients were excluded if they had moderate to severe ascites, high WBC count (12 x 103 / mm3), CTP Class B and C, cirrhotic individuals experiencing encephalopathic symptoms, bacterial peritonitis or hepatorenal syndrome. Patients who were already on other antibiotics within previous 2 week before admission were also excluded.

Participants were divided into two groups; antibiotic (Group A) and control (Group B) arms using an alternate assignment method. The first eligible patient was assigned to Group A, the next to Group B, and this pattern continued sequentially throughout the enrollment period. The arms were as follows:

Group A: Standard of care along with Inj Ceftriaxone 1 gm daily

Group B: Standard of care + Placebo

Informed consent was obtained. Patients were initially screened for eligibility by Site Investigators and Research Physicians. The enrollment form included patient's biodata, clinical evaluation and baseline workup.All patients received standard of care for acute variceal bleeding including hemodynamic resuscitation, IV fluids, vasoactive drugs and blood transfusions if indicated. Upper GI endoscopy was performed after hemodynamic stability within 12 hours of

admission by senior consultant gastroenterologists. All the patients had daily follow up sessions by investigator for five days after enrollment. Follow up included assessment for control of bleeding along with parameters of Infection which included rise in WBC or development of fever, worsening of ascites, and requirement for re-endoscopy. Patients were at liberty to drop out of study any time they wanted. Primary endpoint of study was discharge of patient or death. Secondary end points were development of fever with or without localizing symptoms including abdominal pain, cough with sputum or dysuria. In case of symptoms patients were managed on lines of standard of care for the infection developed.

IBM SPSS Statistics (version 20) was utilized for data analysis. Means and standard deviations were used for quantitative data, while qualitative data were described using frequencies and percentages. Patient with antibiotics use were compared with control group using two tailed unpaired t test for quantitative variables and chi square for qualitative variables with normal distribution. Results with p-values below 0.05 were regarded as statistically significant. We calculated Infection probability score (IPS) for each patient and identified its cut off value for predicting risk of infection using Receiver Operating Characteristic (ROC) curve and assessed its accuracy by determining sensitivity, specificity, positive and negative predictive value.

Results

This study involved 120 participants. The mean age of the patients was 57.42 (SD ± 12.135) years. Amongst these patients, 58.3% (n=70) were male, and 41.7% (n=50) were female. All of the included patients were from CTP Class A and none of them in hepatic encephalopathy. The mean Glasgow-Blatchford Score was 10.13 (SD ± 3.151). The mean serum creatinine was 0.823 (SD ± 0.2602). The mean WBC count on Day 1 was 7.491 (SD ± 0.9945), while on Day 5, it was 7.886 (SD ± 1.4337). The mean Infection Probability Score (IPS score) calculated was 8.42 (SD ± 1.510).

These patients were categorized into two comparable groups. Group A was given antibiotic while Group B was given placebo in addition to standard of care treatment for upper GI bleeding. The mean age for Group A was 56.42 years (SD ± 13.05) and for Group B the mean age was 58.38 years (SD ± 11.201) , difference being non significant (p = 0.380). Mean Glasgow-Blatchford Score was 10.46 (SD ±3.169) in Group A, compared to 9.82 (SD ±3.128) in group B (p = 0.269). Comparison of baseline variables between group A and B has been shown in Table-1 depicting that both groups were similar.

Table 1. Comparison of baseline variables between Group A and Group B

Variable	Antibiotic Group (Mean ± SD)	Placebo Group (Mean ± SD	p- value
Age (years)	56.42 ± 13.05	58.38 ± 11.20	0.380
Glasgow-Blatchford Score	10.46 ± 3.17	9.82 ± 3.13	0.269
Serum Creatinine (mg/dL)	0.85 ± 0.26	0.79 ± 0.26	0.206
WBC Day 1 ($\times 10^9$/L)	7.42 ± 0.92	7.56 ± 1.06	0.437
WBC Day 5 ($\times 10^9$/L)	7.81 ± 1.51	7.96 ± 1.36	0.555
Serum Albumin (g/dL)	3.09 ± 0.24	3.13 ± 0.22	0.314

Infection Probability Score	8.34 ± 1.25	8.49 ± 1.73	0.581

Endoscopy was done within 12 hours and patients were followed for outcomes. Endoscopy showed that 95 patients (79.2%) had small to medium varices, while 21 (17.5%) had large varices without red signs, and 4 (3.3%) had large varices with red signs. The results indicated no significant disparity in variceal size distribution between Group A and B (p = 0.584).

Table 2. Distribution of Variceal Size on Endoscopy.

Variceal size	n (%)	p-value
Small to medium varices	95 (79.2)	
Large varices without red signs	21 (17.5)	
Large varices with red signs	4 (3.3)	
Total	120 (100)	0.584

Participants were observed in hospital for 5 days. A total of 3 (2.5 %) patients (1 case from Group A and 2 cases from Group B) developed encephalopathy but statistical analysis revealed no significant difference between the two groups (p = 0.579). Worsening ascites was seen in 6 (5%) patients (4 cases from Group A and 2 cases from group B) but again the groups did not differ significantly (p = 0.379). Repeat endoscopy was needed in 4 (3.3%) patients (2 cases from each group), showing comparable outcomes across both groups. (p = 0.973). Blood transfusions were required in 20 (16.7%) patients with 9 cases from Group A and 11 cases from Group B (p=0.684). Fever was documented in 8 (6.7 %) patients (3 cases from Group A and 5 cases from Group B), (p = 0.494). Increase in WBC count above 11 was seen in 4 (3.3 %) patients (2 cases from each from group). Mortality was seen in 5 (4.2%) patients (2 cases from Group A and 3 cases from Group B), with statistically similar results between the groups (p = 0.675).

Table 3. Outcomes in Group A (antibiotic) versus Group B (placebo group).

Outcome	Group A (n=60)	Group B (n=60)	Total (n=120)	p-value (Chi square)
Development of encephalopathy	1 (1.7%)	2 (3.3%)	3 (2.5%)	0.579
Worsening	4 (6.8%)	2 (3.3%)	6 (5.0%)	0.379
ascites				
Repeat endoscopy needed	2 (3.4%)	2 (3.3%)	4 (3.3%)	0.973
Blood transfusion needed	9 (15.3%)	11 (18.0%)	20 (16.7%)	0.684
Increase in WBC > 11	2 (3.4%)	2 (3.3%)	4 (3.3%)	0.973
Death	2 (3.4%)	3 (4.9%)	5 (4.2%)	0.675
Fever	3 (5.1%)	5 (8.2%)	8 (6.7%)	0.494

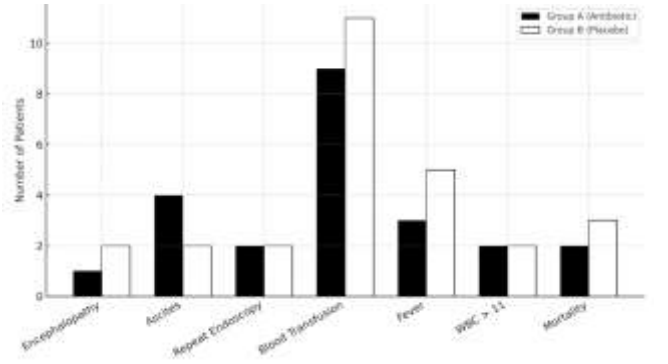

Figure 1. Distribution of Clinical Outcomes Between The Groups

Infection probability score (IPS) was derived by summing points for six clinical parameters including temperature, pulse, respiratory rate, WBC count, CRP and SOFA score. IPS was used as a tool to predict infection risk. The mean IPS was 8.34 (SD ± 1.254) in group A and 8.49 (SD ±1.728) in Group B, not

significantly different (p = 0.581) between the groups. Patients who were alive at follow up had mean IPS value of 8.23 (SD ± 1.079) while 5 patients who died had mean IPS value of 12.60 (SD ± 3.435), with a p value < 0.001. This showed that IPS was significantly associated with mortality (p < .001), making it a strong predictor of poor outcomes. However IPS score was not different between patient of CTP class A with variceal bleeding who were given antibiotics and those with no antibiotic treatment.

Table 4. Mean IPS Score amongst survivors and non-survivors

Mortality Outcome	Mean IPS Score	Standard Deviation	p-value
Survivors (n = 115)	8.23	1.079	< .001
Non-survivors (n = 5)	12.60	3.435	< .001

The Receiver Operating Characteristic (ROC) curve was drawn to ascertain the diagnostic accuracy of IPS in identifying mortality risk. Area under the Curve (AUC) was 0.877, indicating high accuracy.

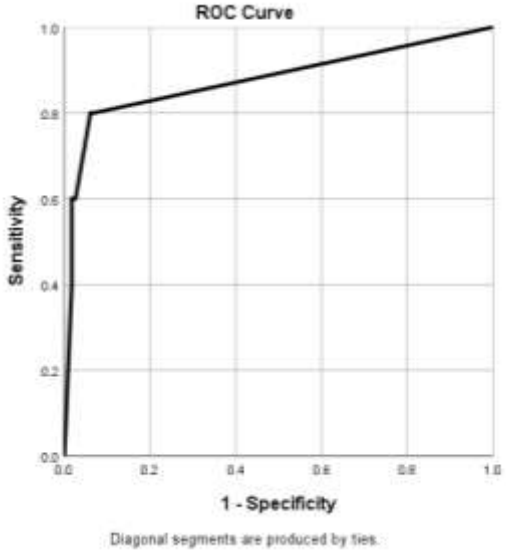

Figure 2. ROC curve of IPS for predicting Mortality in patients with variceal bleeding.

We identified IPS cutoff value considered best for predicting death above 10, with:
Sensitivity = 80%
Specificity = 93.9%
Accuracy = 93.3%
Positive Predictive Value (PPV) = 36.4%
Negative Predictive value (NPV) = 99.1%
This suggests that IPS is a reliable predictor of mortality, with higher scores correlating with worse outcomes.

Discussion

Acute variceal bleeding is a frequent complication of cirrhosis, associated with adverse clinical outcomes (21). This study aimed to determine the need of prophylactic antibiotic for prevention of infectious complications and improving clinical outcomes in CTP Class A patients presenting with bleed due to ruptured varices. By demonstrating that routine antibiotic prophylaxis does not significantly impact infection rates, mortality, or other adverse outcomes in this population, the study contributes to a growing body of evidence advocating for a more nuanced, risk-adapted approach to antibiotic use rather than the broad application of prophylactic treatment. We also identified that Infection Probability Score (IPS) is a strong predictor of morbidity and mortality in variceal bleeding and can be used to identify patients in need of antibiotic prophylaxis. Patients who died had a mean IPS of 12.60 (SD ± 3.435), compared to 8.23 (SD ± 1.079) in survivors.

The study aligns with the recommendations of the Baveno VII guidelines, which calls for reassessing the routine use of antibiotics in well-compensated cirrhotic patients (7). By reinforcing the idea that routine prophylactic antibiotic may not be required for patients having Child-Pugh A cirrhosis, it helps guide clinical practice toward personalized

treatment strategies based on individual risk profiles (22).

Previous studies by Bernard et al. and Fernandez et al. showed that prophylactic antibiotics reduced infection rate, occurrence of spontaneous bacterial peritonitis, and death in cirrhotic individuals with acute variceal bleed, supporting their routine use (23,24). Gan M. et al. demonstrated that individuals with acute upper gastrointestinal bleed show improvement with prophylactic antibiotic use to reduce mortality, particularly in patients above 65 years of age and in patients requiring endotracheal intubation or endoscopic intervention (9). However, these studies mostly included Child-Pugh B and C patients with compromised immunity are vulnerable to risk of infections. In contrast, our study focused on Child-Pugh Class A patients only and found no significant advantage, suggesting that routine prophylactic antibiotics may not be necessary in well-compensated cirrhosis. Several other studies, including large cohort investigations and meta-analyses, have echoed these findings. These studies suggest that modern endoscopic techniques and improvements in cirrhosis management have lessened the requirement for universal antibiotic prophylaxis, especially in individuals with better liver function Child-Pugh A cirrhosis (5, 6, 19, 22).

Ichita et al., in a large cohort study, observed no substantial variation in mortality, rebleeding, or development of spontaneous bacterial peritonitis between patients who received prophylactic antibiotics and other group who did not receive antibiotics following acute variceal bleed (6). Similarly, Aguirre-Villarreal et al. discussed the decreasing requirement of routine prophylaxis in light of modern endoscopic techniques and improved cirrhosis management (25). Chang et al. further demonstrated that in cirrhotic having CTP class A and B cirrhosis, prophylactic antibiotics showed limited clinical impact, suggesting that initial functional capacity of liver is essential inin determining the necessity for antibiotic therapy (19). Additionally, the meta-analysis by Gao et al. reported that although prophylactic antibiotic lower the likelihood of infectious complications and fatal outcomes, overall the advantages are primarily observed in individuals with more advanced hepatic dysfunction (5). Similarly, Tandon et al. carried out a retrospective cohort analysis showing that cirrhotics with variceal bleeding categorized as CTP Class A had decreased infectious complications and death rates without preventive antimicrobials, compared to those in CTP Class B or C.

Utilization of the Infection Probability Score (IPS) in this study is a notable advancement in risk stratification (26). Our study shows that IPS can be a reliable predictor of adverse outcomes, and integrating IPS in clinical settings may assist in recognizing high-risk individuals who would gain from prophylactic antibiotics while minimizing unnecessary exposure in low-risk individuals.

The broader implications of this approach are significant, particularly in terms of antimicrobial stewardship. Unnecessary antibiotic use contributes to the global challenge of multidrug-resistant organisms, making it all the more crucial to tailor treatment approaches guided by patient-specific risk assessments. Integrating clinical risk scores such as IPS to guide antibiotic use in cirrhotic patients with acute variceal bleeding will be helpful in this regard.

Conclusion

This study advocates for a shift away from routine prophylactic antibiotic therapy in low-risk (Child-Pugh A) cirrhotic individuals admitted with variceal bleeding, suggesting that a risk-adapted strategy, supported by tools like the IPS, could optimize patient outcomes while minimizing unnecessary antibiotic use.

Study Limitations

It is a single center design, relatively small sample size, and the absence of blood cultures, which could affect the generalizability of the findings. To validate these results and better define the role of IPS-guided antibiotic therapy, future multicenter trials with more extensive data collection and longer follow-up periods are essential.

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Conflict of Interest: None

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Data acquisition, analysis and interpretation	WF, SS,MAS,MR,SM,KS
Manuscript writing and approval	MAS,

All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.