Identification of Risk Factors Associated with Bacterial Infections in Child-A Cirrhosis with Variceal Bleeding

Dear editor,

Infections are an important determinant of outcomes in patients with cirrhosis after an episode of acute variceal bleeding (AVB). The presence of advanced liver disease along with hepatic encephalopathy and the need for endotracheal intubation have emerged as potential predictors of infections after AVB in the era of antibiotic prophylaxis.[1] While ample evidence about the prevalence and risk factors of infections is available in those with advanced liver disease, this still remains an unanswered question in patients with Child-Pugh A cirrhosis. This risk, although lowest among those with cirrhosis, is not negligible. A recent multicentre study showed it to be around 8%, whereas a previous retrospective study showed it to be around 2%, irrespective of the use of antibiotics.[2] We, therefore, report our experience from a prospectively recruited cohort of patients with Child-A cirrhosis, presenting with AVB between the period of January 2020–March 2021 from a tertiary care centre from India.

Our cohort comprised patients with Child-A cirrhosis (n = 131), presenting with the AVB [mean age: 44 ± 11 years, 80% males, median MELD score: 11(8–12)] of alcoholic liver disease (49%), non-alcoholic steatohepatitis (21.3%), viral cirrhosis (10%) and other aetiologies (19.7%) who were included and analysed for outcomes (Table-1). Patients were managed according to standard protocols described from our centre described elsewhere.[3] Intravenous cefixime was administered to all patients at presentation. Overall, the 6-week mortality, after an episode of AVB, was 4.5%. The incidence of failure to control bleed and early re-bleeding at 6 weeks was 7.6% and 4.6%, respectively. Twenty-five out of the 131 patients (19%) had active bleeding on endoscopy. Fourteen patients (10.6%) developed post-bleeding bacterial infections. The most common site was the respiratory tract (n = 6), followed by cellulitis (n = 3), spontaneous bacterial peritonitis (n = 1, after the onset of ascites post bleeding) and urinary tract infection (n = 1). Three patients developed bacteraemia without any localising site. Multidrug organisms were isolated from four patients, and septic shock developed in four patients. Bacterial infections were more frequent in those presenting with active bleeding on endoscopy (28% vs. 6.6%, P = 0.006) and in those with hypotension at presentation (36% vs. 2%, P = 0.001). A multivariate analysis showed that hypotension at presentation [odds ratio (OR) 95% CI: 11.55 (1.61–111.72), P = 0.019] could independently predict the risk of post-bleed infections, whereas the MELD score [OR: 0.95 (0.75–1.21), P = 0.695] and active bleeding [OR: 1.71 (0.22–8.61), P = 0.536] were non-significant.

The incidence of bacterial infections after AVB in our cohort was slightly higher than that shown by Martinez *et al.*[1] and much higher than what was shown by Tandon *et al.*[2] The prospective consecutive recruitment, higher incidence of hypotension and active bleeding in our study could have resulted in these differences. Our results show that hypotension could independently predict the risk of infections. Gut barrier dysfunction is postulated central to the pathogenesis of post-bleeding infections. Mucosal ischaemia secondary to hypotension promotes gut-barrier dysfunction, which can trigger subsequent bacterial translocation and infections.

The utility of prophylactic antibiotic administration is uncertain in patients with Child-A cirrhosis with AVB, based on the current evidence. The Baveno-VII consensus supports this practice, but the data are largely extrapolated from those with advanced disease.[4] The consensus stressed upon the need for randomised trials evaluating the need for antibiotics in these patients. Our results show that the incidence of a post-bleeding bacterial infection is lower in the sub-group presenting without hypotension and in those without active bleeding. We believe that it is this subgroup that should be the target population for conducting such trials.

In conclusion, results from our cohort outline certain high risk features, which are associated with the risk of bacterial infections in patients with Child-A cirrhosis after AVB, and highlight the importance of prophylactic antibiotics, especially, in this specific subgroup among the otherwise low-risk strata of patients with cirrhosis.

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Table.1 Baseline chracteristics and outcomes in patients with Child-A cirrhosis presenting with variceal bleed

Variable	Child-A cirrhosis with post-bleed infection (n = 13)	Child-A cirrhosis without post-bleed infection (n = 118)	*P* value
Age (years)	44.3 ± 14.2	44.9 ± 11.6	0.972
Males (n%)	12 (92.3)	95 (79.8)	0.429
MELD score	13 (10–15)	11 (9–13)	0.06
Aetiology (n%) ALD NAFLD Viral cirrhosis Other aetiologies	 4 (30.7) 6 (46.2) 3 (23.1) 0	 58 (49.2) 23 (19.5) 14 (11.8) 23 (19.5)	0.669
PVT (n%)	1(6.9)	15 (8.8)	0.653
HCC (n%)	4(18.2)	5 (4.8)	0.001
SBP (mmHg)	96.9 ± 19.1	102.4 ± 11.4	0.128
Heart rate (beats/min)	114 ± 21	99 ± 16	0.006
Hypotension at presentation (n%)	7 (53.8)	4 (3.4)	<0.001
Endotracheal intubation (n%)	6 (46.2)	1 (0.9)	<0.001
Lactate (mmol/L)	7.6 ± 6.7	2.7 ± 2.2	<0.001
Haemoglobin (g/dl)	6.7 ± 1.8	8.5 ± 2.3	0.006
TLC (mm3)	6540 ± 1952	7230 ± 3372	0.449
Platelets (X1000/ mm3)	72 ± 30	82 ± 44	0.281
Bilirubin (mg/dl)	2.58 ± 0.7	1.83 ± 1.4	0.069
Albumin (g/dl)	3.3 ± 0.5	3.3 ± 0.4	0.547
INR	1.32 ± 0.12	1.28 ± 0.17	0.466
Creatinine (mg/dl)	0.98 ± 0.5	0.81 ± 0.2	0.09
Endoscopic findings **EV related** **GV related**	11 (84.6) 2 (15.4)	110 (89.8) 12 (10.2)	0.461
Active bleeding on endoscopy (n%)	7 (53.8)	19 (15.4)	0.003
Failure to control bleed (n%)	7 (53.8)	4 (3.4)	<0.001
Early rebleeding (n%)	1 (8.5)	3 (2.5)	0.861
Treatment for failure to control bleed No therapy EBL Glue Stent placement TIPS	0 0 0 2 5	0 0 2 1 1	
6-week mortality (n%)	6 (46.2)	3 (2.5)	<0.001

Data are presented as Mean ± SD for normally distributed quantitative variables, median (Range) for non-normally distributed quantitative variables and as n(%) for qualitative variables.

List of abbreviations: ALD, alcoholic liver disease; ALT, alanine transferase; AST, aspartate transferase; ALP, alkaline phosphatase; EBL, endoscopic band ligation; EV, oesophageal varices; GV, gastric varices; HCC, hepatocellular carcinoma; INR, international normalised ratio; MELD, model for end stage liver disease; NAFLD, non-alcoholic fatty liver disease; PVT, portal vein thrombosis; PEBU, post endoscopic band ligation; PRBC, packed red blood cells; SBP, systolic blood pressure; TLC, total leucocyte count; TIPS, transjugular intrahepatic portosystemic shunt; UTI, urinary tract infection.

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CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Sanchit Sharma: Data collection and writing of draft.

Samagra Agarwal: Statistical analysis.

Anoop Saraya: Conceptualisation and critical revision of draft.

CONFLICTS OF INTEREST

None.

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