Impact of Liver Impairment on Severity and Outcome of *Staphylococcus aureus* Bacteremia

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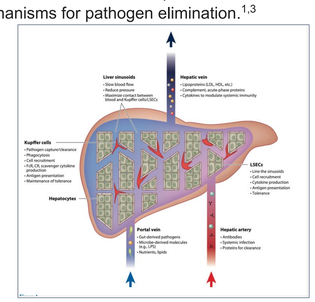
Background

- There is limited information in the relationship between liver impairment and *Staphylococcus aureus* infection. A 2017 study found a 20,000 annual number of deaths due to *S. aureus* bacteremia in the U.S., it's attributed to its virulence factors and immune evasive factors.[1,2]
- The hepatic system plays a role in an infection response that's dependent on the liver's structure and function. Kupffer cells in the liver is a paramount host defense mechanisms for pathogen elimination.[1,3]



- According to the CDC data in 2018, there are 4.5 million U.S. adults who have been diagnosed with liver diseases.[4] Patients with liver disease and admitted for acute care are more susceptible to hospital acquired infections, this immunocompromised population face a higher mortality rate due to a bloodstream infection.[3]
- This would suggest patients with liver impairment such as cirrhosis and its accompanying complications spontaneous bacterial peritonitis (SBP), gastrointestinal variceal bleeding, portal hypotension and hepatic encephalopathy would further the patients immunocompromised state thereby affecting the severity and outcome of infection.[3,4]

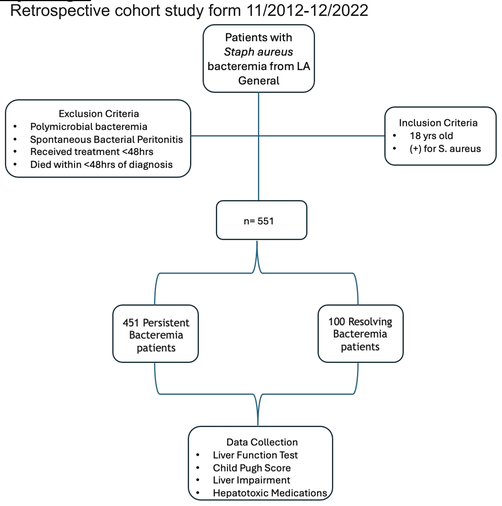
Objectives

- To evaluate the impact of liver impairment on the clinical severity and outcome of patients with *Staphylococcus aureus* bacteremia

Methods

Study Design:

- Retrospective cohort study form 11/2012-12/2022



Study Endpoints:

- Severity of presentation measured by ICU admission, need for vasopressor (septic shock), baseline thrombocytopenia
- Outcome measures include length of stay and 30-day mortality

Statistical Analysis:

- Patients will be grouped based on presence or absence of liver impairment compared to the severity of clinical presentation and outcome. Graphpad prism, t-test, chi square, and Fisher's exact test analyses was used for continuous and categorical variables where appropriate

Results

Table 1: Patient Characteristics

Characteristics	Patients with SAB (N= 551), n (%)	Cirrhosis (N= 68), n (%)	Non-Cirrhosis (N= 483), n (%)	P-value
Sex				
Male	414 (75)	52 (76)	362 (75)	0.881
Female	135 (25)	16(24)	119(25)	
Age (yrs)				
18-34	66 (12)	2 (3)	64 (13)	0.219
35-64	388 (71)	55 (81)	333 (69)	
65+	95 (17)	11 (16)	84 (18)	
Comorbidities				
Cardiovascular	355(64)	37 (54)	318 (65)	0.078
Diabetes	227 (41)	32 (47)	195 (40)	0.296
Lung Disease	26 (5)	2 (3)	24 (4)	0.758
Liver Disease	104 (19)	68 (100)	44 (9)	<0.001
Renal Disease	117 (21)	15 (22)	102 (21)	0.874
History of *S. aureus* Infection	68(12)	8(12)	60(12)	>0.999
Pitt Bacteremia Score				
0-3	470 (85)	60(88)	410(85	0.584
≥4	81(15)	8(12)	73(15)	
Source Risk of SA Bacteremia				
Low risk	144(26)	17(25)	127(26)	0.808
Intermediate risk	234(42)	32(47)	202(42)	
High risk	164(30)	19(27)	145(30)	
Top 5 Sources of Infection				
SSTI	106(19)	16(23)	90(19)	0.328
Endocarditis	84(15)	6(8)	78(16)	0.148
Pneumonia	55(10)	10(15)	45(9)	0.191
Meningitis	50(10)	0	50(10)	0.002
Non-Spinal Abscess	55(10)	8(12)	47(10)	0.664

Figure 1. Child Pugh score classification in patients with cirrhosis (n=68)

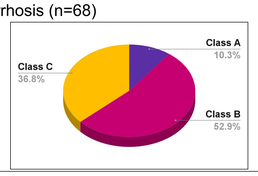


Figure 2. Percentage of Patients with Elevated LFTs at Baseline and at Highest during SAB in patients with cirrhosis (n=68) and patients without cirrhosis (n=442)

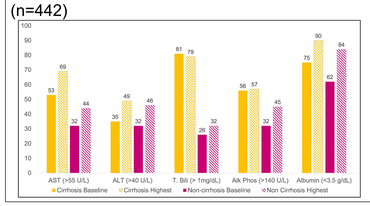


Figure 3. Top 5 most common hepatotoxic medications administered during the course of infection in patients with cirrhosis (n=68) and patients without cirrhosis (n=476)

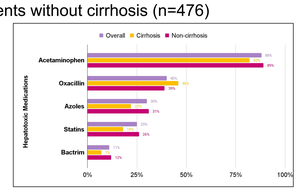


Figure 4. Severity and outcome endpoints measured by lengths of time (days) between patients with and without cirrhosis. **A**, shows the duration of vasopressor therapy. **B**, measures the duration of hospital stay. **C**, measures the number of days spent in the ICU. **D**, indicates the number of days positive for SAB.
**Reported as median with interquartile range
One outlier removed from (C**) and 9 from (**B**) because duration >100 days

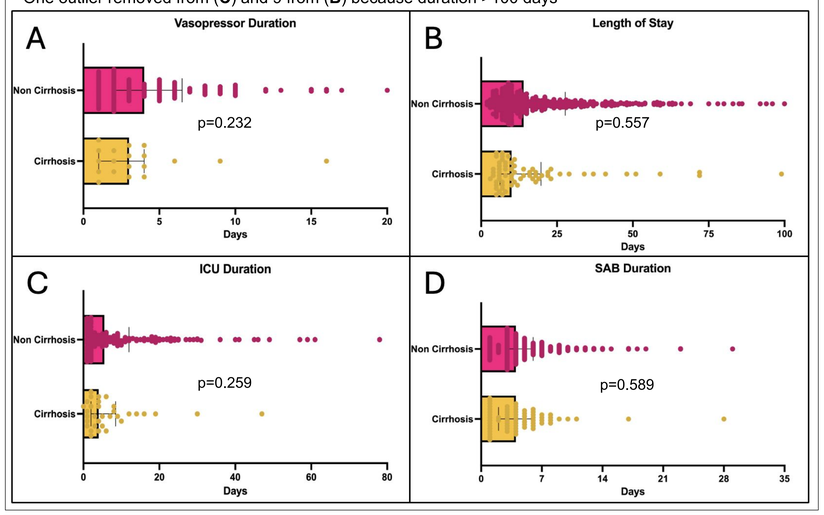


Figure 5. Outcomes and severity endpoints measured by percentage of 30-day mortality, need for vasopressor therapy, ICU admission and thrombocytopenia in patients with cirrhosis (n=68) and without cirrhosis (n=442).

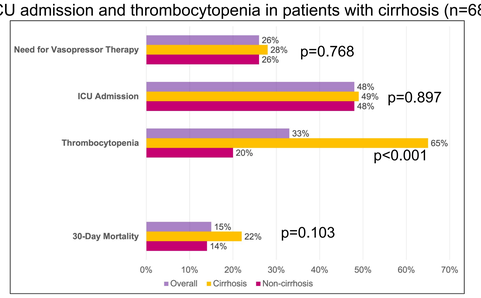
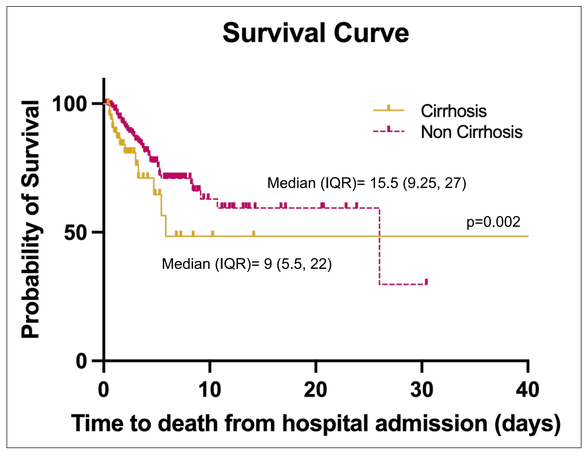


Figure 6. Kaplan Meier survival curve between patients with cirrhosis (n= 68) and patients without cirrhosis (n=473). A Gehan-Breslow-Wilcoxon test showed statistical significance between the survival curves (p=0.002).
*n=541, excluded 10 patients for either a missing mortality date, hospital discharge date, or having no record of survival, and 1 patient was treated as an outlier because their time to death >40 days.



Discussion

- Both groups did not differ in age, history of SA infection, PBS, and source risk of bacteremia regardless of underlying liver disease.
  - SAB cases involved more males (75%) and most are within the age of 35-64 (71%) with a trend towards higher proportion in the cirrhosis group than those without (81% vs 69%; p=0.219)
  - An intermediate risk of death hold a greater percentage across both groups (47% vs 42%; p=0.808)
- Patients with cirrhosis were less likely to have underlying cardiovascular disease compared to those without cirrhosis (54% vs 65%).
- SSTI was the most common source of infection overall (19%); patients with cirrhosis had slightly higher rate of SSTI (23% vs 19%) and pneumonia (15% vs 9%).
- Most of the patient with cirrhosis had a Child Pugh Class of B or C, 52.9% and 36.8%, respectively.
- Both patients with cirrhosis and non-cirrhosis were on the same top 5 hepatotoxic medications during hospital stay. The percentage of patients on these top 5 medications was similar across both groups.
  - The lower percentage of patient with cirrhosis vs non-cirrhosis administered hepatotoxic medications suggests that clinicians are already cautious in using these medications in patients with liver impairments.
- There were significantly more patients with cirrhosis who had elevated LFTs at baseline and elevated LFTs at the highest values during hospital stay compared to non-cirrhosis patients (p<0.001) in AST, ALT, T. Bili, Alk Phos, and decreased Albumin levels.
- Patients with cirrhosis had a higher incidence of thrombocytopenia at baseline compared to those without cirrhosis (65% vs 20%, p <0.001).
- Patients with cirrhosis had a 50% higher 30-day mortality compared to their non-cirrhotic counterparts, whereas ICU admission and need for vasopressor therapy were relatively similar across groups. Patients with cirrhosis had a shorter time to death in the hospital, median of 9 days from admission vs 15.5 days for their non-cirrhotic counterparts, leading to a reduced duration of ICU stay, vasopressor therapy, SAB, and LOS.

Conclusion

Nearly half of all patients recorded required ICU admission, more than 25% required vasopressor support, and 15% had 30-day mortality. ICU admission and vasopressor support were similar across cirrhosis and non-cirrhosis groups (49% vs 48% and 28% vs 26%), whereas 30-day mortality was >50% higher in cirrhosis patients vs non-cirrhosis patients (22% vs 14%). While the underlying liver impairment did not correlate with severity of acute presentation, it likely compromised the host's overall ability to recover from the acute insult from the infection. Future studies should investigate in detail potential complications such as secondary infections or metabolic derangements that may have contributed to the cause of death in patients with cirrhosis.

Limitations

- Single center study
- Missing data, including:
  - Liver Function Test
  - INR
  - Baseline and bacteremia onset values
- Missing MRN and FIN numbers
- Cannot determine causation, only association

References

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