

Cellulitis in Chronic Liver Disease in Tertiary Care Centre in South India

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Abstract: ***Background and Aim:** Cellulitis represents a significant complication in patients with chronic liver disease. This study aimed to investigate the incidence, clinical characteristics, and microbiological profile of cellulitis in patients with chronic liver disease at a tertiary care center in South India. **Methods:** This prospective observational study included 55 patients with chronic liver disease who developed cellulitis between January 2023 and December 2023. Patient demographics, etiology of liver disease, comorbidities, site of infection, microbiological data, and outcomes were analyzed. **Results:** Among 470 hospitalized cirrhotic patients, 55 (11.7%) developed cellulitis. The mean age was 52.8 ± 10.4 years, with male predominance (88%). Alcohol (45.5%) and NASH (29.1%) were the predominant etiologies of cirrhosis. Most patients had advanced liver disease (Child-Pugh C: 52.7%, B: 43.6%). Diabetes mellitus was the most common comorbidity (40%). Lower limb involvement was predominant (63.6%), with 45.5% showing bilateral involvement. Culture positivity was observed in 52% of cases, with gram-negative organisms predominating. *E. coli* and *Acinetobacter baumannii* were the most common isolates, with 61% showing multidrug resistance. The overall mortality rate was 3.6%. **Conclusion:** Cellulitis is a common complication in chronic liver disease, particularly in advanced stages. Gram-negative organisms with high antimicrobial resistance predominate, emphasizing the need for appropriate empirical antibiotic selection. Early recognition and appropriate management result in favorable outcomes despite the severity of underlying liver disease.*

Keywords: Chronic Liver Disease; Cellulitis; Cirrhosis; Bacterial Infections; Antimicrobial Resistance; Gram-Negative Bacteria; Liver Failure

1. Introduction

Chronic liver disease (CLD) represents a significant global health burden, with particularly high prevalence rates in South Asian countries including India (1). The condition encompasses a spectrum of progressive disorders characterized by hepatic dysfunction and ultimately leading to cirrhosis. Patients with CLD are notably susceptible to various infectious complications due to their immunocompromised state and altered protein metabolism (2).

Cellulitis, a common bacterial skin infection affecting the deep dermis and subcutaneous tissues, presents a significant challenge in patients with chronic liver disease. The compromised immune system, coupled with decreased protein synthesis and portal hypertension in these patients, creates an environment conducive to the development and progression of soft tissue infections (3). The incidence of cellulitis in CLD patients is reported to be significantly higher than in the general population, with some studies suggesting a 10-15 fold increase in risk (4).

The pathophysiology underlying the increased susceptibility to cellulitis in CLD patients is multifactorial. Reduced complement levels, impaired neutrophil function, and decreased opsonization capacity contribute to weakened host defenses against bacterial invasion. Additionally, the presence of edema secondary to hypoalbuminemia and portal hypertension provides an ideal environment for bacterial growth and spread (5). The compromised lymphatic drainage in these patients further complicates the resolution of infections and may lead to prolonged healing times.

In the context of South India, where the prevalence of chronic liver disease is notably high due to various factors including viral hepatitis, alcoholic liver disease, and metabolic syndrome, understanding the relationship between CLD and cellulitis becomes particularly relevant (6). The tropical climate, coupled with socioeconomic factors and healthcare access disparities, may influence both the incidence and outcomes of cellulitis in this population.

Early recognition and appropriate management of cellulitis in CLD patients is crucial, as these infections can progress rapidly and lead to severe complications including sepsis, which carries a particularly high mortality rate in this vulnerable population (7). The diagnosis of cellulitis in CLD patients can be challenging due to the overlap of symptoms with other complications of liver disease, such as edema and skin changes related to portal hypertension.

Current literature suggests that the microbial etiology of cellulitis in CLD patients may differ from that seen in the general population, with a higher prevalence of gram-negative organisms and resistant pathogens (8). This altered microbial spectrum has important implications for empiric antibiotic selection and overall management strategies. Furthermore, the presence of portal hypertension and associated complications may affect drug distribution and metabolism, necessitating careful consideration of antimicrobial dosing (9).

The economic burden of treating cellulitis in CLD patients is substantial, with prolonged hospital stays and increased healthcare utilization compared to non-CLD patients with cellulitis. This impact is particularly significant in developing countries where healthcare resources may be limited (10). Understanding the incidence and patterns of

cellulitis in this population can help in resource allocation and development of preventive strategies.

The present study aims to investigate the incidence of cellulitis among patients with chronic liver disease in a tertiary care center in South India. By analyzing the demographic patterns, risk factors, and clinical characteristics of cellulitis in this population, we seek to provide valuable data that can inform clinical practice and improve patient outcomes.

2. Methodology

Study Design and Setting:

This retrospective observational study was conducted at a tertiary care center in South India, from January 2023 to December 2023. The study protocol received approval from the Institutional Ethics Committee.

Study Population

A total of 55 patients with diagnosed chronic liver disease who developed cellulitis during the study period were included. The diagnosis of chronic liver disease was based on clinical, biochemical, and radiological criteria, while cellulitis was diagnosed based on standard clinical criteria including erythema, warmth, tenderness, and swelling of the affected area.

Data Collection

Patient data were collected using a standardized data collection form. Demographic information including age and sex was recorded at admission. The length of hospital stay was calculated from the dates of admission and discharge.

Clinical Assessment

A comprehensive clinical evaluation was performed for all patients, including:

- Detailed history of chronic liver disease and its etiology
- Presence of comorbidities including diabetes mellitus and hypertension
- Associated complications such as Acute Respiratory Distress Syndrome (ARDS) and tuberculosis
- Physical examination with particular attention to the site and characteristics of cellulitis

Laboratory Investigations

The following laboratory parameters were assessed:

- a) Liver Function Tests:
 - Total protein and albumin levels
 - Prothrombin Time (PT) and International Normalized Ratio (INR)
- b) Complete Blood Count with total leukocyte count
- c) Renal Function Tests including serum creatinine
- d) Serum ammonia levels

Microbiological Assessment

Multiple cultures were obtained including:

- Ascitic fluid culture
- Wound swab culture from the cellulitis site
- Blood culture
- Urine culture

The number and types of organisms isolated were documented. Antimicrobial sensitivity patterns were recorded to guide antibiotic therapy.

Disease Severity Assessment

The severity of liver disease was assessed using:

- 1) Model for End-Stage Liver Disease (MELD) score
- 2) Child-Turcotte-Pugh (CTP) score

Treatment Documentation

Detailed records were maintained regarding:

- Types of antibiotics used
- Duration of antibiotic therapy
- Response to treatment
- Any modifications in antibiotic regimen based on culture sensitivity

Outcome Measures

Patient outcomes were categorized as:

- Complete recovery and discharge
- Discharge against medical advice
- Mortality

Data Management

All collected data were entered into a structured database using Microsoft Excel. Data validation was performed to ensure accuracy and completeness of entries.

Statistical Analysis

Statistical analysis was performed using statistical software SPSS version 25. Continuous variables were expressed as mean \pm standard deviation or median with interquartile range based on the distribution of data. Categorical variables were expressed as frequencies and percentages.

The following analyses were performed:

- Descriptive statistics for demographic and clinical characteristics
- Correlation analysis between various clinical parameters and outcomes
- Assessment of risk factors for adverse outcomes
- Analysis of microbiological patterns and antibiotic sensitivity

Quality Control Measures

To ensure data quality:

- All laboratory investigations were performed in accredited laboratories
- Standard operating procedures were followed for sample collection and processing
- Regular calibration of laboratory equipment was maintained
- Double verification of critical data points was performed

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants or their legal representatives. Patient confidentiality was maintained throughout the study period.

3. Results

The study population demonstrated a predominance of alcohol-related liver disease (45.5%), followed by NASH (29.1%) and viral hepatitis B (21.8%). Diabetes mellitus was the most common comorbidity, affecting 40% of patients, followed by hypertension (27.3%). The majority of patients had advanced liver disease, with 52.7% classified as Child-Pugh C and 43.6% as Child-Pugh B, indicating a significantly compromised patient population.

Table 1: Patient Demographics and Disease Characteristics (N=55)

Characteristic	Category	n (%)
Etiology of CLD	Alcohol (ETOH)	25 (45.5%)
	NASH	16 (29.1%)
	HBV	12 (21.8%)
	HCV	1 (1.8%)
	Cryptogenic	1 (1.8%)
Comorbidities	Diabetes Mellitus	22 (40.0%)
	Hypertension	15 (27.3%)
	CKD	7 (12.7%)
	Hypothyroidism	3 (5.5%)
	Hyperthyroidism	1 (1.8%)
CTP Classification	Class A	2 (3.6%)
	Class B	24 (43.6%)
	Class C	29 (52.7%)

The pattern of cellulitis showed a predilection for unilateral limb involvement (63.6%), though bilateral involvement was also substantial (45.5%). A significant proportion of patients developed ulcers (43.6%), while necrotizing fasciitis was rare (3.6%). Microbiological analysis revealed a predominance of polymicrobial infections (68.2% of cultured cases), with gram-negative organisms, particularly *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, being the most common pathogens.

Table 2: Clinical Manifestations and Microbiology (N=55)

Parameter	Category	n (%)
Site of Infection	Unilateral limb	35 (63.6%)
	Bilateral limb	25 (45.5%)
	Ulcers	24 (43.6%)
	Necrotizing fasciitis	2 (3.6%)
Culture Results (n=22)	Monomicrobial growth	7 (31.8%)
	Polymicrobial growth	15 (68.2%)
Predominant Organisms	<i>Acinetobacter baumannii</i> , <i>Pseudomonas aeruginosa</i>	

The mortality analysis of two cases revealed several common features: both patients were elderly (63 and 74 years), had significant comorbidities, and presented with ACLF Grade 2 with an AARC score of 9. Both cases showed substantial organ dysfunction, as evidenced by elevated bilirubin, altered coagulation profiles, and renal impairment. Despite the overall mortality rate being relatively low (3.6%), these cases highlight the potential severity of cellulitis in patients with advanced liver disease and multiple comorbidities.

Table 3: Mortality Cases Analysis (n=2)

Parameter	Case 1	Case 2
Age/Gender	63/Female	74/Male
Etiology	NASH	ETOH
Comorbidities	DM, CVA	CAD, CKD
Site	Right lower limb	Left lower limb
Organism	Klebsiella	Pseudomonas
ACLF Grade/AARC Score	02-Sep	02-Sep
Lab Parameters		
- Total Bilirubin (mg/dL)	6.0	10
- INR	1.8	2.5
- Lactate	2	2
- Creatinine (mg/dL)	2.5	3

4. Discussion

The present study demonstrates that cellulitis represents a significant complication in patients with chronic liver disease, with an overall prevalence of 11.7% among hospitalized cirrhotic patients. This finding aligns with previous studies from South India, including Sanglodkar et al. who reported a prevalence of 7.4% [11] and Revathy et al. who found an 11.0% prevalence [12]. The consistency in these figures suggests that cellulitis remains a persistent challenge in the management of chronic liver disease in the South Indian population.

Demographics and Risk Factors

Our patient cohort demonstrated a male predominance (88%) and a mean age of 52.8 ± 10.4 years, which closely mirrors the demographic patterns reported by Sanglodkar et al. [11] and Mohan et al. [13]. The etiology of cirrhosis in our study showed alcohol (45.5%) and NASH (29.1%) as the predominant causes, reflecting the changing patterns of liver disease in India. This distribution differs slightly from earlier studies where alcohol was more heavily predominant, suggesting a potential shift in the epidemiological pattern of chronic liver disease in South India [13, 14].

Diabetes mellitus was present in 40% of our patients, comparable to the findings of Sanglodkar et al. (36%) [11] and higher than reported by Jain et al. (30.8%) [14]. This high prevalence of diabetes may contribute to the increased susceptibility to cellulitis, as diabetes is a well-established risk factor for skin infections.

Disease Severity and Clinical Presentation

A notable finding in our study was the correlation between disease severity and cellulitis occurrence. The majority of our patients had advanced liver disease (Child-Pugh C: 52.7%, B: 43.6%), consistent with findings from previous studies [11, 13]. This pattern supports the hypothesis that deteriorating liver function increases susceptibility to bacterial infections, likely due to compromised immune function and altered protein metabolism.

Microbiological Profile

The culture positivity rate in our study was 52%, comparable to the 53.8% reported by Revathy et al. [12] and 52% by Sanglodkar et al. [11]. The predominance of gram-negative organisms, particularly *E. coli* and *Acinetobacter baumannii*, aligns with previous findings but shows some evolution in the bacterial spectrum. While earlier studies by Mohan et al. [13] and Jain et al. [14] reported primarily *E. coli* and

Klebsiella, our study noted an emergence of Acinetobacter species, suggesting a possible shift in local bacterial ecology.

Antimicrobial Resistance

The high prevalence of multidrug-resistant organisms (61%) in our study is particularly concerning and comparable to the findings of Jain et al. (69%) [14]. This trend of increasing antimicrobial resistance poses a significant therapeutic challenge and necessitates careful consideration in empirical antibiotic selection.

Clinical Outcomes

Despite the severity of underlying liver disease and high prevalence of multidrug-resistant organisms, our study showed a relatively low mortality rate (3.6%) compared to earlier studies by Mohan et al. (19%) [13] and Jain et al. (22.2%) [14]. This improvement in outcomes might be attributed to:

- 1) Earlier recognition of infection
- 2) More appropriate empirical antibiotic selection
- 3) Better supportive care measures
- 4) Improved understanding of the disease process

Site of Infection

Lower limb involvement was predominant in our study (63.6%), consistent with findings across all referenced studies [11-14]. This consistent pattern suggests that local factors such as edema, compromised circulation, and portal hypertension play crucial roles in the pathogenesis of cellulitis in cirrhotic patients.

Clinical Implications

Our findings have several important implications for clinical practice:

- 1) The high prevalence of multidrug-resistant organisms necessitates careful consideration in empirical antibiotic selection
- 2) Regular surveillance of local antimicrobial resistance patterns is crucial
- 3) Early recognition and intervention may improve outcomes
- 4) Preventive strategies may be particularly important in patients with advanced liver disease

Study Limitations

The single-center nature of our study and the relatively short follow-up period may limit the generalizability of our findings. Additionally, the impact of prophylactic antibiotics and long-term outcomes could not be assessed in this study design.

5. Future Directions

Future research should focus on:

- 1) Development of predictive models for cellulitis risk in cirrhotic patients
- 2) Evaluation of preventive strategies
- 3) Assessment of the role of antibiotic prophylaxis in high-risk patients
- 4) Long-term follow-up studies to assess recurrence rates and outcomes

6. Conclusion

Our study demonstrates that cellulitis is a significant complication in patients with chronic liver disease, with a prevalence of 11.7% among hospitalized cirrhotic patients. Gram-negative organisms, particularly E. coli and Klebsiella, were the predominant pathogens, with a concerning rate of multidrug resistance (61%). The study highlights that advanced liver disease (Child-Pugh C) and presence of comorbidities significantly impact the development of cellulitis. Despite the severity of infection, appropriate antibiotic therapy resulted in favorable outcomes in most cases, with a relatively low mortality rate of 3.6%.

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