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Non-Invasive Assessment of Hepatic Fibrosis in Sickle Cell Disease Using Shear Wave Elastography

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Abstract: ***Background: Sickle cell disease (SCD) is associated with chronic hemolysis and progressive multi-organ involvement, including hepatic injury. Early detection of liver fibrosis is essential for preventing long-term complications. Shear wave elastography is a non-invasive technique used to assess liver stiffness as a surrogate marker of fibrosis. Methods: This hospital-based cross-sectional study included 50 patients with sickle cell disease. Liver stiffness was measured using shear wave elastography and expressed in kilopascals (kPa). The primary objective was to assess hepatic fibrosis based on liver stiffness measurements. Results: The mean age of participants was 18.20 ± 6.24 years. The mean liver stiffness was 6.62 ± 1.35 kPa. Fibrosis grading revealed 22.0% of patients in F0–F1 stage, 62.0% in F2 stage, and 16.0% in F3 stage. No patient was in F4 stage. Conclusion: Shear wave elastography is a reliable and effective non-invasive modality for assessing hepatic fibrosis in sickle cell disease. The high prevalence of significant fibrosis in this predominantly young, asymptomatic cohort highlights the need for routine hepatic surveillance in SCD patients. Shear wave elastography should be considered for early detection of liver involvement and timely clinical management.***

Keywords: Sickle cell disease, Liver fibrosis, Shear wave elastography, Liver stiffness

1. Introduction

Sickle cell disease (SCD) is an inherited hemoglobin disorder characterized by chronic hemolysis, vaso-occlusive episodes, and progressive multi-organ damage. With improved survival, chronic complications such as hepatic involvement have become increasingly important contributors to morbidity (1,2).

The liver is particularly vulnerable in SCD due to recurrent vaso-occlusion, ischemia–reperfusion injury, and ongoing inflammation, leading to hepatocellular damage and fibrosis. Early hepatic fibrosis is often asymptomatic and may remain undetected until advanced stages, highlighting the need for timely evaluation (3,4).

Although liver biopsy is the gold standard for fibrosis assessment, its invasive nature limits routine use. Shear wave elastography is a non-invasive ultrasound-based technique that measures liver stiffness and serves as a reliable surrogate marker of fibrosis, making it suitable for repeated assessment in chronic conditions like SCD (5,6).

Aim: To study the liver stiffness in sickle cell disease patients and assess the proportion of patients with different grades of liver fibrosis.

Objective: To estimate the proportion of sickle cell disease patients with liver fibrosis.

2. Methodology

Study Design and Setting

This was a hospital-based prospective cross-sectional observational study conducted at Assam Medical College and Hospital, Dibrugarh for a period of 1 year.

Study Population

A total of 50 patients diagnosed with sickle cell disease were included in the study (7).

Inclusion Criteria

1) Confirmed diagnosis of Sickle cell disease based on hemoglobin electrophoresis or high-performance liquid chromatography (HPLC).
2) Age more than 13 years.
3) Sickle cell disease patients attending Outpatient and Inpatient department in General Medicine.
4) Willingness to provide informed consent to participate in the study.

Exclusion Criteria

1) Presence of cirrhosis, hepatocellular carcinoma, or decompensated liver failure.
2) Significant co-morbidities affecting liver function or iron metabolism (e.g., chronic hepatitis B or C infection, significant alcohol use disorder, MASLD).
3) Pregnant or lactating females due to potential confounding effects on liver stiffness and serum ferritin levels.
4) Inability to undergo shear wave elastography procedure due to technical limitations (e.g., Body Mass Index > 40,

ascites, or other conditions that preclude reliable elastography measurements).
5) Unwilling to give consent.

Ethical Clearance and Consent
Approval for the study was obtained from the Institutional Ethics Committee of Assam Medical College and Hospital. Informed written consent was obtained from patients or their guardians after explaining the study's purpose.

Data Collection
A detailed clinical evaluation was performed, including demographic characteristics and relevant medical history.

Liver Stiffness Measurement
Liver stiffness was assessed using shear wave elastography, a non-invasive ultrasound-based technique. The procedure was performed by an experienced radiologist.

Patients were examined after overnight fasting in the supine or slight left lateral position. Following B-mode ultrasonography, a region of interest was placed in the right hepatic lobe (3–5 cm below the capsule), avoiding vascular and biliary structures. Measurements were obtained during brief breath-hold. Multiple readings were recorded, and the median value was taken as liver stiffness (kPa). Values were interpreted as a surrogate marker of hepatic fibrosis and categorized into stages (F0–F4) using standard cut-offs.

Statistical Analysis
Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 20.0 (SPSS Inc., Chicago, USA) along with Microsoft Excel 2010. Continuous variables were summarized as mean with standard deviation (mean ± SD), whereas categorical variables were described in terms of frequency and percentage. A p-value of less than 0.05 was considered to indicate statistical significance.

3. Results and Discussion

Age Distribution
Patients ranged from childhood to middle age, with a strong predominance in the ≤20 years group (40; 80%). Smaller proportions were seen in 20–29 years (6; 12%), 30–39 years (3; 6%), and 40–49 years (1; 2%), with no patients ≥50 years. The mean age was 18.20 ± 6.24 years.

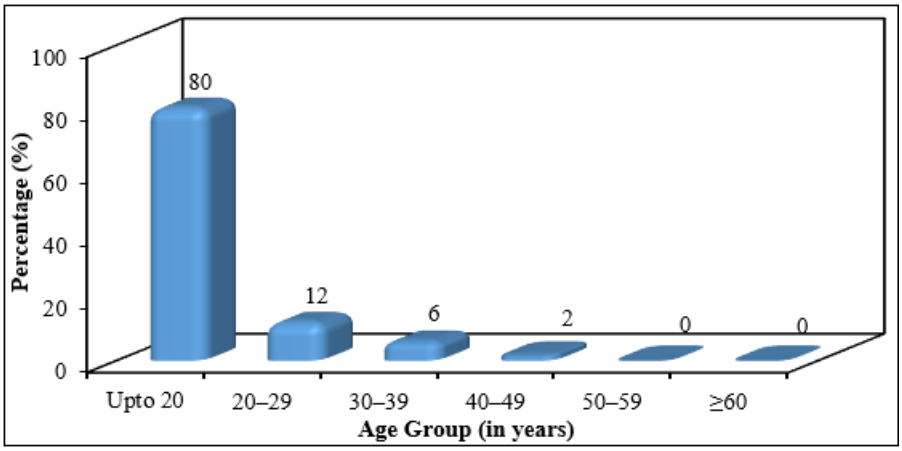

Figure 1: Age Distribution

In a study by Alvarez et al., age of patients was between 10 and 21 years with a mean age of 15.9 years (8). In a study by Sukla et al., the mean age was between 20 and 30 years with a median of 27 years (9). These findings are broadly consistent with our predominantly young study population.

Gender Distribution
Out of 50 patients, 27 (54.0%) were male and 23 (46.0%) were female. The male-to-female ratio was 1.17:1, indicating a slight male predominance in the study population.

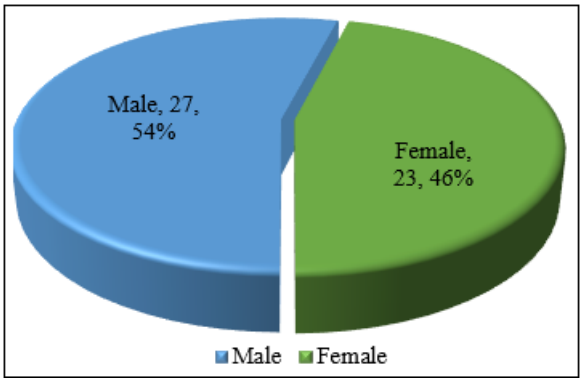

Figure 2: Gender Distribution

Alvarez et al. found that out of nineteen patients, 12 were male (8). The slight male predominance seen in our study is consistent with these reports.

Distribution of Patients According to Ethnicity
Of the total 50 study participants, 37 (74.0%) belonged to the tribal population, while 13 (26.0%) were from the non-tribal

population. The majority of patients with sickle cell disease in the present study were from the tribal community, reflecting the known higher prevalence of SCD among tribal populations in northeastern India.

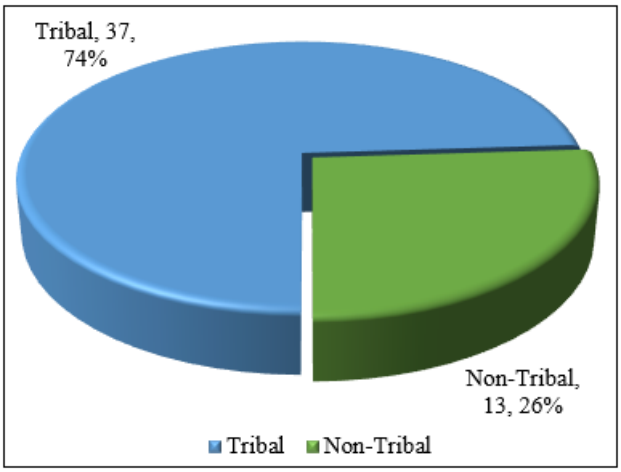

Figure 3: Distribution of patients according to Ethnicity

Distribution Based on Sickle Cell Genotype

The most common genotype was HbSS, seen in 18 patients (36%), followed by HbS/HbE in 12 patients (24%), HbAS in 11 patients (22%), and HbS/β-thalassemia in 9 patients (18%).

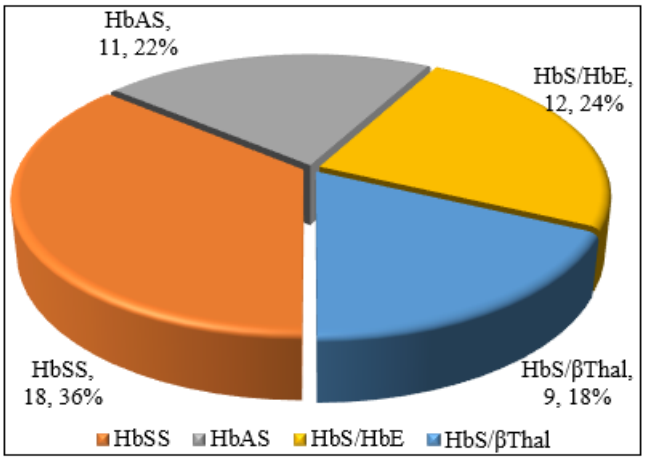

Figure 4: Distribution Based on Sickle Cell Genotype

Distribution of Patients Based on Transfusion History

The majority of patients (46; 92.0%) had received blood transfusions, while 4 patients (8.0%) had no history of blood transfusion.

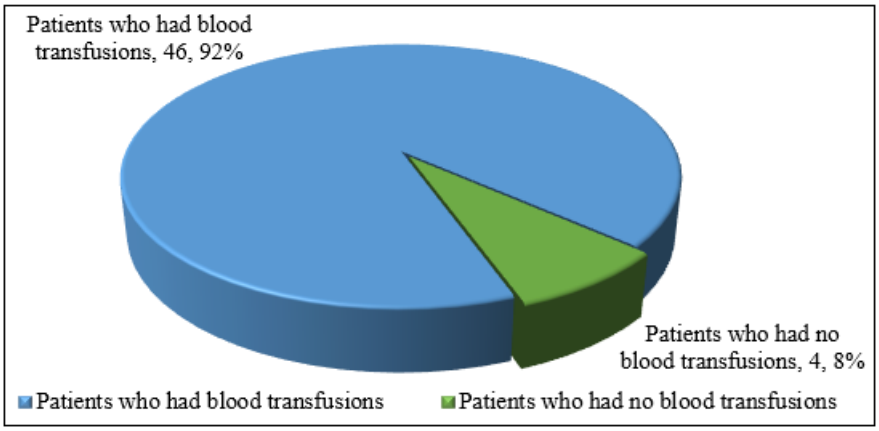

Figure 5: Distribution of patients based on Transfusion History

Distribution of Patients According to Number of Blood Transfusions per Year

With respect to frequency, 26 patients (52.0%) received fewer than 5 transfusions per year, 18 patients (36.0%) received 5–10 transfusions, and 6 patients (12.0%) received more than 10 transfusions per year.

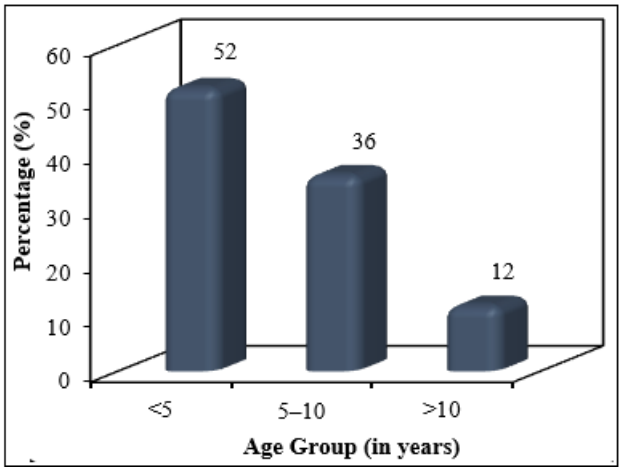

Figure 6: Number of Blood Transfusion per year

Fibrosis Grading Based on Liver Stiffness Measurement (LSM)

Fibrosis grading based on liver stiffness measurement (LSM) revealed that 11 patients (22.0%) were in the F0–F1 stage, 31

patients (62.0%) were in F2 stage, and 8 patients (16.0%) were in F3 stage. No patients were observed in the F4 stage. The mean liver stiffness measurement was 6.62 ± 1.35 kPa.

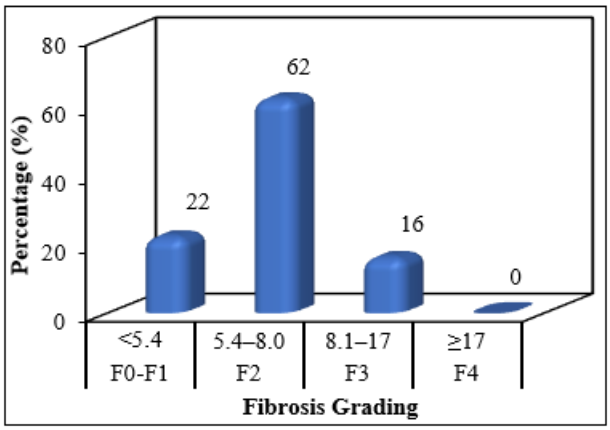

Figure 7: Fibrosis Staging Based on LSM

The preponderance of F2 fibrosis indicates that patients with SCD frequently have moderate hepatic fibrosis even in the absence of obvious clinical liver failure. Since early stages of fibrosis are frequently asymptomatic, this finding underscores the importance of non-invasive screening.

Castera et al. showed that early to moderate fibrosis phases are correlated with LSM values between 5 and 9 kPa (10). Similarly, Ziol et al. found that patients with F2 fibrosis had median LSM values of roughly 7–9 kPa (11). The mean LSM in our study (6.62 kPa) falls within this early-to-moderate fibrosis range. Singh et al.'s meta-analysis reported pooled cut-off values of approximately 7 kPa for significant fibrosis (≥F2) and more than 12–14 kPa for cirrhosis (12), which explains the absence of F4 fibrosis in our cohort.

These findings are consistent with previous reports demonstrating increased liver stiffness in SCD patients even in the absence of overt clinical liver disease. Shear wave elastography proved to be a reliable, safe, and reproducible non-invasive modality suitable for repeated evaluation, particularly in resource-limited settings. The high proportion of patients with moderate fibrosis (F2 stage) highlights the need for early screening and regular monitoring of hepatic involvement in SCD.

4. Conclusion

Hepatic fibrosis is a common and clinically significant complication in patients with sickle cell disease, even among a predominantly young population. Using shear wave elastography, we found that a substantial majority of patients had significant fibrosis corresponding to the early-to-moderate range, with many in the F2 and F3 stages. Importantly, most of these patients were asymptomatic from a hepatic standpoint, underscoring the silent but progressive nature of liver involvement in SCD.

Shear wave elastography proved to be a safe, reliable, and reproducible non-invasive modality for evaluating hepatic fibrosis in this patient population. Its non-invasive nature makes it particularly suitable for repeated longitudinal monitoring, which is essential for a chronic condition like SCD. Routine incorporation of shear wave elastography into the follow-up protocol for SCD patients may enable early detection of liver fibrosis, allowing for timely therapeutic interventions and potentially preventing progression to advanced fibrosis or cirrhosis.

5. Limitations

The present study has certain limitations. The sample size was relatively small, and the study was conducted at a single centre, which may limit the generalizability of the findings. Additionally, histopathological confirmation with liver biopsy was not performed to validate the elastography-based fibrosis staging. Future studies with larger, multicentre cohorts and biopsy correlation are recommended to further establish the diagnostic accuracy of shear wave elastography in SCD.

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