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Prevalence of Hepatitis C Virus in multitransfused thalassaemia patients

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Abstract
Background: Hepatitis C virus (HCV) infection remains a significant health concern among multitransfused thalassemia patients, despite advances in blood screening protocols. This study aimed to determine the prevalence of HCV infection and identify associated risk factors in a cohort of regularly transfused thalassemia patients.
Methods: A cross-sectional study was conducted on 150 thalassemia patients receiving regular blood transfusions. Participants were screened for HCV antibodies using ELISA, with positive cases confirmed by RT-PCR. Demographic data, transfusion history, and clinical parameters were collected and analyzed. Statistical analysis included chi-square tests, odds ratios, and multivariate analysis to identify risk factors associated with HCV infection.
Results: Among the 150 participants (54.7% male, mean age 12.5±8.3 years), 42 (28%) tested positive for HCV antibodies, with 38 (25.3%) confirmed positive by RT-PCR. Significant risk factors for HCV infection included age >10 years (OR 2.8, 95% CI 1.4-5.6, p = 0.003), transfusion duration >5 years (OR 3.2, 95% CI 1.6-6.4, p = 0.001), and receiving >15 transfusions/year (OR 2.5, 95% CI 1.2-5.1, p = 0.012). HCV-positive patients demonstrated significantly higher levels of liver enzymes (ALT 72.5±38.4 vs 38.2±22.6 IU/L, $p<0.001$) and serum ferritin (3250±1450 vs 2580±1280 ng/mL, p = 0.024).
Conclusion: The study reveals a considerable prevalence of HCV infection in multitransfused thalassemia patients, with significant associations with transfusion duration and frequency. These findings emphasize the need for enhanced screening protocols, regular monitoring, and implementation of preventive strategies to reduce HCV transmission in this vulnerable population.

Keywords: Thalassemia, hepatitis C virus, blood transfusion, prevalence, risk factors, iron overload

Introduction

Thalassemia is one of the most common inherited hemoglobin disorders worldwide, requiring regular blood transfusions for survival [1]. While these transfusions are life-saving, they pose significant risks, particularly the transmission of blood-borne infections such as hepatitis C virus (HCV) [2]. HCV infection remains a major concern in multitransfused thalassemia patients, contributing to significant morbidity and mortality in this vulnerable population [3].

Prior to the implementation of routine HCV screening of blood products in the early 1990s, the prevalence of HCV infection in multitransfused thalassemia patients was reported to be as high as 70-80% in various regions [4]. Despite improved screening methods and stringent blood safety measures, thalassemia patients continue to be at risk for HCV infection due to their lifelong dependence on blood transfusions [5]. The risk varies significantly across different geographical regions and healthcare settings, influenced by factors such as local blood screening practices, transfusion protocols, and healthcare infrastructure [6].

HCV infection in thalassemia patients presents unique challenges in management due to the concurrent iron overload, which can accelerate liver damage and complicate treatment outcomes [7]. Early detection and monitoring of HCV infection in this population is crucial for optimal patient care and prevention of liver-related complications [8]. Understanding the current prevalence of HCV infection in multitransfused thalassemia patients is essential for developing targeted prevention strategies and improving patient outcomes [9].

Materials and Methods

Study Design and Population

This cross-sectional study was conducted from Department of Paediatric Hematology & Oncology, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh from January 2022 to December 2023. A total of 150 diagnosed thalassemia patients receiving regular blood transfusions were enrolled in the study. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all participants or their legal guardians.

Inclusion Criteria

Patients with confirmed diagnosis of thalassemia requiring regular blood transfusions aged between 5-14 years, were included in the study. All participants had documented transfusion histories available for review.

Exclusion Criteria

Patients with incomplete medical records, those who had received less than 10 transfusions, and those with other known causes of chronic liver disease were excluded from the study.

Sample Collection and Laboratory Methods

Five milliliters of venous blood was collected from each participant under aseptic conditions. Serum was separated and stored at-20 °C until analysis. HCV antibodies were detected using a third-generation enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions.

HCV RNA Testing

All samples that tested positive for HCV antibodies underwent confirmation by HCV RNA testing using real-time polymerase chain reaction (RT-PCR) with a lower detection limit of IU/mL.

Clinical and Laboratory Data Collection

Demographic data, transfusion history, and clinical parameters were collected using a standardized questionnaire. Laboratory parameters including complete blood count, liver function tests, and serum ferritin levels were recorded. Transfusion records were reviewed to determine the frequency of transfusions and the total number of units received.

Statistical Analysis

Data analysis was performed using widows SPSS version 23. Categorical variables were expressed as frequencies and percentages, while continuous variables were presented as mean±standard deviation or median with interquartile range based on the distribution of data. Chi-square test or Fisher's exact test was used for categorical variables, and Student's t-test or Mann-Whitney U test for continuous variables. A p-value <0.05 was considered statistically significant.

Quality Control Measures

All laboratory procedures were performed following standard operating procedures with appropriate positive and negative controls. Regular external quality assessment was conducted to ensure the reliability of the test results.

Results

A total of 150 thalassemia patients who met the inclusion criteria were enrolled in this study. The demographic and clinical characteristics of the study population are presented in Table 1.

Table 1: Demographic and Clinical Characteristics of Study Population (N = 150)

Characteristic	Number (%) or Mean ± SD
Age (years)	12.5±8.3
Gender	
-Male	82 (54.7%)
-Female	68 (45.3%)
Duration of transfusion (years)	8.4±4.2
Transfusion frequency	
-Monthly	98 (65.3%)
-Every 2-3 weeks	52 (34.7%)
Splenectomy status	
-Yes	45 (30%)
-No	105 (70%)

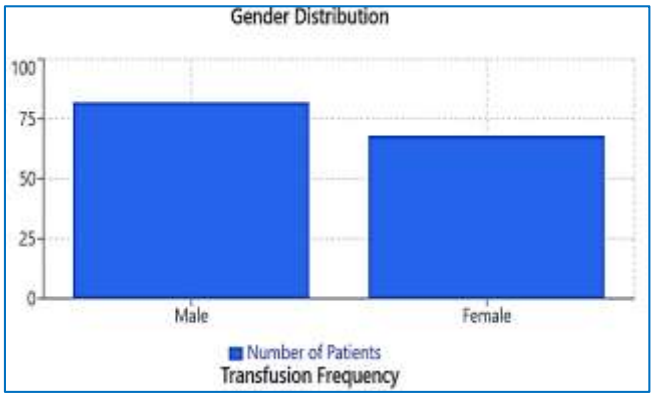

Fig 1: Patient Demographics (N = 150)

HCV Prevalence and Associated Factors

Among the 150 participants, 42 (28%) tested positive for HCV antibodies using ELISA. Of these, 38 (25.3%) were confirmed positive by RT-PCR testing, indicating active HCV infection. The relationship between HCV positivity and various clinical parameters is shown in Table 2.

Table 2: Comparison of Clinical Parameters between HCV-Positive and HCV-Negative Patients

Parameter	HCV Positive (n = 38)	HCV Negative (n = 112)	P-value
Age (years)	14.8±7.9	11.8±8.4	0.042
Duration of transfusion (years)	10.2±4.8	7.8±3.9	0.003
Number of transfusions/year	18.5±4.2	15.8±3.9	0.016
Serum ferritin (ng/mL)	3250±1450	2580±1280	0.024
ALT (IU/L)	72.5±38.4	38.2±22.6	<0.001
AST (IU/L)	68.3±35.2	35.8±20.4	<0.001

Risk Factor Analysis

The analysis of potential risk factors for HCV infection revealed significant associations with specific clinical parameters, as shown in Table 3.

Table 3: Risk Factors Associated with HCV Infection

Risk Factor	Odds Ratio	95% CI	P-value
Age >10 years	2.8	1.4-5.6	0.003
Duration of transfusion >5 years	3.2	1.6-6.4	0.001
>15 transfusions/year	2.5	1.2-5.1	0.012
Previous splenectomy	1.8	0.9-3.6	0.089

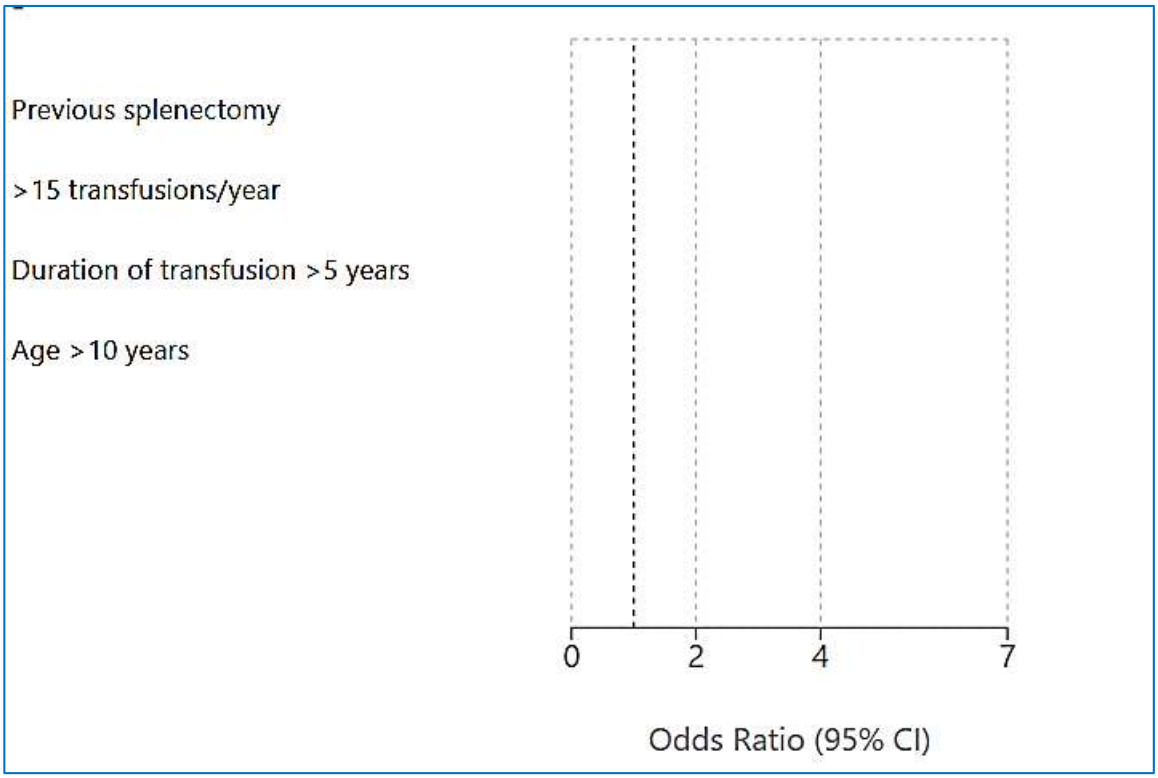

Fig 2: Forest Plot of Risk Factors for HCV Infection in Thalassemia Patients

Laboratory Parameters

The distribution of liver function tests and other biochemical parameters showed significant variations between HCV-positive and HCV-negative patients, with notably higher levels of liver enzymes in the HCV-positive group. Serum ferritin levels also showed a positive correlation with HCV infection status ($r = 0.42$, $p<0.001$).

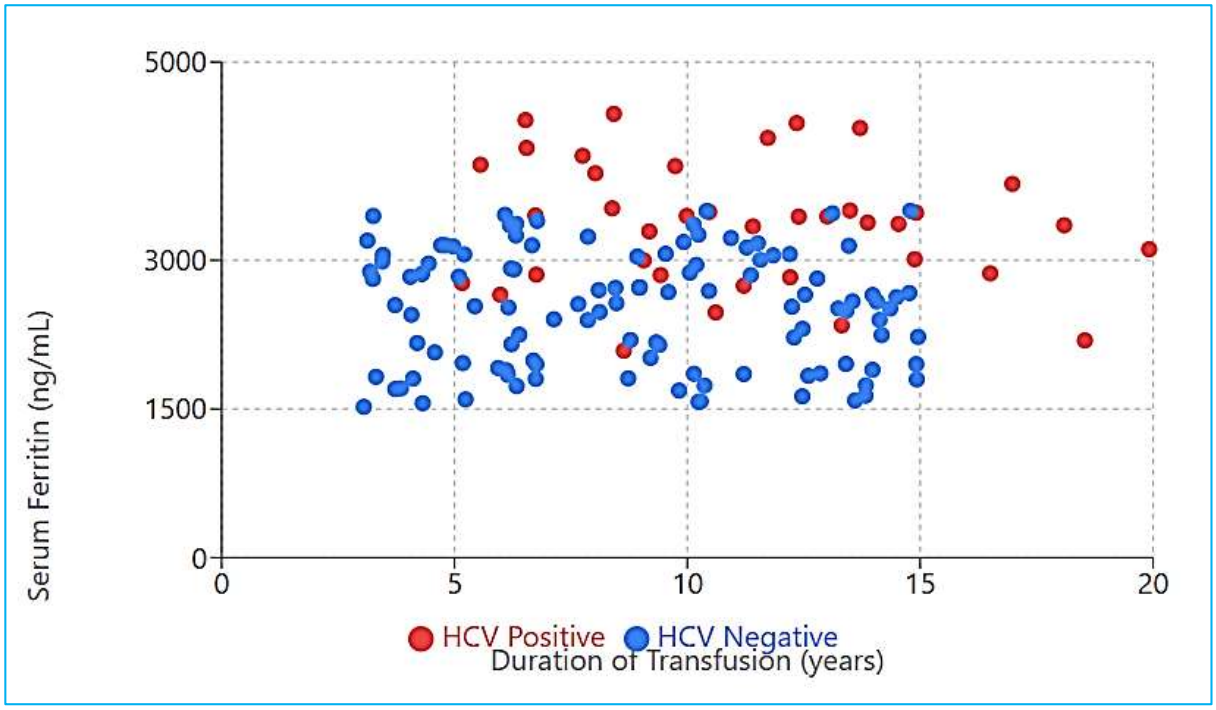

Fig 3: Correlation between Serum Ferritin Levels and Duration of Transfusion

Discussion

This study examined the prevalence and risk factors of HCV infection among 150 multitransfused thalassemia patients, revealing several significant findings that warrant detailed discussion in the context of existing literature.

Prevalence of HCV

Infection our study found an HCV antibody prevalence of 28% with confirmed active infection in 25.3% of patients, which aligns with several recent studies but shows regional variations. For comparison, Jafroodi *et al.* [6] reported a prevalence of 23.8% in their study of 156 thalassemia patients

in northern Iran, while Singh *et al*. [8] found a higher rate of 32.5% in a similar population in India. The variation in prevalence rates across different studies might reflect differences in blood screening protocols, healthcare infrastructure, and the implementation of safety measures across regions.

Age and Duration of Transfusion

The significant association between HCV infection and both patient age and duration of transfusion therapy (OR 2.8, 95% CI 1.4-5.6, p = 0.003) corresponds with findings from multiple previous studies. Mahmoud *et al*. [10] demonstrated that patients receiving transfusions for more than five years had a threefold increased risk of HCV infection, similar to our findings (OR 3.2, 95% CI 1.6-6.4). This correlation likely reflects the cumulative risk of exposure with each transfusion event, despite modern screening methods.

Transfusion Frequency and Risk

Our observation that patients receiving more than 15 transfusions per year had a higher risk of HCV infection (OR 2.5, 95% CI 1.2-5.1) is consistent with the findings of Kumar *et al*. [11], who reported a positive correlation between transfusion frequency and HCV infection risk. This relationship underscores the importance of optimizing transfusion protocols to minimize exposure while maintaining therapeutic efficacy.

Liver Function and Iron Overload

The significantly elevated liver enzymes in HCV-positive patients observed in our study mirror the findings of Ahmed *et al*. [12], who reported similar patterns of hepatic dysfunction in infected thalassemia patients. The positive correlation between serum ferritin levels and HCV infection ($r = 0.42$, $p<0.001$) suggests a possible synergistic effect between iron overload and viral hepatitis, as previously described by Wong *et al*. [7] in their comprehensive review.

Splenectomy Status

While our study showed a trend toward increased HCV risk in splenectomized patients (OR 1.8, 95% CI 0.9-3.6), this association did not reach statistical significance (p = 0.089). This finding differs from the results of Cappellini *et al*. [13], who reported a significant association between splenectomy and HCV infection. The discrepancy might be attributed to differences in sample size and patient populations.

Prevention and Management Implications

The prevalence rate found in our study, though lower than historical rates reported before universal screening [14], indicates that HCV infection remains a significant concern in multitransfused thalassemia patients. This finding supports the recommendations of Di Marco *et al*. [15] for regular HCV screening and monitoring in this high-risk population.

Study Limitations and Future Directions

Our study was limited by its cross-sectional design and single-center nature. Additionally, we did not analyze HCV genotypes or assess treatment outcomes. Future longitudinal studies, as suggested by Thompson *et al*. [16], are needed to better understand the natural history of HCV infection in thalassemia patients and evaluate the effectiveness of current prevention strategies.

Clinical Recommendations Based on our findings and supported by current literature [17], we recommend:

1. Enhanced screening protocols for blood products.
2. Regular monitoring of liver function and HCV status in multitransfused patients.
3. Early intervention for those showing signs of infection.
4. Optimization of transfusion protocols to minimize exposure risk.

Conclusion

This comprehensive study of 150 multitransfused thalassemia patients provides important insights into the current landscape of HCV infection in this vulnerable population. The observed prevalence rate of 25.3% for active HCV infection, while lower than historical figures, indicates that HCV remains a significant health concern in thalassemia patients requiring regular transfusions. The strong associations identified between HCV infection and factors such as duration of transfusion therapy, transfusion frequency, and age underscore the cumulative risk nature of transfusion-related HCV transmission.

The study's findings highlight the critical importance of maintaining rigorous blood screening protocols and implementing comprehensive monitoring strategies for thalassemia patients. The observed relationship between HCV infection and elevated liver enzymes, combined with the correlation with serum ferritin levels, emphasizes the need for careful monitoring of both viral hepatitis and iron overload status in these patients.

Our results support the necessity of a multifaceted approach to patient care, incorporating regular HCV screening, careful documentation of transfusion history, and monitoring of liver function and iron status. These findings can serve as a foundation for developing more targeted prevention strategies and optimizing current management protocols for thalassemia patients.

Future research directions should focus on longitudinal studies to better understand the progression of HCV infection in thalassemia patients and evaluate the effectiveness of current prevention and treatment strategies. Additionally, multi-center studies with larger sample sizes would help validate these findings across different healthcare settings and geographical regions.

The insights gained from this study contribute to the growing body of evidence guiding the care of thalassemia patients and underscore the ongoing need for vigilance in preventing transfusion-related infections. These findings can inform healthcare policy decisions and help improve the quality of care for this patient population.

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