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Frequency of Hepatitis B Virus and Hepatitis C Virus Infection in Beta Thalassemia Major Children in Tertiary Care Hospital

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ABSTRACT

Introduction: The study aimed to determine the frequency of hepatitis B virus and hepatitis C virus infection in children with beta thalassemia major receiving treatment at a tertiary care hospital. **Methodology:** This descriptive cross-sectional study was conducted over six months, from April 2024 to October 2024, in the Department of Pediatrics at PIMS Hospital, Islamabad. A total of 161 beta-thalassemia major patients, aged 1 to 15 years, were included using non-probability consecutive sampling. Participants with prior HBV or HCV diagnoses, liver disease, or a history of antiviral treatment were excluded. Data on demographics, transfusion history, and infection status were collected. Blood samples were analyzed for HBV and HCV RNA levels using Real-Time PCR. Statistical analysis was performed using SPSS version 26, with infections stratified by age, gender, and transfusion frequency. A p-value ≤0.05 was considered statistically significant. **Results:** The mean age of participants was 7.98±4.29 years, with an average of 15.95±8.57 transfusions. Males constituted 59.6% of the sample. HBV was detected in 9.9% of patients, and HCV in 31.7%. HBV positivity was significantly associated with age (>10 years: 17%, p=0.036) and number of transfusions (>20 transfusions: 17%, p=0.036). Similarly, HCV positivity dramatically increased with age (>10 years: 83%, p=0.000) and transfusions (>20 transfusions: 83%, p=0.000). Gender differences in infection rates were not statistically significant. **Conclusion:** Hepatitis B and C infections pose significant risks for beta-thalassemia major patients, with HCV showing a higher prevalence. Older age and increased transfusions significantly elevate infection risk, underscoring the need for enhanced screening protocols and targeted preventive strategies.

INTRODUCTION

Beta thalassemia major, is an inherited blood problem that results from mutations in the beta-globin gene, leading to a reduction or absence in the production of hemoglobin.[1] It usually presents within the first two years of life and is characterized by severe anemia and skeletal deformities resulting from bone marrow expansion.[2] Children with beta thalassemia major must undergo regular hemoglobin maintenance through blood transfusions, which increase the risk of emergencies from iron overload and complications in vital organs.[3] Successful management involves de-chelating to reduce extra iron and monitoring for infections brought on by the many transfusions that are typically done, sometimes presenting a major problem within patients.[4]

Children with beta thalassemia major are more prone to Hepatitis B infection since the path of transmission is repetitive transfusions.[5] Although successful blood screening and vaccination programs already exist, in countries with poor medical resources, HBV remains a concern.[6] Chronic HBV infection can lead to liver fibrosis, cirrhosis, and hepatocellular carcinoma and is thus a condition that may threaten life and quality of life among children.[7] The main measure is already vaccination against HBV; regular serological follow-up is necessary due to breakthrough infections and non-responsiveness to vaccines.[8]

Another critical issue in children with beta thalassemia major is the infection of hepatitis C virus (HCV), since it is also transmitted by blood transfusion.[9] Unlike HBV, there is no vaccine for HCV. Thus, strict screening of donor blood and the use of nucleic acid testing are very important in prevention.[10] The result, if left neglected, is usually chronic liver diseases that may reach the stage of cirrhosis or liver malignancy with a longer duration of the disease.[11] Currently, antiviral therapies-needless to emphasize-are much potent, especially DAA, hence bringing about considerably improved outcomes with complete cure possibilities for patients infected with HCV.[12] Early detection of HCV status and timely interventions in thalassemia patients

play a very major role in terms of minimizing long-term liver damage as well as optimizing overall prognosis in cases of thalassemia.[13] A study conducted by Nadir R, et al. reported that the overall prevalence of HBV and HCV infections was 9.3% and 31.7%, respectively, among children with beta-thalassemia major.[14]

Their higher vulnerability owing to frequent blood transfusions and deranged immunity conditions makes it quite imperative that the frequencies of hepatitis B virus and hepatitis C virus infections should be studied among children with beta-thalassemia major. Knowing the prevalence among these subjects would lead to specific programs for its screening, improve policies for ensuring the safety of transfusions, and include necessary measures to avoid such conditions or their complications for an improved quality of life in later years.

METHODOLOGY

This study was conducted over a period of 6 months, from April 2024 to October 2024, in the Department of Pediatrics at PIMS Hospital, Islamabad. A total of 161 children were included in the study. The sample size was calculated using the WHO sample size calculator, assuming a 9.3% expected frequency of hepatitis B virus in beta thalassemia major children,[14] with a 95% confidence level and a 4.5% margin of error.

The study employed non-probability consecutive sampling. Eligible participants included children aged 1 to 15 years of both genders diagnosed with beta thalassemia major as per predefined operational definitions. Beta thalassemia major was defined as chronic hemolytic anemia lasting more than six months, diagnosed via complete blood count (CBC) showing low hemoglobin (Hb), low mean corpuscular volume (MCV), and increased red cell distribution width (RDW), along with Hb electrophoresis results indicating absent HbA1, elevated HbA2 (>3%), and HbF (>90%). Children with a history of liver transplantation, those who had received antiviral treatment for Hepatitis B or C, those previously diagnosed with HBV or HCV, or those with chronic liver disease (AST and ALT > 40 IU/L) were excluded.

Basic demographic information, such as age, gender, and the number of transfusions, was recorded. After obtaining informed consent from parents or caregivers, ensuring confidentiality and no associated risk to participants, about 3 ml of venous blood was drawn. Blood samples were sent to the hospital's laboratory for screening of Hepatitis B and C viruses to minimize bias. Hepatitis B virus infection was defined as the persistence of HBV RNA levels (>50 IU/ml) detected through Real-Time PCR in serum. Similarly, Hepatitis C virus infection was defined as the persistence of HCV RNA levels (>50 IU/ml) detected through Real-Time PCR in serum. Data regarding Hepatitis B and C virus infections were documented as per operational definitions and recorded using a structured proforma. Data analysis was conducted using IBM-SPSS version 26. Quantitative variables, such as age and number of transfusions, were expressed as means and standard deviations. Qualitative variables, including gender and Hepatitis B and C virus infections, were presented as frequencies and percentages. Infections were stratified by age, gender, and the number of transfusions. Post-stratification, a chi-square test was applied, and a p-value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of patients was 7.98±4.29 years, and they had undergone an average of 15.95±8.57 transfusions. While 59.6% were male (n=96) and 40.4% were female (n=65) as shown in Table-1.

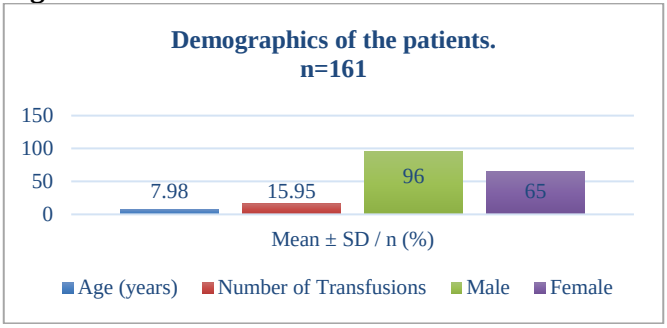
Table 1

Demographics of the patients.

Demographics	Mean ± SD / n (%)
Age (years)	7.98 ± 4.29
Number of Transfusions	15.95 ± 8.57
Male	96 (59.6%)
Female	65 (40.4%)

n=161

Figure 1



HBV was present in 9.9% (n=16) of children, while HCV was present in 31.7% (n=51) children as shown in Table-2.

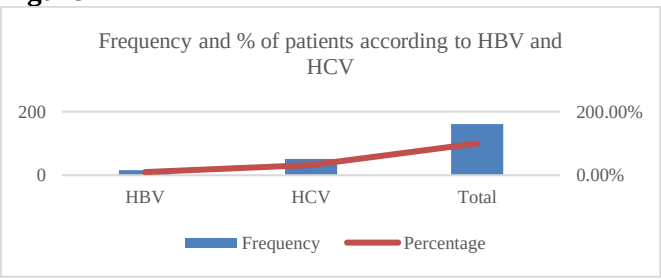
Table 2

Frequency and % of patients according to HBV and HCV

Infection	Frequency	Percentage
HBV	16	9.9%
HCV	51	31.7%
Total	161	100%

n=161

Figure 2



For HBV, individuals aged 1-10 years had a positivity rate of 6.5%, while those older than 10 years had a higher

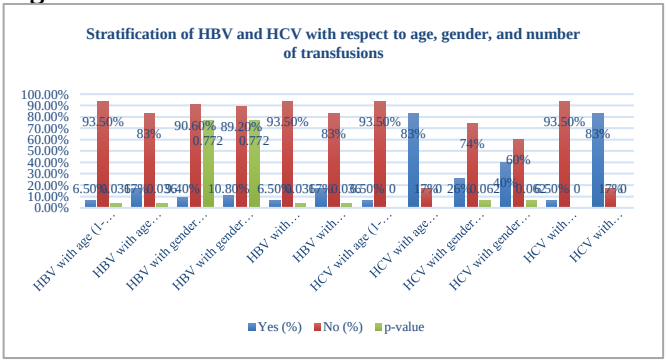
positivity rate of 17%. The p-value of 0.036 indicates a significant association between age and HBV. Similarly, for HCV, positivity in individuals aged 1-10 years was 6.5%, while it significantly increased to 83% in those older than 10 years, with a highly significant p-value of 0.000. In terms of gender, HBV positivity was 9.4% in males and 10.8% in females, with a p-value of 0.772, indicating no significant difference. For HCV, males had a positivity rate of 26%, while females had a higher rate of 40%, but the p-value of 0.062 suggests this difference is not statistically significant. Regarding the number of transfusions, HBV positivity was 6.5% for those receiving ≤20 transfusions and 17% for those with >20 transfusions. The p-value of 0.036 indicates a significant association between transfusions and HBV. For HCV, individuals with ≤20 transfusions had a positivity rate of 6.5%, which rose dramatically to 83% for those with >20 transfusions, with a highly significant p-value of 0.000. These findings highlight significant differences in positivity rates for age and transfusions in both HBV and HCV cases, while gender differences were not statistically significant as shown in Table-III.

Table 3

Stratification of HBV and HCV with respect to age, gender, and number of transfusions

Stratification	Yes (%)	No (%)	p-value
HBV with age (1-10 years)	7 (6.5%)	101 (93.5%)	0.036
HBV with age (>10 years)	9 (17%)	44 (83%)	0.036
HBV with (Male)	9 (9.4%)	87 (90.6%)	0.772
HBV with (Female)	7 (10.8%)	58 (89.2%)	0.772
HBV with transfusions (≤20)	7 (6.5%)	101 (93.5%)	0.036
HBV with transfusions (>20)	9 (17%)	44 (83%)	0.036
HCV with age (1-10 years)	7 (6.5%)	101 (93.5%)	0.000
HCV with age (>10 years)	44 (83%)	9 (17%)	0.000
HCV with gender (Male)	25 (26%)	71 (74%)	0.062
HCV with gender (Female)	26 (40%)	39 (60%)	0.062
HCV with transfusions (≤20)	7 (6.5%)	101 (93.5%)	0.000
HCV with transfusions (>20)	44 (83%)	9 (17%)	0.000

Figure 3



DISCUSSION

The study reveals significant insights into hepatitis virus prevalence among beta thalassemia major children. The average age of children was 7.98±4.29 years, along with 15.95±8.57 mean transfusions, represents a typical profile of young thalassemia patients requiring regular blood transfusions. The gender distribution showed a slight male predominance (59.6% vs 40.4% females), which is expected as thalassemia, being an autosomal recessive disorder, affects both genders similarly. Perhaps the most clinically significant finding was the strong correlation between transfusion numbers and viral infection rates. For HBV, patients receiving more than 20 transfusions showed higher positivity (17% vs 6.5%, p=0.036), while HCV rates dramatically increased from 6.5% to 83% in patients with over 20 transfusions (p=0.000). This striking correlation emphasizes the critical role of multiple transfusions as a risk factor for viral hepatitis transmission, despite modern blood screening techniques. Our study found an HBV prevalence of 9.9%, which is higher than the rates reported in studies by Muhammad Mahmood Iqbal et al.[15] (0.7%), Sohail Akhtar and Jamal Abdul Nasir[16] (pooled prevalence of <5%), and G. Mirzaei et al.[17] (0%). However, it is closer to the prevalence reported by Raheel Nadir et al.[18] (9.3%) and Sumaira Khalil et al.[19] (5%). The relatively higher HBV rate in our study may be due to differences in vaccination coverage, donor screening, or other regional healthcare disparities. Notably, our study demonstrated a significant association between HBV positivity and the number of transfusions (p=0.036) and age (p=0.036), consistent with findings from studies like Raheel Nadir et al.[19], where frequent transfusions were a key risk factor.

The HCV prevalence in our study was 31.7%, aligning closely with the findings of Sumaira Khalil et al.[19] (38.7%) and Raheel Nadir et al.[18] (31.7%). It was also within the range reported by Tasneem Kousar et al.[20] (33.3%) but higher than the pooled prevalence in Sohail Akhtar and Jamal Abdul Nasir's[16] meta-analysis (36.21%) and the study by G. Mirzaei et al.[17] (3.4%). These variations may result from differences in healthcare infrastructure, transfusion safety measures, and regional prevalence of HCV. Our study's finding of a dramatic increase in HCV positivity with more than 20 transfusions (p=0.000) echoes the findings of studies like those by Asad Ullah et al.[21] and Tasneem Kousar et al.[20] which highlighted transfusion frequency as a critical risk factor.

In terms of demographic differences, our study observed that males constituted 59.6% of the population, and gender differences in HBV and HCV positivity rates were not statistically significant (p=0.772 and p=0.062, respectively). These findings align with the results of studies by Tasneem Kousar et al.[20] and Raheel Nadir et

al.[18] which also did not report significant gender disparities. However, our study's age-related trends for HBV and HCV positivity were significant, with older children (above 10 years) having much higher positivity rates for both infections. This is consistent with the findings of Golam Sarower Bhuyan et al.[22] and Sumaira Khalil et al.[19], who reported higher infection rates in older children due to cumulative transfusions over time.

Our findings contrasts from studies such as G. Mirzaei et al.[17] which reported significantly lower HCV prevalence in East Azerbaijan due to improved blood screening practices post-1996. This contrast underscores the impact of regional differences in blood safety measures, with regions implementing stringent screening protocols experiencing reduced infection rates.

The higher prevalence of both HBV and HCV in patients receiving more than 20 transfusions aligns with almost all studies reviewed, including Muhammad Mahmood Iqbal et al.[15] and Tasneem Kousar et al.[20] reinforcing the critical role of transfusion safety in managing infection risks. The differences in infection prevalence between our study and others could also be attributed to variations in study periods, methodologies, and the implementation of nucleic acid testing or other advanced donor screening techniques in some regions.

These findings underscore the urgent need for enhanced blood screening protocols, particularly for HCV, and the importance of developing preventive strategies for multi-transfused thalassemic patients.

CONCLUSION

Our study has concluded that hepatitis B and C infections pose significant risks in thalassemia major patients, with HCV showing higher prevalence than HBV. The infection risk increases significantly with patient age and number of transfusions received, though gender shows no significant impact. These findings emphasize the need for enhanced blood screening protocols and preventive strategies, particularly for HCV, in the management of thalassemia patients requiring multiple transfusions.

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