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Frequency of Hepatitis B or C in Patients of Beta Thalassemia Registered in the Thalassemia Centre, Pak Emirates Military Hospital, Rawalpindi

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ABSTRACT

Objective: To determine the frequency of Hepatitis B or C and associated factors in patients with beta Thalassemia registered in the Thalassemia Centre, Pak Emirates military hospital, Rawalpindi.

Study Design: Cross sectional study.

Place and Duration of Study: Thalassemia Centre, Pak Emirates military hospital, Rawalpindi Pakistan, from Aug 2019 to Apr 2020.

Methodology: This study involved 280 children of both genders aged between 2-12 years managed for beta-Thalassemia Major and having transfusions at the or Thalassemia Centre. Laboratory testing for hepatitis B and C was performed on all the patients by the ELISA method. Age, gender, duration of receiving transfusions, and ALT levels were also associated with the seropositivity of any of the viruses.

Results: The Mean age of the patients was 7.26±4.26 years. There were 150 (53.5%) male and 130 (46.5%) female patients in the study patients. Out of 280 patients, 238(85.0%) were negative for both viruses, 9(3.2%) were hepatitis B positive, and 33(11.8%) were hepatitis C positive. Raised ALT levels (p-value <0.001) and increased frequency of red cell transfusions (p-value=0.006) had a significant relationship with seropositivity of any of the viruses.

Conclusion: Seropositivity of hepatitis B and C was not an uncommon finding among our target population. Hepatitis C was more common of the two viruses studied. Raised ALT levels among these patients should not be ignored, and patients with increased duration of being transfused should be considered at high risk for acquiring these viral infections.

Keywords: β-Thalassemia Major; Hepatitis B; Hepatitis C, Thalassemia.

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INTRODUCTION

Thalassemias are a group of inherited disorders of haematological origin that usually manifest in early childhood in severe forms and make the child transfusion-dependent for the rest of his life.[1] Though survival of patients becomes linked to repeated transfusions he/she undergo but still clinical scenario is not complete here, and the patient may suffer from a lot of transfusion-related problems.[2] Disease-related and transfusion-related problems together make the quality of life of the patient severely compromised in a large number of cases.[3]

Transfusion-related complications among patients with Thalassemia might be of various types. They may be linked to iron overload affecting the liver, spleen, kidneys, brain, heart, and almost all the vital organs.[4] In developing countries where viral infections have been common and screening has been compromised at any stage, transmission of these blood-borne viral infections has been relatively standard.[5] Hepatitis B and C may be found among patients dependent on repeated transfusions for any disorder.[6]

Singh *et al*., in 2003 published a study in our neighbouring country, India, to look for hepatitis B virus among patients of beta-thalassemia. They found that around 5% were Hepatitis B surface antigen (HBs Ag) positive and around 20% were antibody positive. Vaccination responders and non-responders were not different in this regard. Frequency of transfusions had a statistically significant relationship with hepatitis B positivity among their target population.[7] Amarapurkar *et al*., way back in 1992 studied hepatitis B, C and HIV among Beta thalassemia patients and revealed that hepatitis B, C and HIV were present in considerable number of patients with HCV the most common viral infection of the three studied in target population. Another concerning finding they observed was the presence of co-infection. Around 10% of the patients belonged to the group that were positive for both hepatitis B and C.[8] A local study published by Saeed *et al*., in 2015 showed alarming results in this regard. A considerable chunk of patients were HBV

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and HCV positive, with most of them having HCV. A concerning finding was that all patients above 20 years of age were HCV positive. Being positive for these infections also accounted for other clinical and biochemical findings. ALT levels were higher than usual in patients positive for HBV or HCV. Hepatomegaly and splenomegaly were also a consistent finding among the patients positive for HBV or HCV. Serum ferritin levels were also markedly raised in patients having any one of these viral infections.[9]

Despite numerous awareness campaigns on the modes of transmission of thalassemia genes and the transmission of viruses from one individual to another, neither the incidence of thalassemia nor the incidence of new cases of different types of hepatitis has declined.[6,10] It has been high time for a developing country like ours with minimal health resources, where already there has been much burden on the health care system and parents of children due to repeated transfusions for the management of Thalassemia. If the situation becomes more complicated and they also harbour a viral infection, then things can become more difficult. We designed this study to determine the frequency of Hepatitis B or C and associated factors in patients with beta thalassemia registered at the Thalassemia Centre, Pak Emirates Military Hospital, Rawalpindi.

METHODOLOGY

The cross sectional study was conducted at the Thalassemia Centre, Pak Emirates military hospital, Rawalpindi, Pakistan from August 2019 to April 2020. Ethical approval was obtained (IREB letter number 171) from the Ethical Review Committee at the start of our study. The sample size was calculated with an expected frequency of Hepatitis B seropositivity of 12% in children with Thalassemia in Pakistan.[11]

Inclusion Criteria: Children of any gender aged between 2-12 years diagnosed with β-Thalassemia Major, having received repeated blood transfusions, were included.

Exclusion Criteria: Children with a diagnosis of hepatitis C before the start of transfusions or diagnosis of Thalassemia or children of Hepatitis B or Hepatitis C positive mothers (antenatal record of the mother) or children with any other comorbid liver pathology or having any reason for transfusion or any repeated invasive procedure were excluded.

Patients were included in the study using the Non-Probability, Consecutive Sampling technique. Diagnosis of Thalassemia was made upon patients having repeated blood transfusions (≥10) and haemoglobin electrophoresis reporting 100% HbF (foetal haemoglobin). 123ml of blood was acquired by venepuncture from the cubital fossa. The sample was allowed to clot, and a separate third-generation ELISA kit for Hepatitis B and C was used to determine seropositivity from the isolated serum of the sample. An immediate single line (≤5sec) was a marker of an accurate test, and a double line within 5 minutes was taken as a marker of seropositivity.[12,13]

Subsequently, 280 paediatric patients managed at the Thalassemia Centre, Pak Emirates Military Hospital, Rawalpindi, who met the inclusion and exclusion criteria, were enrolled in this study. Detailed history and written informed consent were obtained from the patient's attendants. 3 ml of blood was taken by venipuncture from the cubital fossa, and seropositivity for hepatitis B and C was checked. Patient's demographic details along with basic laboratory tests and seropositivity for hepatitis B and C were noted and recorded into the attached proforma. A single resident performed all the samples and tests to eliminate bias. Confounding variables were controlled through detailed history taking and a thorough review of all records.

Statistical Package for Social Sciences (SPSS) version 23.0 was used for the data analysis. Quantitative variables were presented as Mean±SD. Categorical variables were presented as frequency and percentage. The chi-square test was applied, with a *p*-value of ≤0.05 considered significant, to evaluate the relationship between age, gender, duration of transfusions, and ALT levels, and their association with seropositivity for any virus.

RESULTS

After the application of inclusion and exclusion criteria, 280 patients with Thalassemia underwent relevant investigations to look for the frequency of the understudy viral infections. Table-I shows that the mean age of the patients was 7.26±4.26 years. The mean duration of patients being transfused was 4.15±2.35 years. There were 150(53.5%) male and 130(46.5%) female patients in the study group. Out of 280 patients, 238(85%) were negative for both viruses, 9(3.2%) were hepatitis B positive, and 33(11.8%) were hepatitis C positive. Table-II showed that raised ALT levels and longer duration of receiving transfusions

had a statistically significant relationship with seropositivity of any of the viruses (p-value<0.05). In contrast, age and gender had no such association (p-value-0.234 and 0.065).

Table-I: Baseline Characteristics of Study Participants (n=280)

Characteristics	n(%)
Mean Age (years)	7.26±4.26
Mean Duration of getting Transfusions (years)	4.15±2.35
Age Groups	
2-5 years	101(36.1%)
6-9 years	99(35.3%)
10-12 years	80(28.6%)
Gender	
Male	150(53.5%)
Female	130(46.5%)
Hepatitis Virus	
Hepatitis B	09(3.2%)
Hepatitis C	33(11.8%)
ALT (Alanine Transaminase) Levels (IU/L)	
10-40	259(92.5%)
>40	21(7.5%)

Table-II: Association of Various Factors with the Seropositivity of any of the Two Viruses (Hepatitis B or C) (n=280)

	Hepatitis B & C Negative	Hepatitis B or C Positive	p-Value
Age			
≤8 year o	185(77.7%)	29(69.1%)	0.234
>8 years	53(22.3%)	13(30.9%)	
Gender			
Male	133(55.8%)	17(40.5%)	0.065
Female	105(44.2%)	25(59.5%)	
ALT (Alanine Transaminase) Levels			
10-40 IU/L	227(95.3%)	32(76.2%)	<0.001
>40 IU/L	11(4.7%)	10(23.8%)	
Duration of Getting Transfused			
≤3 years	103(43.3%)	09(21.4%)	0.006
>3 years	135(56.7%)	33(78.6%)	

DISCUSSION

Thalassemias have been considered primarily hematological disorders requiring lifelong transfusion in severe cases. However, the disease itself and repeated transfusions may involve all systems of the body, and overall homeostasis of the body gets disturbed, requiring various interventions.[14,15] Multiple blood-borne infections may be transmitted to the children who receive regular transfusions for their survival. Hepatitis viruses B & C have been the most common infections seen in these patients in our setting. If not detected timely, they may lead to fatal complications like chronic liver disease and hepatocellular carcinoma. We therefore conducted this study to determine the frequency of Hepatitis B or C and associated factors in beta Thalassemia patients registered at the Thalassemia Center, Pak Emirates Military Hospital, Rawalpindi.

Bhattacahriya *et al.*, (2018) concluded in a study in India that 25% of thalassemia patients were found to be HCV positive by enzyme-linked immunosorbent assay (ELISA). Among them, 49 (65%) were HCV RNA positive, having a significant viral load in their blood, and the remaining 26(35%) were below the detection level, which signifies auto-clearance of the virus in those patients. According to our study, HCV genotype 3 was the significant circulating strain (92.59%), followed by genotype 1. Liver enzymes, such as alanine aminotransferase, aspartate aminotransferase, and total bilirubin, were significantly elevated among HCV seroreactive individuals.[13] We did not study the viral load, and less number of our patients were infected with the virus, as compared to the Indian population.

Biswas et al. in 2018 investigated the association of HCV viraemia and genotype with clinical parameters in HCV seroreactive individuals with beta thalassemia. They summarized that Liver enzymes, such as ALT, AST, and serum total bilirubin, were significantly elevated in all age groups with hepatitis C virus compared to control groups.[16] We only included ALT as a laboratory parameter in our study. There was a very strong association with raised ALT levels and the presence of HBV or HCV among the patients suffering from Thalassemia. Explanation of this may be direct liver injury by the virus, which causes a rise in the liver enzymes, including ALT.

Jang *et al.,* in 2017 discussed this subject in a broader perspective and evaluated transfusion-dependent Taiwanese patients for the presence of hepatitis B and C. They concluded that the seropositivity for hepatitis B antibody and hepatitis C antigen was higher in this group as compared to the normal population.[17] Age, serum ALT levels, and platelet counts were the factors that were statistically significantly correlated with the presence of viral infection among these patients. Our statistics differed from theirs because the frequency of both viruses was low in our sample population. Association of raised ALT was a common finding in both studies.

Akhtar et al. published an interesting meta-analysis of local studies in this regard and concluded that the pooled prevalence of HCV in β-thalassemia patients in Pakistan was more than one in three, and higher than in neighboring countries. It varies

regionally within the country. With the use of standard prevention procedures during blood transfusion, the risk of HCV transmission in β-thalassemia patients could be controlled, and the prevalence of HCV in β-thalassemia patients reduced.[18] In our study, the prevalence of both viruses was low compared to other studies, but HCV was found more frequently in patients than HBV.

CONCLUSION

Seropositivity of hepatitis B and C was not an uncommon finding among our target population. Hepatitis C was more common of the two viruses studied. Raised ALT levels among these patients should not be ignored, and patients with increased duration of being transfused should be considered at high risk for acquiring these viral infections.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

KZ AR: Conception, study design, drafting the manuscript, approval of the final version to be published.

FI: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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