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Original Article

Incidence of Hepatitis B due to Multiple Transfusions in Patients of β-Thalassemia Major

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ABSTRACT

β-Thalassemia is one of the most prevalent childhood hemolytic disorders. Multiple blood transfusions of unscreened blood can result in infection transmission. After many transfusions, Hepatitis B infection in thalassemia patients was reported. **Objective:** To determine the incidence of Hepatitis B in β-thalassemia major patients, associated with multiple blood transfusion strategies. **Methods:** This cross-sectional study was executed in Pediatric department of DHQ teaching hospital Dera Ismail khan with the collaboration of the Regional Blood center, and comprised 360 patients, diagnosed with β-Thalassemia Major and maintained on multiple transfusions. **Results:** The average weight of the subjects was 43.50±18.76 Kg and their mean age was 13.10±2.1 years. The significantly high population of the patients ($p<0.05$) was not immunized against Hepatitis B (73.88%), while only 26.66% (94/360) were immunized. The patients having less than 10, 11-20 and more than 20 transfusions per annum comprised 72 (20%), 157 (43.61%) and 131 (36.38%) patients, respectively. The affected patients had significantly altered hematological parameters ($p<0.05$). The highest number of β-Thalassemia Major patients affected with Hepatitis B belonged to the Group having more than 25 transfusions of blood annually, with an incidence rate of 11.53. **Conclusions:** The greatest risk factor for Hepatitis B infection in β-thalassemia major patients is concluded to be multiple blood transfusions. It was also found that a huge population of Thalassemia patients was not immunized against HBV despite the severe risk. Therefore, health education and awareness campaigns are needed for the significance of Hepatitis B immunization and transfusion of screened blood.

INTRODUCTION

The most widespread autosomal recessive genetic disorder, beta thalassemia is caused by an aberrant beta hemoglobin gene, yielding Globin chain and clinically characterized by moderate to stern hemolytic anemia. The wide-reaching carrier frequency of β-thalassemia is approximately 3%, and it is estimated that approximately 600,000 children with thalassemia major are born per annum. There is more than 10 million β-thalassemia trait carrier in Pakistan, where the peculiarity frequency ranges from 5 to 8% and around 5,000 kids are diagnosed with β-thalassemia major per annum. Lack of education, illiteracy and consanguineous marriages (70%) are the crucial causes of Pakistan's high carrier fraction. According to World Health Organization, an effectual screening program should be implemented whenever the birth rate of afflicted newborns surpasses 0.1/1000 for any disease [1]. β-Thalassemia Major patients entail monthly blood transfusions to sustain normal hemoglobin levels. Patients who entail multiple transfusions are always predisposed to contracting transfusion-transmitted maladies [2]. Patients with β-thalassemia major experience numerous difficulties as a result of multiple blood transfusions (MBTs)

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including iron excess and infection transmission of contagious maladies. Inadequate screening procedures upshot in the transmission of infections, among which the most prevalent are Hepatitis B and C infections, rendering increased morbidity and mortality of these patients. According to local and regional studies, the prevalence of HBV and HCV is 5 and 38.7%, respectively [3]. The treatment of patients with β-thalassemia major imposes a significant economic burden. In Punjab (Pakistan), there is a single government-funded project (The Punjab Thalassemia Prevention Program), which provides free beta thalassemia screening and prenatal diagnosis. Complete blood count and hemoglobin electrophoresis remain the initial screening test, although chorionic villi sample and amplification refractory mutation system method is the most common molecular tests for β-thalassemia diagnosis. Modern molecular approaches, and non-invasive prenatal and pre-implantation diagnosis are currently in the testing phase [1]. The current research was conducted to determine the incidence of Hepatitis B in β-thalassemia major patients, associated with multiple blood transfusion strategies and to evaluate the efficacy of blood screening before transfusion.

METHODS

This cross-sectional study was completed in the Pediatrics Department DHQ Teaching hospital, Dera Ismail Khan in the collaboration with the Regional Blood Centre Dera Ismail Khan from February 2022 to December 2022. The study comprised 360 patients of both sexes (259 males; 101 females) aged less than 18 years, diagnosed with β-Thalassemia Major, who were maintained by MBTs. Participants who met the inclusion criteria were enrolled in the study by non-probabilistic convenience sampling. Cases of B-Thalassemia Major with microcytic hypochromic anemia (Hb<10, MCH<25 and MCV<70) and blood transfusions undergoing along with follow-up at tertiary care hospitals in District Dera Ismail Khan, during the study period were enrolled. While the exclusion criteria concluded patients diagnosed previously with hepatitis B or chronic liver disease. The relevant hematological, and demographic parameters of the patients were noted and compiled in the MS Excel sheets (Version 2010), and were compared to the normal hematological values of hemoglobin (12-18g/dl), RBCs count (4.1-6 x 10^{12}/L), PCV (36-51%), MCH (27-33 pg/cell) and MCV (79-96 FL/cell) [4]. Their frequency of blood transfusions per annum was also kept on record and statistically analyzed. Before all transfusions in B-Thalassemia Major patients, complete history along with their vaccination status was recorded on the pre-designed questionnaire and their blood specimens, comprising 3ml each in EDTA (whole blood) and gel tube (for serum extraction) were sent to the laboratory facility of the center for screening of Hepatitis B (3rd generation ELISA and PCR), CBC (Hematology Analyzer) and other maladies. All these medical procedures were executed under the strict compliance of Ethical norms and policies of our institute, and informed consent from the enrolled patients for the subject research was signed by the parents of patients. The gathered data were statistically analyzed using SPSS software (Version 20.0). The continuous variables were expressed in frequency, percentage, means and standard deviations and the treatment groups were instigated through One-Way ANOVA and Chi-square testing, while, a p-value of less than 0.05 was deemed statistically significant.

RESULTS

The blood disorder β-Thalassemia reduced hemoglobin synthesis and is characterized by abnormal erythrocyte production. The affected persons have a deficiency of erythrocytes (anemia), resulting in pale skin, weakness and more severe consequences. Those with beta thalassemia are more likely to have irregular blood profiles. Depending on the severity, it is divided into thalassemia major (transfusion-dependent thalassemia or Cooley's anemia) and thalassemia minor (non-transfusion-dependent). Therefore, this cross-sectional study was conducted to determine the incidence of hepatitis B due to multiple transfusions in patients of β-Thalassemia Major in Dera Ismail Khan from February 2022 to December 2022 and comprised 360 participants including 259 males and 101 females. The average weight of the subjects was 43.50±18.76 Kg and their mean age was 13.10±2.1 years. The significantly high population of the patients ($p<0.05$) was not immunized against Hepatitis B (73.88%), while only 26.66% (94/360) were immunized. The patients having less than 10, 11-20 and more than 20 transfusions per annum comprised 72 (20%), 157 (43.61%) and 131 (36.38%) patients, respectively. The statistically significant difference was found among these three groups and most of the patients ($p<0.05$) were maintained on 11-20 transfusions/annum (Table 1).

S. No	Variable	No. of subjects n (%)	p-value
Age			
1	<7 years	89 (24.72)	0.0004*
	8-14 years	142 (39.44)	
	15-20 years	129 (35.83)	
Weight			
2	>10 Kg	13 (3.55)	0.00001*
	11-20 Kg	47 (13.05)	
	21-30 Kg	83 (23.05)	
	>30 Kg	217 (60.27)	
Gender			
3	Male	259 (71.94)	0.00001*
	Female	101 (28.05)	

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	Female	101 (28.05)	
Vaccination against HBV			
4	Immunized	94 (26.11)	0.00001*
	Not immunized	266 (73.88)	
No. of transfusions			
5	<10	72 (20.0)	0.00001*
	11-20	157 (43.61)	
	>20	131 (36.38)	

Table 1: Demographic characteristics of the patients with β-Thalassemia Major

* Indicated that the value of p is significant at p<0.05

Whole blood was collected from all the participants for the evaluation of their hematological parameters and complete blood count and the values were compared to the normal (Table 2). All the collected values were analyzed and mean and standard deviations were calculated. The hemoglobin (6.89±0.53), erythrocytic counts (7.01±1.10), packed cell volume (39.76±7.68), mean corpuscular hemoglobin (19.19± 4.32) and mean corpuscular volume (55.88±16.73) of the patients affected with β-Thalassemia were compiled (Table 2).

S. No	Hematology parameters	Normal values	Range of subjects	Mean + SD
1	Hemoglobin (g/dL)	12-18	5.2-10.1 4	6.89+0.53
2	RBCs count (x1012/L)	4.1-6.0	4.02-7.87 4	7.01+1.10
3	PCV (%)	36-51	27-44 4	39.76+7.68
4	MCH (pg/cell)	27-33	17-27 4	19.19+ 4.32
5	MCV (FL/cell)	79-96	45-69 4	55.88+16.73

Table 2: Analysis of hematological parameters of β-Thalassemia Major patients

Normal values retrieved from Williams Manual of Hematology, 9th Edition

Based on a number of blood transfusions, the patients were categorized into four groups i.e., Group A (1-7 transfusions/annum), B (8-15 transfusions/annum), C (16-24 transfusions/annum) and D (>25transfusions/annum). It was found that the highest number of β-Thalassemia Major patients affected with Hepatitis B belonged to Group D having more than 25 transfusions of blood annually (Figure 1), followed by Group C, B and A characterized by the incidence rate of 11.53, 5.75, 2.91 and 2.50%, respectively (Table 3).

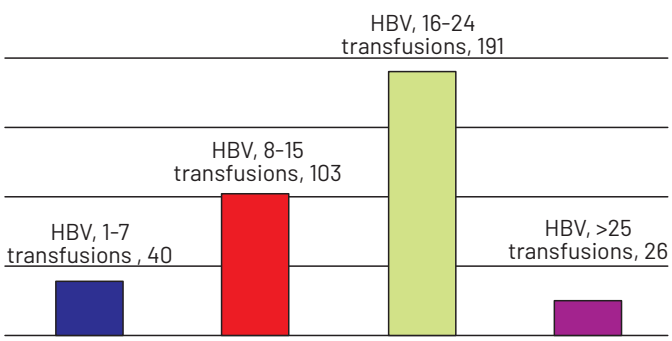

Figure 1: Relationship of HBV with β-Thalassemia

S. No	Groups	No. of transfusions per annum	No. of Subjects (n)	Patients diagnosed with Hepatitis B (n)	Incidence of HBV (%)	p-value
1	A	1-7	40	01	2.50	0.00005*
2	B	8-15	103	03	2.91	
3	C	16-24	191	11	5.75	
4	D	>25	26	03	11.53	

Table 3: Prevalence of Hepatitis B in β-Thalassemia Major patients due to multiple transfusions

* Indicated that the value of p is significant at p<0.05

DISCUSSION

β-Thalassemia is one of the most prevalent childhood hemolytic disorders. Multiple blood transfusions can result in infection transmission. After many transfusions, Hepatitis B infection in thalassemia patients was reported. Our findings revealed that significantly the highest (p<0.05) numbers of β-Thalassemia Major patients (11.53%) were affected with Hepatitis B for having more than 25 transfusions of blood annually. Our results were in accordance with the study conducted at the Department of Pediatric Medicine, Mayo Hospital, Lahore, in which 28 patients (9.3%) tested positive for HBV, with an average age of 9.76±5.26 years [3]. Another descriptive retrospective investigation conducted in Swat in Thalassemia patients undergoing multiple transfusions revealed comparable findings to our study, whereby 10 patients (5.88%) tested positive for hepatitis B surface antigen (HBsAg), through ELISA, in patients who were maintained on MBT strategies. It was also suggested that adequately screened blood must be utilized through a reliable approach to minimize transfusion-transmitted illnesses [5]. A similar nature study was close to our findings in which 250 and 152 multi-transfused thalassemia patients in Cacopardo's and Sicily, had HBV incidences of 8.40 and 8.0%, respectively [6]. Our results were also supported by the research performed in Fauji Foundation Hospital Rawalpindi including 80 Thalassemia patients undergoing MBTs and their results revealed that 5% (4/80) patients were infected with HBV [2]. Another study in East Azerbaijan reported that frequent blood transfusions in people with beta-thalassemia major rendered them to contract blood-borne viral infections among which HBV and HCV were the most significant. 116 beta-thalassemia patients who received blood in Tabriz's Shahid Ghazi hospital were examined by ELISA for the serum markers HCV-Ab, and HBsAg, revealing only four patients (3.4%) positive for HCV-Ab [7]. Our results coincided with the study conducted to assess the prevalence, genotype distribution and risk factors of hepatitis B virus (HBV) infection in individuals with β-thalassemia. Of 126 thalassemia patients, 4 cases (3.17%) were positive for HBsAg, 23 cases (18.25%) were positive for HBcAb, and 6 cases (4.76%) had HBV viremia with

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genotype D [8]. A study reported 3% incidence of β-thalassemia in Bandar-Iran [9], only 1.5% in India in 2020 [10], and incidence of HCV in Pakistan was found to be 36.21% in 2020 [11]. Our findings were corroborated with the study conducted in Bahawalpur and Peshawar to investigate of incidence of Hepatitis B and revealing 9.0 and 7.5%, respectively [12, 13]. Burki *et al.* reported 3.90% incidence of HBsAg in Pakistan in 2009 [14]. Our findings were supported by a study conducted at Quetta, Pakistan and reported 18.3% prevalence of HBsAg in β-thalassemia patients [15], 13.51% in Dhaka, Bangladesh and 10.0% in Palestine through diagnosed through ELISA [16, 17]. Patients with thalassemia who had undergone many blood transfusions were more susceptible to infection as a result of a deterioration in their immunological function [18]. Moreover, in the event of an emergency, it is normal practice in Bangladesh to accept dangerous blood donations from professional donors, the majority of whom are drug abusers [19]. Today, effective and safe blood transfusions have lowered the mortality rate, but complications such as hepatocellular carcinoma are becoming more prevalent in individuals with thalassemia, possibly related to the carcinogenicity of iron overload and chronic infections [20].

CONCLUSIONS

The greatest risk factor for Hepatitis B infection in β-thalassemia major patients is concluded to be multiple blood transfusions. It was also found that a huge population of Thalassemia patients was not immunized against HBV despite the severe risk. Therefore, health education and awareness campaigns are needed for the significance of Hepatitis B immunization and transfusion of screened blood.

Conflicts of Interest

The authors declare no conflict of interest.

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