ORIGINAL ARTICLE

The Burden of Transfusion related Infections on Thalassemia Major Children

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ABSTRACT

Aim: To determine the frequency of transfusion related infections in multi-transfused beta thalassemia major patients.

Methods: It was a descriptive cross-sectional study conducted indepartment of Hematology and Oncology, The Children's Hospital and Institute of Child health, Lahore, from March 2014 to September 2014. A total 470 patients were included in the study between 1 to 15 years. An informed written consent from the parents was taken and information was recoded on a predesignedPerforma. Sera of the patients was sent to the hospital laboratory and tested forhepatitis B surface antigen (HBsAg), anti-hepatitis C virus antibodies (HCV Abs), anti HIV antibodies and CMV IgM antibodies by using third generation enzyme linked immunosorbent (ELISA) technique.

Results: Among 470 patients diagnosed with Beta thalassemia major, 37 (7.87%)were positive for hepatitis B surface antigen, 216 (45.96%) cases were positive for hepatitis C antibodies and 22 (4.68%) cases were positive for both HBsAg and ant HCV Abs. Only 02 (0.42%) patients were positive for CMV IgM antibodies and none was positive for anti HIV antibodies. There were 306 (65.1%) male and 164 (34.9%) female patients. Predominately, 206 (43.82 %) patients lied in age group of 1 to 5 years. The number of blood transfusions received in majority of cases (246, 52.3%) was in the range of 1-50 times.

Conclusion:The frequency of transfusion related viruses especially HCV , isvery high among multi-transfused beta thalassemia major children. This ignitesthe need of proper pre-transfusion screening of blood by third generation ELISA for these viruses in the blood banks and transfusion centers.

Keywords: Burden, Transfusionrelatedinfections,Thalassemiamajor.

INTRODUCTION

Thalassemias, also called Cooley's anemia or Mediterranean anemia, are a group of genetic disorders in the globin chain (alpha and beta) production, leading to ineffective erythropoiesis and anemia. Beta thalassemia are a group of hereditary disorders in which there is either a complete absence of beta globin production called as beta thalassemia major or a partial reduction in globin chain synthesis called as beta thalassemia minor. Children with thalassemia major usually present clinically within first two years of life with severe anemia requiring regular red blood cells transfusions which necessarily begin in second month to two year of life[1].

Beta thalassemia is a worldwide problem, with a higher prevalence among Mediterranean population in the Middle East, in parts of India, Pakistan and South Asia. The average life expectancy is 10 years and at present the disease burden is of 90000 to 100000 patients in Pakistan[2]. Five out of 100 people in Pakistan are suffering from thalassemia. About 6000 children born in Pakistan are suffering from thalassemia annually[3].

A total of 350 million people were reported by World health organization with chronic hepatitis B virus infection and 170 million people with chronic hepatitis C virus infection worldwide. Hepatitis B and C viruses are among the principal causes of severe liver disease and cirrhosis related end stage liver disease. The annual deaths from hepatitis B are estimated to be 563,000 and from hepatitis C are 366,000. Pakistan is among the worst afflicted nations. In Punjab province of Pakistan, the prevalence of hepatitis B and C is 4.3% and 2.4% where as in Sindh, their prevalence is 1.8% and 2.3% respectively[4]. It is estimated overall that atleast 9 million people harbor hepatitis B and over 14 million are suffering chronic infection with hepatitis C in Pakistan[5].

Prevalence of hepatitis B has increased from 3% in 2000 up to 8.06% in 2009 among general population and has escalated from 3.3% in 2002 up to 5.07% in 2009 in blood donors. Whereas hepatitis C incidence has elevated from 6.5% in 1996 up to 33.7% in 2008 among general population and has proliferated from 1.2% (1996) up to 7.5% (2008) in blood donars[6,7].

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The prevalence of HIV in general population in Pakistan was estimated as 0.1% and 1-2% in high risk population. Contaminated blood or blood products contribute to the second most common mode of HIV transmission[8].

Thalassemia children are at high risk of transfusion related infections such as HIV and CMV, hepatitis B and C viruses[9,10]. A study from Egypt showed that out of 97 beta thalassemia major pediatric patients, 36 (37.11%) had positive serology for HCV, 4 (3.88%) patients were positive for each HbsAg and CMV IgM antibodies, 2(1.94%) patients had both HCV and HBV and 1 patient had both HCV and CMV infections while none had HIV infection[10]**.** A study done in India showed that hepatitis B surface antigen, anti-hepatitis C antibodies and human immunodeficiency virus antibodies were positive in 1 of 96 (1.04%), 24 of 96 (25%) and 1 of 96 (1.04%) respectively in beta thalassemia major patients who had received multiple blood transfusions[11]. A study has been found in Pakistan,carried on 160 patients with thalassemia major, the seroprevalence of HBV, HCV and HIV was 21 (13.1%), 2 (1.25%) and 0 (0%) respectively[12]**.**

Thalassemia patients receive multiple blood transfusions every year, which may result in the development of transfusion related infections[8]. Moreover, there is an increase in the incidence of hepatitis B and C infections in general population andblood donors in Pakistan in the last decade[6,7] and hence their increase transmission to thalassemia children. This study was done to determine the burden of transfusion transmitted infections in beta thalassemia major children presenting to a tertiary care hospital for blood transfusion.

MATERIAL AND METHODS

This cross-sectional study with non-probable consecutive sampling was done in Hematology and Oncology department, The Children's Hospital and Institute of Child Health, Lahore, from March till September 2014. An approval from the Hospital Ethics Committee and informed written consent of the parents were obtained for the study. A total of 470 confirmed thalassemia major children including male and female with age ranging from 1 year to 15 years, admitted were enrolled in the study. Thalassemia minor patients and thalassemia major children who had past history of surgery were excluded. Under strict aseptic measures 5ml of blood was obtained and sent to the hospital laboratory for screening hepatitis B surface antigen and anti-hepatitis C virus, CMV IgM and anti HIV antibodies by using third generation enzyme linked immunosorbent assay. All investigations were done in the same laboratory. Confounding variables were controlled by strictly following exclusion criteria. All the information was recorded through a pre-designed Performa.

Data analysis: The collected data was analyzed statistically by using SPSS 16.0 software. The results were presented in the forms of tables. Frequencies and percentages were calculated for categorical variables like gender, hepatitis C antibodies and hepatitis B surface antigen. Mean $\pm$ S.D was calculated for continuous variable like age and number of blood transfusions. Data is stratified among age, gender,frequency of HBV, HCV, CMV, HIV and number of blood transfusions to deal with the effect modifiers. Chi-square test was applied post-stratification with P-value ≤0.005 was taken as significant.

RESULTS

A total of 470 thalassemia major patients were tested for hepatitis B surface antigen (HBsAg) and hepatitis C, CMV IgM and HIV antibodies. Out of 470 cases, 37(7.87%) cases were positive for HBsAg, 216 (45.96%) cases were positive for HCV-Ab and 22(4.68%) cases of thalassemia major were positive for both HBsAg and HCV-Ab. Only **2**(0.42%) cases had positive CMV IgM Ab and none had HIV Ab (Table 1). All cases were divided into various groups regarding their age. Minimum age taken was 01 year and maximum age included was 15 years with a mean age of 4.8121±3.4537. Most of the patients, 206 (43.82%) belonged to age group 1-5 years. Out of 470 patients, 177(37.66%) cases were in the age group of 5-10 years whereas 87(18.51%) cases belonged to age group of 10-15 years.Out of total 470 cases, 306(65.1%) were male and 164(34.9%) were female with male to female ratio of 1.86:1.0. (Fig.1)

The number of blood transfusion in majority of cases, 246(52.3%), was in the range of 1-50 times. In 102(21.7%) cases blood was transfused from 51 to 100 times. In 3(7.7%) cases, the total number of blood transfusions ware 101-150 times. There were 150-200 times blood transfusion in 30(6.4%) patients. In 56 (11.9%) cases blood was transfused more than 200 times. Minimum blood was transfused was for 10 times and maximum was 500 times with a mean of 38.02±73.29.

There was a statistically significant association between the number of blood transfusion and the age of the patients (p=0.00) but no relation (p=0.44) between the gender of the patients and the number of blood transfusions (Table 2).

Fig. 1: Gender wise distribution of Thalassemia major children

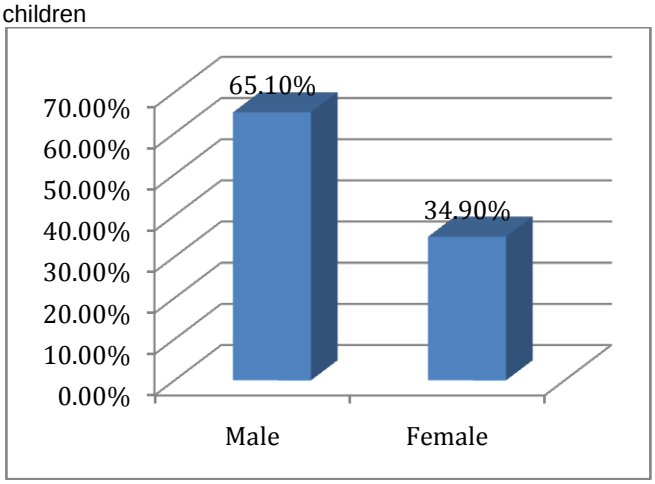

Table 1: Frequency of hepatitis B and C viruses in multi-transfusedThalassemia major children

Type of Infection	Frequency of Patients	%age
Hepatitis B surface	37	7.87
Antigen		
Hepatitis C virus	216	45.96
Antibodies		
CMV IgM Abs	02	0.42
Anti HIV Abs	00	00
HBs Ag +HCV Abs	22	4.68
Positive cases		
Patients with Negative	193	41.06

Table 2: Cross tabulation of number of blood transfusion, ageand gender of the patients:

No. Of blood transfusions		Age				Gender		Total
		1-5	6-10	11-15	Total	Male	Female	
1-50	Count	204	42	0	246	160	86	246
	%age	43.4%	8.9%	0.0%	**52.3%**	34.0%	18.3%	**52.3%**
51-100	Count	2	100	0	102	65	37	102
	%age	0.0%	7.7%	0.0%	**7.7%**	4.5%	3.2%	**7.7%**
101-150	Count	0	0	30	**30**	24	6	**30**
	% age	0.0%	7.7%	0.0%	**7.7%**	4.5%	3.2%	**7.7%**
151-200	Count	0	0	30	**30**	24	6	**30**
	% age	0.0%	0%	6.4%	**6.4%**	5.1%	1.3%	**6.4%**
>200	Count	0	0	56	**56**	36	20	**56**
	% age	0.0%	0%	11.9%	**11.9%**	7.7%	4.3%	**11.9%**
Total	Count	206	178	86	**470**	306	164	**470**
	% age	43.8%	37.9%	18.3%	**100%**	65.1%	34.9%	**100%**

DISCUSSION

Transfusion related infections are one of the serious complication in patients who receive multiple blood transfusions. Thalassemia major patients are one of the frequently transfused children in Pakistan[11].

In this study, 470 patients suffering from thalassemia major were investigated for HBsAg and anti HCV, HIV and CMV IgM antibodies. It was found that 37(7.87%) cases were positive for HbsAg, 216 (45.96 %) cases were positive for anti HCV antibodies and 22 (4.6%) cases were suffering both from HBV and HCV infection. Our result shows higher frequency of HBV as compared to a study in India which showed frequency of HBV and HCV as 1.04% and 25% respectively[11]. Similarly, a study done in Iran shows much lower figures than our study in which prevalence of HBV and HCV was 1.5% and 19.3% respectively[13]. The frequency of hepatitis C virus infection in thalassemia patients has been reported to be up to 60% in Italy[14].While, in few other studies hepatitis C virus wasdetected in 86 to 100% patients[15,16]. A local study shows that out of 79 thalassemiapatients, 34 (43%) were positive for hepatitis C virus and 4 (5.1%) were positive for Hepatitis B surface antigen[17] which is almost comparable to our study in which 7.87% cases were positive for HBs Ag and 45.96 % cases were positive for anti HCV Ab.

This study shows a very high frequency of HCV (45.96%) as compared to HBV (7.87%) infection in thalassemia major children. This is because of the protective role of vaccination against HBV and no vaccine available against hepatitis C virus [17,18]. A hepatitis B vaccine, available since 1982, has a high efficacy in the prevention of HBV transmission and has brought about remarkable changes in the global epidemiology of HBV infection[19,20]. Our results showed that in only 18%cases of thalassemia, history of HBV vaccination was positive. A study was conducted to assess the efficacy of HBV vaccine in thalassemia children and it was concluded that

hepatitis B vaccine is highly immunogenic for thalassemia children and particularly well tolerated[21]. In one local study it was found that most of patients were vaccinated and they found only 1.7% of patient who was hepatitis B positive[22]. Moreover, the prevalence of HCV is also higher in general population and blood donors as compared to hepatitis B virus [19,20]. Manny other studies also showed a higher prevalence of HCV as compared to HBV in thalassemia patients[1,11,12,14,22].

In Pakistan, variation in frequency of HBV and HVC infections in thalassemia patients were observed by different local studies. A study conducted by Shah MA et al at Khyber Medical College and Fatimid Foundation, Peshawar revealed that out of 250 multi-transfused thalassemia major patients, 8.4% were positive for HbsAg and 56.8% patients were found to be positive for anti-HCV antibodies[23].

Another local study conducted by Mohammad J and colleagues reported that among 80 thalassemia children, 7.59% were positive for HBsAg and 36.25% for anti-HCVantibodies[24]. A study carried out in Karachi, shows that out of 79 thalassemiapatients, 34 (43%) were positive for hepatitis C virus and 4 (5.1%) were positive for Hepatitis B surface antigen[17]. In another study done by Ansari SH and his colleagues reported that out of 160 thalassemia major children who received multiple blood transfusions, 13.1% cases (n=21) were anti-HCV Abs positive and 1.25% (n=20) were hepatitis B surface antigen positive[12]. In our study, the frequency for HBs Ag and anti HCV antibodies positivity were 7.87%and 45.96%respectively. This reflects that the magnitude of these infections varies in each province of Pakistan[2,4].

In our study, CMV was found in 02 cases and none of the patients showed positive serology for HIV. Similar results for CMV and HIV were found in a study done on 97 thalassemia patients in Egypt[10]. However, a local study carried on 1257 patients showed a higher frequency of HIV (0.5%) as compared to our study[25].

Male predominance was observed in our study with the frequency of 65.1% as compared to females who were in lower frequency of 34.9% with male to female ratio of 1.88**:**1. Many other local and international researchers have also shown in their studies male predominance in thalassemia major children[9,15,23,26,27,28]. A study done by Iqbal and his colleagues in Rawalpindi showed that among 95 patients, 60% (n=57) were male and 40% (n=38) were female patients[29]. In 2012, a study conducted in Iran also reported that out of 466 cases, number of male and female patients were 270 (58.3%) and 193 (41.7%) respectively[30]. However, in contrast to these studies and our results, another study conducted in Iran reported more female cases, 64 (56.64%) than males which were 49 (43.36%)[31].

In our study that the number of older patients was less while the number of younger patients was increasing. It is obvious that most of the patients, 206 (43.82 %), suffering from thalassemia major belonged to younger age group of 1 to 5 year age. There were only 87 cases in the age group 11 – 15 years. The oldest patient in our study was 15 year age while the youngest patient was of 1 year age. Several other studies have reported different age groups. In a local study conducted by Shah MA and his colleagues included in their study the children from 1.5 year to 19 years age[23]. In another study, the age group reported in thalassemia patients was 3 years to 12 years[32].

Frequency of transfusion transmitted viruses is very high in thalassemia patients because of frequent blood transfusions[33,34]. A study done by Shah et al states that the frequency of HCV infection is more than double when 50 or more than 50 times of blood transfusion was done as contrary to those with less than five blood transfusion[34]. Our study shows that the number of blood transfusion increased with increase in age (p= 0.00). However, there was no relation between the number of blood transfusions and gender of the patients (p=0.44). A study carried out by Lee WS et al stated that in 72 children there were 2,605 blood transfusions and 4,154 units of blood transfused at 0.88 transfusion episode per patient per month and 1.41 units of blood transfused/ patient/per month[26].In our study the number of blood transfusion range from minimum 10 times to maximum of 500 times with a mean of 38.02 +/- 73.29.

CONCLUSION

The frequency of transfusion related viruses especially HCV and HBV infections, is very high among multi-transfused beta thalassemia major children. This ignites the need of proper pre-transfusion screening of blood by third generation ELISA for these viruses in the blood banks and transfusion centers. Moreover, vaccination against hepatitis B in all transfusion dependent thalassemia children must be ensured.

Conflict of interest: The authors has no conflict of interest in this study.

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