Original Article

Transfusion Transmitted Hepatitis B Virus among Multitransfused Thalassaemic Children in a Tertiary Health Care Centre in Bangladesh

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Abstract

Background: *Repeated blood transfusion is the main life line support for thalassaemic children and so they are more prone to be infected with HBV. In Bangladesh the main source of blood for transfusion is the professional donors and so the possibility of HBV infection is higher.* ***Objective:*** *To assess the frequency of HBV among children who received more than 3 blood transfusions.* ***Materials and Methods:*** *This cross sectional analytical study was conducted in Pediatrics ward of Bangabandhu Sheikh Mujib Medical University, Dhaka during the period of July 2003 to June 2004. Ninety five children aged less than 15 years, suffering from β thalassaemia major and Hb E β thalassaemia having blood transfusion more than three times and 20 controls of similar age and sex were included in this study. Seromarkers of HBV were tested and the results were analyzed using SPSS version Windows 11.0.* ***Results:*** *Out of 115 children 68 were β thalassaemic (mean age 6.8 ± 2.84 yrs and male:female is 4.2:1), 27 were Hb E β thalassaemic children (mean age 8.78 ± 2.99 yrs and M:F 1.4:1) and 20 were nontransfused, age and sex matched controls (mean age 6.23 ± 1.88 yrs and M:F 1:2.3). Out of 95 thalassaemic children 21 (22.1%) were positive for HBsAg. Among them 13 were β thalassaemic and 8 were Hb E β thalassaemic. None of the controls showed HBsAg positivity indicating a significant statistical difference (p=0.033). 28 (29.5%) children were positive for anti-HBc. Among them 23 were β thalassaemic and 5 were Hb E β thalassaemic and there was no core antigen positivity among the controls showing a significant statistical difference (p=0.022). Four (4.2%) patients showed HBeAg positivity, out of whom 3 were β thalassaemic and 1 was Hb E β thalassaemic. But this antigen was not found in any control and thereby, no statistical significant difference was observed (p=0.637). Among 20 controls, 2 were positive for anti-HBe antibody, but none of the thalassaemic children was positive for this antibody showing statistically significant difference (p=0.008).*
Conclusion: *A significantly higher sero-prevalence of hepatitis B viral marker was observed among the multitransfused thalassaemic children.*

Key words: *β thalassaemia, Transfusion*

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Introduction

The prevalence of transfusion transmitted virus is high in multiple transfused patients with thalassaemia, but varies geographically according to the source of the blood administered to patients, and according to

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geographical region. The second commonest cause of death in thalassaemic patients is liver disease due to blood borne viral hepatitis.[1]

Children with β thalassaemia and Hb E β thalassaemia are dependent on regular blood transfusions.[2] This is a well-established method of transfusion of HBV and it is well known that exposure to blood and blood products is a risk factor of such virus. Despite the existence of effective vaccine for HBV for the last two decades, the initial strategy for vaccination which targeted the high risk groups including IV drug users was ineffective.[3] The emergence of newly identified hepatitis B viral variance that was found to be resistant to lamivudine and not easily prevented by the widely used recombinant viral vaccine added more complexity and confusion.[4]

Though the risk of transmission of HBV has decreased substantially in developed countries with the introduction of pre-transfusion screening program, this is still a health hazard in developing countries. Studies among thalassaemic children in different countries showed the prevalence rate of transmission of HBV ranging from 0.53% to 4.5%.[5]

In Bangladesh the main source of blood for transfusion is the risky professional donors (Bangladesh Ministry of Health and Family Welfare Program 2001). The WHO ranked Bangladesh in the moderate to high risk group of countries for HBV infections (Weekly Epidemial Rec, 2002). The prevalence of HBV among professional donors ranges from 19% to 29% and it is 2.4% among voluntary donors.[6] In 2000 to 2001 (July to April), a study found HBs Ag marker is positive in 13.82% of thalassaemic children.[7]

Materials and Methods

This cross sectional analytical study of one year duration from July 2003 to June 2004 was conducted in Pediatrics ward of Bangabandhu Sheikh Mujib Medical University, Dhaka in collaboration with Z. H. Sikder Women's Medical College, Dhaka. Ninety five children aged less than 15 years, suffering from β thalassaemia major and Hb E β thalassaemia having blood transfusion more than three times and 20 controls of similar age and sex were included in the study. Thalassaemic children were identified based on complete history, physical examination and Hb electrophoresis. Controls were selected from the non-transfused children attending the OPD of BSMMU.

3mL of venous blood was collected for screening of hepatitis B virus. The laboratory technique for analysis was done by using the 3rd generation of ELISA.

The data were expressed as mean ± SD. Statistical differences between two groups were calculated by Student's 't' test, ANOVA and χ^2 test. All statistical analyses were performed with the software SPSS version 11.0 for windows.

Results

Table I: Demographic characteristics of study children (N=115)

Study children	No	Mean age	SD (±)	Male:Female
β thalassaemic children	68	6.8	2.86	4.2:1
Hb E βthalassaemic children	27	8.78	2.99	1.4:1
Controls	20	6.23	1.88	1:2.3

One hundred and fifteen children were included in this study. Among them 68 were β thalassaemic, 27 were Hb E β thalassaemic and 20 were controls. The mean ages in years of β thalassaemic and Hb E β thalassaemic children were 6.8 ± 2.84 and 8.78 ± 2.99 respectively. The mean age of controls was 6.23 ± 1.88. The male to female ratio was 4.2:1 in β thalassaemic and 1.4:1 in Hb E β thalassaemic children. The male to female ratio of controls was 1:2.3.

Table II: Number of transfusions in different categories of patients

Number of transfusions	β-thalassaemic children (n=68)	Hb E β thalassaemic children (n=27)	Controls (n=20)	χ2	p value
4 times	37	9	None		
5 to 10 times	16	6	None	121.289	0.000
More than 10 times	15	12	None		

p value is significant

Out of 68 β thalassaemic children 37 received 4 transfusions, 16 received 5-10 transfusions and 15 were transfused more than 10 times. Among 27 Hb E β thalassaemic children 9 received 4 transfusions, 6 received 5-10 transfusions and 12 were transfused more than 10 times.

Table III: Frequency of transfusions in different categories of patients

Frequency of transfusions	β thalassaemic children (n=68)	Hb E β thalassaemic children (n=27)	Controls (n=20)	χ^2	p value
Monthly	26	3	None	123.116	0.000
2 to 6 monthly	42	24	None		

p value is significant

26 β thalassaemic and 3 Hb E β thalassaemic children were transfused monthly and 42 β thalassaemic and 24 Hb E β thalassaemic children received 2-6 monthly transfusions.

Table IV: Duration of transfusions received in different categories of patients

Duration of transfusions	β thalassaemic children (n=68)	Hb E β thalassaemic children (n=27)	Controls (n=20)	χ^2	p value
Less than 1 year	4	0	None		
1 to 5 years	49	14	None	123.766	0.000
More than 5 years	15	13	None		

p value is significant

4 β thalassaemic children had been transfused for less than one year, 49 for 1 to 5 years and 15 for more than 5 years. 14 Hb E β thalassaemic children had received transfusions for 1 to 5 years and 13 for more than 5 years.

Table V: Number and percentage of patients in respect to sources of transfused blood

Patient categories	Professional donors		Voluntary donors	
	No.	(%)	No.	(%)
β thalassaemic (n = 68)	54	79.4	14	20.6
Hb E β thalassaemic (n=27)	22	81.4	5	18.6

Fifty four (79.4%) β thalassaemic and 22 (81.4%) Hb E β thalassaemic children were transfused with blood obtained from professional donors. Fourteen (20.6%) β thalassaemic children and 5 (18.6%) Hb E β thalassaemic children were given blood from voluntary donors.

Table VI: Number and percentage of patients in accordance with the status of transfused blood

Patient category	Not screened		Screened	
	No.	(%)	No.	(%)
β thalassaemic (n=68)	37	54.4	31	45.6
Hb E β thalassaemic (n=27)	14	51.9	13	48.1

Thirty seven (54.4%) β thalassaemic and 14 (51.9%) Hb E β thalassaemic children received unscreened blood. Thirty one (45.6%) β thalassaemic and 13 (48.1%) Hb E β thalassaemic children were transfused with screened blood.

Table VII: Number and percentage of serologically positive viral markers in thalassaemic children (n=95)

Viral markers	Number	Percentage
HBsAg	21	22.1
Anti-HBc total (IgM or IgG)	28	29.5
HBeAg	4	4.2

Out of 95 thalassaemic children 21 (22.1%) were positive for HBsAg. Among them 13 were β thalassaemic and 8 were Hb E β thalassaemic. None of the controls showed HBsAg positivity indicating a significant statistical difference (p = 0.033). Twenty eight (29.5%) children were positive for anti-HBc. Among them 23 were β thalassaemic and 5 were Hb E β thalassaemic and there was no core antigen positivity among the controls showing a significant statistical difference (p = 0.022). Four (4.2%) patients showed HBeAg positivity, out of whom 3 were β thalassaemic and 1 was Hb E β thalassaemic. But this antigen was not found in any controls.

Table VIII: Status of anti-HBe total IgM & IgG in different categories of patients

Status of Anti HBe	β children (n=68)	Hb E β thalassaemic children (n=27)	Controls (n=20)	χ^2	p value
Positive	0	0	2	9.668	0.008
Negative	68	27	18		

p value is significant

Among 20 controls, 2 were positive for anti-HBe antibody but none of the thalassaemic children was positive for this antibody showing statistically significant difference (p=0.008).

Table IX: Number and percentage of viral markers positivity in accordance with the number of transfusions

	HBsAg positive cases (21)		Anti HBc positive cases (28)		HBeAg positive cases (4)	
Number of transfusion	No.	(%)	No.	(%)	No.	(%)
More than 10	12	57.14	12	42.86	0	0.0
5-10 times	6	28.57	11	32.29	2	50.00
4 times	3	14.29	5	17.86	2	50.00

Table X: Number and percentage of viral markers positivity in respect to sources of transfusion

Viral markers positivity	Professional donors		Voluntary donors		χ^2	p value
	No.	**(%)**	No.	**(%)**		
HBsAg (n=21)	21	100.00	00	00	6.645	0.021

p value is significant.

Discussion

The survival rates of children with thalassaemia and other chronic haemolytic anaemias have improved with the development of thalassaemia clinics and centres. These children require multiple transfusions and iron chelation and are at increased risk of viral transmitted infection.

Bangladesh is a developing country where HBV infection is prevalent. Akbar et al demonstrated a prevalence of HBV infection ranging from 19% to 29% among professional donors and 2 to 4% among voluntary donors.[6] WHO also ranked Bangladesh in the moderate to high risk group countries for HBV infections. Repeated blood transfusions, the main life line support for thalassaemic children, are provided mainly by professional donors in our country.[8]

In our study, 22.1% of thalassaemic children were HBsAg positive. This result is lower than that reported by Banarjee from India. He observed 25.9% HBsAg positive cases among multitransfused thalassaemic children. This comparatively low prevalence rate in our observation might be due to introduction and implementation of 'Safe blood transfusion 2002', a nationwide blood screening programme in 97 centres throughout the country and awareness among the parents of thalassaemic children about HBV vaccination and active immunization against HBV.[9] But the result of our observation is higher than that reported from other countries, where this ranged from 0.53% to 3.5%.[5]

Studies conducted in early 1990s in India showed a much higher prevalence of HBsAg ranging from 22% to 45%.[10] The differences in the results may be due to various factors such as (1) the sensitivity of ELISA, (2) the absence of HBsAg during the window phase and the convalescent phase, (3) very low levels of viremia, (4) effectiveness of screening programmes of blood and (5) the immune status of recipient of multiple transfusions.[11]

In our observation we found none of the healthy controls was positive for HBsAg and there is a significant difference (p=0.033) between the diseased children and the controls in respect to HBsAg positivity.

We found anti-HBc total IgM and IgG more often among the thalassaemic children than among controls (p=0.022). Positive anti-HBc total IgM and IgG indicates an HBV infection.[12] This is the most valuable single serological marker in diagnosing HBV infection even when HBsAg remains negative.[13]

Although none of the controls was positive for HBeAg in our study, this

marker was found in 4 thalassaemic HBsAg positive children. That did not differ significantly between the thalassaemics and the controls (p=0.637). This result is consistent with that of the another study.[7] On the other hand, 2 of the controls were positive for anti-HBe and all of the thalassaemics were negative. The difference was statistically significant (p=0.008). The reason for this is not known. Unlike our study, Alsheyyab et al reported 3.5% HBeAg and 22% anti-HBe positivity among Arabian children suffering from hereditary haemolytic anemia.[5]

Positive HBeAg indicates that the virus replicates, encodes and infects liver cells when it remains highly infectious.[14] On the other hand anti-HBe antibody indicates seroconversion and appearance of anti-HBe is a strong evidence that the patient will recover.[15]

As the thalassaemic children are dependent on blood transfusion mostly from professional donors, they can be infected with HBV as the professional donors harbour HBV more often than voluntary donors.[7]

In our study, one of the thalassaemic children had both HBV and HCV infections. Concomitant infection of both HBV and HCV has ominous impact in the pathogenesis of chronic viral hepatitis[16], leading to rapid progression towards cirrhosis of liver (hepatitis C-global prevalence, 2000). So, HBV vaccination should be considered for the thalassaemic children as a preventive measure. Considering the fatal outcome of concomitant HBV and HCV infection, it is mandatory to transfuse blood which is screened strictly before transfusion, and transfusion of infected blood must be stopped.

In our observation, it revealed that the prevalence rate of hepatitis B viral marker positivity increased with the increment of the number of transfusions. Among the thalassaemic children who were transfused more than 10 times, 57.14% were positive for HBsAg and 42.86% were anti-HBc positive. On the other hand, 14.29% and 17.86% of the diseased children who were transfused 4 times were positive for HBsAg and anti-HBc respectively. It was evident that all of the HBsAg positive thalassaemic children were transfused with blood from the professional donors. This indicates that the professional donors in comparison to the voluntary donors play the major role in transmitting transfusion related HBV with a statistical significance (p=0.021).

Akbar et al demonstrated a prevalence of HBV infection ranging from 19% to 29% among the professional donors and 2 to 4% among the voluntary donors.[6] The WHO also ranked Bangladesh in the moderate to high risk group countries for HBV infections.[17]

A significantly higher sero-prevalence of hepatitis B viral marker was observed among the multi-transfused thalassaemic children. Since these children depend mostly on professional donors for transfusion, there always remains a possibility of acquiring these infections through blood transfusion.

We acknowledge the potential limitation of our study. The sample size was not sufficiently large. Study subjects were not cohort, collected from the urban set-ups and were not randomly selected. We, therefore, suggest that a multi-centre study should be conducted with a larger sample size from a wider geographic area to reach a firm conclusion on the potential risks of transfusion-transmitted infections among multitransfused thalassaemic children.

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