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Original Research Article

Prevalence of transfusion transmitted infections amongst multiple blood transfused patients of β-thalassemia major in a tertiary care hospital

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ABSTRACT

Background: The β-thalassemias are the most common autosomal recessive inherited hemoglobin disorder in the Indian subcontinent, with an uneven distribution among different endogenous populations. Present study was planned to estimate the prevalence of transfusion transmitted viral diseases in multiple transfused patients of β-thalassemia and factors affecting it.
Methods: It was a Prospective observational study carried out at Thalassemia day care center of tertiary health care institute.
Results: 211 patients were enrolled in the study. 151 were males and 60 females. Maximum numbers of children were in age group of 6- 10 years. 75 (35.5%) patients with HCV (Hepatitis C Virus) and 5 (2.36%) patients with Hepatitis B virus (HBV) infection were found at the end of study. No new HIV (Human Immunodeficiency Virus) infection was detected. There was significant association between prevalence of transfusion transmitted infections (TTI) with number of transfusions but no significant association detected with age, sex and blood group of the patients
Conclusions: Thalassemia is a chronic transfusion dependent disease complicated by the effects of iron overload on various organs leading to increased morbidity and mortality. The risk of transmission of TTI in thalassemia increases with time as number of transfusions increase. Use of advanced technology in blood screening, voluntary donations, donor selection, asepsis during blood transfusion should be used to curtail the transmission.

Keywords: Thalassemia, Transfusion transmitted infection, HBV, HCV, HIV

INTRODUCTION

The β-thalassemias are the most common autosomal recessive inherited hemoglobin disorder in the Indian subcontinent, with an uneven distribution among different endogenous populations.[1] It occurs due to reduced or absent production of β-globin chains with relative excess of α-chains, resulting in decreased production of adult hemoglobin in bone marrow and extramedullary sites. The relatively excessα-globin chains in comparison to β and ϒ-globin chains forms alpha-globin tetramers (α4) and these inclusions interact with the red cell membrane; shorten red cell survival, all resulting in ineffective erythropoiesis and anemia.

Adequate and safe blood transfusions with regular iron-chelation therapy remain the cornerstone therapy to improve the quality of life and survival of these patients.[2] If there is a breach in "safe blood transfusion" practices, these patients are confronted to new clinical challenges, particularly in the form of transfusion transmitted diseases, especially HCV (Hepatitis C Virus), HBV

(Hepatitis B Virus) and HIV (Human Immunodeficiency Virus) infections.[2] Present study was planned to estimate the prevalence of transfusion transmitted viral diseases in multiple transfused patients of β-thalassemiaand factors affecting it.

METHODS

Present study was carried out over a period of 15 months in Department of Pediatrics at Pt. B.D. Sharma University of Health Sciences, Rohtak, Haryana, India. All registered patients of β-thalassemia major attending the day care center of this institute fulfilling inclusion criteria (known cases of beta thalassemia major registered in Thalassemia clinic, those who had been transfused at least ten units of blood and received complete course of hepatitis B vaccine) were selected. Patients receiving less than 10 transfusions or had received blood transfusion outside the institute were excluded from the study. Informed written consent from the parents/guardian was obtained. Patients were given regular blood transfusions in order to maintain hemoglobin at least 10g/dl with chelation. Blood was procured from blood bank of the institute. Blood units were screened for HIV, HCV, HBsAg, syphilis and malarial parasite by kit approved by Central Drugs Standard Control Organization. A detailed history and physical examination was done as per study performa. Complete hemogram with absolute platelets count, liver and renal function tests, serum ferritin levels and viral markers HIV, HBsAg (Hepatitis B surface antigen), HCV status were done at beginning of study and thereafter repeated every three months for 15 months. HbsAg in serum was analyzed using Microwell ELISA technique. HIV serological status was detected by Micro well ELISA test for detection of antibodies to HIV-1and HIV-2 in human serum/plasma. Third generation HCV microwell ELISA method was used for detection of antibodies against HCV in plasma.

RESULTS

211 patients were enrolled in the study. 151 were males and 60 females. Maximum numbers of children were in age group of 6- 10 years (Table 1).

Table 1: Distribution of patients in different age groups.

Age (years)	Males	Females	Total
0-5	34	10	44
6-10	40	20	60
11-15	33	14	47
16-20	28	7	35
21-25	13	6	19
>26	3	3	6

Table 2 shows distribution of patients according to average number of blood transfusions. The incidence of transfusion transmitted infections increased with increased number of transfusions. 33.1% children received between10-100 transfusions during study, 29% received between 101-200, 24.1% children had been transfused between 201-300 times, 11.8% between 301-400 and 5.6% children had received more than 400 transfusions since the diagnosis of disease. 38.5% patient of 10-100 transfusion group, 55% of 201-300, 48% of 30-400 and 66.6% of more than 400 transfusion group were found seropositive for various viral markers in the study (Table 2).

Table 2: Distribution of patients according to number of transfusion received and prevalence of TTI in different groups.

No. of blood transfusions	Total no. of patients	Positive for HIV	Positive for HCV	Positive for HBV	Percentage of Seropositivity (%)
10-100	70	0	26	1	38.57%
101-200	47	0	0	0	0
201-300	60	0	31	2	55%
301-400	25	0	12	0	48%
>400	12	0	6	2	66.6

80 (59 males and 21 females) patients were tested seropositive for viral markers during the study. 75 (56 males and19 females) patients were reactive for HCV, 5 (3 males and 2 females) patients were found positive for HBV. No patient was found reactive for HIV. The maximum incidence of transfusion transmitted infection was found in 11-15 years (32.5%, 31.25% HCV, 1.25% HBV) followed by 16-20 years (26.25%, all HCV), less than 10 years (21.25% , 20% HCV, 1.25% HBV) and more than 20 years(20%, 16.25% HCV, 3.75% HBV). (Table 3).

Transfusion group of 200-300 transfusions had highest number of transfusion transmitted infection (41.25%, 38.75% HCV, 2.5% HBV) followed by 10-100 transfusion group (33.75%, 32.5% HCV, 1.25% HBV), 300-400 (15%, all HCV) and more than 400 transfusion group (10%, 7.5% HCV, 2.5% HBV). Surprisingly no

patient was found infected in 101-200 transfusion groups. Patients were divided according to blood groups and Seropositivity for viral markers under study. Blood group B positive had maximum numbers of 91 patients and no patient belonged to AB negative blood group. HBV seroreactivity was seen in two patients of B positive blood group, two patients of O positive blood group and one patient of AB positive blood group. HCV was found seropositive in 34 patients of B positive, 17 patients of O positive blood group, 9 patients of A positive, 7 patients of AB positive, 4 patients of B negative, 3 patients of O negative and 1 patient of A negative blood group.

Table 3: Distribution of various TTI detected during study in various age group.

Age (Years)	HCV		HBV		HIV	
	Males	Females	Males	Females	Males	Females
0-5	03	01	1	0	0	0
6-10	08	04	0	0	0	0
11-15	19	06	0	1	0	0
16-20	16	05	0	0	0	0
21-25	07	02	2	0	0	0
>26	02	02	0	1	0	0

Though there was no significant association between prevalence of transfusion transmitted infections (TTI) with number of transfusions, age , sex, blood group but prevalence of TTI increased with increasing age and number of transfusion.

DISCUSSION

Transfusion transmitted infections (TTIs) are a great concern for safety of multiple transfusion patients. The magnitude of the TTI varies from country to country depending on TTIs' loads in that particular population from where blood units are sourced.[3,4] The major problems are due to high prevalence of asymptomatic carriers in the society, blood donations during the window period of infections, concealing medical history by captive, paid, or professional blood donors who widely exist in developing countries. There is a long list of viruses, parasites, and bacteria, which can be transmitted through blood transfusions.[5,6]

Table 4: Comparison of prevalence of TTI from previous studies.

Study	Country	Year	No. Of patients	HBV (%)	Method	HCV (%)	Method	HIV (%)	Method
Bhavsar[12]	Gujrat (India)	2008	100	6	ELISA	18	ELISA	9	ELISA
Grewal[13]	Punjab	2004	116	0.8	ELISA	59.4	ELISA		
Faramawy[14]	Egypt	2014	100	12	ELISA	45	ELISA		
Jain[15]	Gujarat	2012	115	1.04	ELISA	25	ELISA	1.04	ELISA
Mirmomen[16]	Iran	2006	732	1.5	ELISA	19.3	ELISA	0	ELISA
Mansour[17]	Egypt	2012	200	20	ELISA	40.5	ELISA		
Lee[18]	Malaysia	2005	72	1	ELISA	13	ELISA	0	ELISA
Katabuka[19]	Congo	2013	394	1.6	ELISA	13.5	ELISA	1.3	ELISA
Ansari[20]	Pakistan	2012	160	1.25	ELISA	13.1	ELISA	0	
Mollah[21]	Bangladesh	2003	152	13.5	ELISA	39.5	ELISA	0	ELISA
Vidja[22]	Gujarat	2010	200	3	ELISA	2	ELISA	3	ELISA
Ocak[23]	Turkey	2006	399	0.75	ELISA	4.5	ELISA	0	ELISA
Present study		2014	211	2.3	ELISA	35.5	ELISA	0	ELISA

HCV prevalence was found to be 35.54% in present study, making it most common TTIs. 55 males and 20 females were seropositive. In age group 0-5 years 4 patients out of 44, in age group 6-10 years 12 patients out of 60, in age group 11-15 years 25 patients out of 47, in age group 16-20 years 21 patients out of 35, in age group 21-25 years 9 patients out of 19, in age more than 26 years 4 patients out of 6 patients are found to be

seropositive for HCV. 2.36% patients were found to be HbsAg positive. 3 males and 2 females tested positive for HBV. One male patient belongs to 0-5 year's age group and two male patients belong to 21-25 years age group, while there are two HBV seropositive females patients belonging to 11-15 years and more than 26 years age group each. None of the patient was found to seropositive for HIV, so its prevalence is 0%. Table 4 shows the prevalence of various TTI in our study from the studies done earlier in different region of our country and neighboring countries. HCV is the most prevalent TTIs in all of the studies. Prevalence of HCV ranges from 2- 59.4 %. In present study it comes out 35.5% which is close to previous reports. HBV prevalence in other studies is 0.75-20 %. In present study it is 2.3 %. HIV prevalence ranges from 0-9 % in various studies. In present study no case was detected seropositive for HIV, making prevalence 0%.[12-24]

This high prevalence of HCV infection may be attributed to late starting of screening for HCV in donated blood bags compared to that of anti HIV-1/2.[7] HCV prevalence had shown a decreasing trend after mandatory screening of blood in blood banks. Another factor which might be responsible for high prevalence of HCV as compared to HBV is non-availability of vaccine against HCV.

During window period the HBsAg cannot be detected in the blood, although hepatitis B infection is present. Despite the screening of HBsAg by ELISA for over 20 years, transfusion associated HBV continues to be a major problem in India, more so in patients who receive repeated transfusions. During this "window period," detection of the antibody to the hepatitis B core antigen (anti-HBc) serves as a useful serological marker for hepatitis B infection. So there is a need of more advanced screening tests to limit the transmission of HBV infection.

Some countries with low level prevalence of HBV have implemented HBV NAT testing in plasma pools. The kinetics of viral antigen and antibody appearance during HBV infection create two different window periods in which one or the other test may fail. The "early acute phase", when serological markers are negative and "late chronic phase" when HBsAg may become gradually undetectable, although infectivity remains. NAT can potentially identify and therefore can be of particular benefit in detecting HBV DNA in latent HBV infection in early acute phase/occult HBV infection, when HBV DNA is present in plasma but presence of anti-HBC and HBsAg is variable.

Indian government mandates testing all donated blood for HIV, Hepatitis B, Hepatitis C, Syphillis and Malaria.[7] Blood Banking is governed by the Drugs & Cosmetic Rule in India 1940. According to this rule, only blood tested non-reactive can be transfused to patients. Even after screening of blood, the transmission risk of infections is not obsolete as screening methods are not sensitive enough to detect infections in window period.[8-10]

The magnitude of the TTI varies from country to country depending on TTIs' loads in that particular population from where blood units are sourced. Multiple measures are taken to minimize TTI transmission in the respective population. These strategies may be targeted to prevent transfusion-transmitted diseases in that country. The strategies which may lead to significant decrease in TTI includes adequate screening of blood and blood products, use of advanced techniques like NAT (nucleic acid amplication techniques) which detects infections earlier than convention methods and reduces the the window period of HBV to 10.34 days, HCV to 1.34 days and HIV to 2.93 days.[11]

Promotion of voluntary donation in place of replacement donation of blood, selection of donors after proper history and examination, proper storage and handling of blood and blood products, use of adequate asepsis technique during transmission are some of the measures which can be taken for prevention of TTI.

CONCLUSION

Thalassemia is a chronic transfusion dependent disease complicated by the effects of iron overload on various organs leading to increased morbidity and mortality. The risk of transmission of TTI in thalassemia increases with time as number of transfusions increase. The TTI further complements the suffering of patient leading to increased morbidity. Use of advanced technology in blood screening, voluntary donations, donor selection, asepsis during blood transfusion should be used to curtail the transmission.

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