Prevalence of Transfusion Transmitted Infections in Multiple Blood Transfused β-Thalassemia Patients from a Tertiary Care Centre in North India

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ABSTRACT

Introduction: The mainstay of therapy for patients suffering from beta thalassemia major is regular blood transfusion and chelation therapy due to constraints in bone marrow transplantation. The present study was conducted to estimate the prevalence of transfusion-transmitted infections (TTIs) in multitransfused patients of thalassemia major and to determine the association with relation to the number of blood transfusions received.

Material and Methods: This study was conducted in Department of Microbiology on 126 β- thalassemia major patients registered for regular blood transfusions at Thalassemia Day Care Centre attached to Department of Pediatrics, Government Medical College, Amritsar, Punjab from January to July 2018. The patient's serum samples were screened for TTIs i.e. Human Immunodeficiency Virus (HIV), Hepatitis B virus (HBV) and Hepatitis C virus (HCV). Seropositivity screening for HBV and HCV was done by rapid Immunochromatographic test and confirmed by enzyme-linked immunosorbent assays. (ELISA) while for HIV as per NACO guidelines.

Results: Out of 126 patients, 14.28% (18/126) were sero-reactive for TTIs. Of these sero-reactive patients, 13.4% (17/126) were positive for anti-HCV antibody, 0.79% (1/126) positive for HBsAg and none (0) for anti HIV antibody. Of the anti-HCV reactive cases, 70.5% (12 out of 17) were >12years of age, 58.8% (10 out of 17) had received more than 250 transfusions, and 23.5% (4 out of 17) had received transfusions between 100 to 250. Anti-HCV seroreactivity was thus found to increase with the age and increase in the number of transfusions received.

Conclusion: It is concluded that HCV is the most prevalent TTI in multi-transfused children with thalassemia major and stringent pre-transfusion screening of blood for anti-HCV must be introduced in blood centers. HBV vaccination should also be done before the start of transfusion regimen or as soon as possible after diagnosis of thalassemia.

Keywords: Enzyme-linked Immunosorbent Assay (ELISA), Multitransfused, Thalassemia, Transfusion-Transmitted Infections (TTIs)

INTRODUCTION

Beta thalassemia, also known as Cooley's anemia, is a chronic hemoglobinopathy, characterized by severe hemolysis. Thalassaemias are a group of hemolytic anemia which result from an inherited abnormality of globin chain production. About 150 million people i.e., 3% of world population carry beta thalassaemia gene.[1] It occurs in a particularly high frequency in a broad belt extending from the Mediterranean basin through the Middle East, Indian subcontinent, Burma, Southeast Asia, Melanesia and the island of the Pacific. Defective globin chain synthesis leads to haemolysis of red blood cells and thereby fall in haemoglobin. Patients require frequent blood transfusions to maintain their haemoglobin above the survival level.[2] Definitive treatment of beta thalassemia which is the most common type of thalassemia is bone marrow transplanatation.

Due to the financial constraints and limited availability of matched donors for bone marrow transplantation, patients have to depend on regular blood transfusions and chelation therapy to prevent iron overload. Majority of patients require blood transfusion every two weeks. Due to such high frequency of blood transfusions, patients are at risk for transfusion transmitted infections (TTI). Transfusion transmitted infections include many viral, bacterial or parasitic infections but most gravest of them are HIV, Hepatitis B and Hepatitis C.[16] Nowadays, blood products from the donors are stringently screened for these infections in the blood banks before being transfused, but these infections may be present in their window period which gives a possibility for missing these infections and thereby pose a risk of infection in the recipient.[3] the present study was conducted to know the prevalence of transfusion transmitted infections in beta thallasemic patients.

The aims of this study were to estimate the prevalence of Transfusion Transmitted Infections amongst multiple blood transfused patients of beta thalassemia and to determine association of TTIs in relation to number of transfusions.

MATERIAL AND METHODS

The present was done to investigate the seroprevalence of

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HIV, HBV, HCV infections in 126 multiple blood transfusion dependent thalassemia major patients. The present study was conducted in the Department of Microbiology, and Thalassemia ward attatched to Department of Pediatrics, Government medical college, Amritsar, Punjab from January to July 2018. Thallasemic patients receiving regular transfusions of blood per month at interval of 7- 15 days in order to maintain the hemoglobin levels above 10gm/dl were included in the study. Patient's age ranged between 0 and 25 years. Patients were interviewed using a structured questionnaire and Information regarding serostatus of HIV, HBV and HCV infection was obtained from their case records. HIV, HBV, HCV seropositivity was screened by rapid immunochromatographic test and confirmed by ELISA (Enzyme Linked Immunosorbent Assay). HIV status was detected by Micro well ELISA test for detection of Antibodies to HIV-1and HIV-2 in Human serum/plasma (COMBAIDS-RS Advantage-ST test kit which is dot immunoassay indented for the qualitative detection of IgG/IgM). HBV status was detected by Qualisa or HEPALISA (Micro well Enzyme Immunoassay, ELISA for the detection of Hepatitis B surface antigen (HBsAg) in human serum or plasma). HCV status was detected by HCV-MICROLISA (micro well ELISA TEST for detection of Antibodies to Hepatitis C virus in Human Serum/plasma). Every thalassaemic patient was given vaccine for Hepatitis B on very first day before starting of first blood transfusion, when he/she came for blood transfusion. Serum used in the study was obtained just before packed red blood cells transfusion. All information and test results were kept confidential. Written consent was taken from all patients or from their relatives in case of minor for this study.

RESULTS

A total of 126 patients, 74 males (58.7%) and 52 females (41.2%), multi-transfused thalassemia major patients were included in the study group with mean age of 8.1 years (0.75–23 years). The mean age of diagnosis of thalassemia major was 1.6 years with a range of 3 months to 7 years. A total of 26 (20.6%) patients reported history of receiving blood from other sources in addition to the blood bank of the study hospital. Pre-transfusion mean haemoglobin at hospital visit was 5.9 g/dl with a range of 2–11 g/dl. 40% of the patients did not receive any chelation therapy.

Out of total 126 patients, 14.28% (18/126) were sero-reactive for TTIs. Out of these 18 sero-reactive patients, 13.4% (17/126) were positive for anti-HCV antibody while 0.79% (1/126) were positive for HBsAg (table-1). None of the patient was positive for anti HIV antibody. Of the anti-HCV reactive cases, 70.5% (12 out of 17) were >12years of age, 58.8% (10 out of 17) had received more than 250 transfusions, and 23.5% (4 out of 17) had received transfusions between 100 to 250. Anti-HCV seroreactivity was thus found to increase with the age and increase in the number of transfusions received.

DISCUSSION

Regular blood transfusions are the mainstay of therapy in thalassemia major patients due to financial constraints and limited availability of HLA matched donors. As per guidelines issued by different institutes, hemoglobin level of

	Male (%)	Female (%)	Total
Prevalence of hepatitis C	8 (6.3%)	9 (7.1%)	17 (13.4%)
Prevalence of hepatitis B	1 (0.79%)	0	1 (0.79%)
Prevalence of HIV	0 (0%)	0	0 (0%)
Total TTI	9 (7.14)	9 (7.14%)	18 (14.28%)

Table-1: Burden of transfusion transmitted infections (TTIs)

	Male (%)	Female (%)	Total
Mean haemoglobin level (SD)	5.7 (0.3)	6.1 (0.4)	5.9 (0.2)
History of hepatitis B vaccination			
Complete	11 (14.86)	6 (11.5)	17(13.4)
Incomplete	5 (6.7)	3 (5.7)	8 (6.3)
None	58 (78.3)	43 (82.6)	101(80.15)
Mean age of diagnosis of thalassemia Major (SD)	1.3 (0.4)	2.3 (0.5)	1.6 (0.3)
Mean duration of blood transfusion (SD)	8 (0.4)	5.3 (0.2)	7.2 (0.3)
History of thalassemia major in family	3 (4.0)	2 (3.8)	5 (3.9)
Mean frequency of blood transfusion in days (SD)	19 (2)	18 (3)	18.5 (2.5)
Mean serum ferritin level (SD)	3,378.2 (481.5)	2936.4 (593.1)	3518 (482.7)
Mean SGOT (SD)	62.5 (12.3)	64.1 (7.2)	58.2 (12.4)
Mean SGPT (SD)	52.4 (15.2)	57.5 (4.8)	61.2 (7.1)
Mean serum alkaline phosphatase (SD)	244.5 (14.3)	223.4 (12.1)	230.1 (7.6)

Table-2: Medical history of the study participants

No. of transfusions	No. of cases	Anti HCV	Anti HbSAg	Anti HIV
<50	35	Nil	Nil	Nil
50-100	33	3	1	Nil
100-250	40	4	Nil	Nil
>250	18	10	Nil	Nil

Table-3: Seroprevalence of TTIs with respect to the number of transfusions received by thalassemic patients

at least 9.5 gm/dL is necessary for maintaining the physical growth and development of such patients.[1] Therefore these patients require frequent blood transfusions. Although adequate and safe blood transfusions improve the quality of life of thalassemic patients, they also expose the patients to the risk of acquiring TTIs. The probability of acquiring TTIs is related to the probability of being exposed to the infected units of blood. The probability of being exposed to infectious units of blood depends on the prevalence of carriers among the donor population and the number of units transfused.[4] Thus, the infection rate of TTIs increases with increase in number of transfusions received by the recipient.

In the present study, seropositivity for TTIs was 14.2% (18/126). HBV seropositivity was 0.79% (1/126) and that for HCV was 13.49%. None of the thalassemia patients in the study group was positive for HIV infection (table-2).

Rates of TTIs with studies from other part of India showed different percentages of Anti-HCV positivity and HBsAg and Anti- HIV positivity. Studies with similar prevalence were reported by various authors. In the study done by Jain et al[5], Anti HCV positivity was found to be 25 percent. While Vidija et al[6] and Patel et al[7] showed Anti HCV positivity to be 2 percent and 16.04 percent respectively. In a similar study done by Grewal et al[15] in Punjab, prevalence of HBV was found in 0.8% while prevalence of HCV was found in 59.4 percent of thallasemic patients.

HBV positivity in study done by Jain et al[5] was 1.04 percent, while in the study done by Vidija et al6 showed 2 percent positivity. A little higher prevalence (6%) was found in Bhavasar et al7.

Variations in the prevalence of TTIs amongst thalassemics even after serological screening could be related to geographical differences in prevalence of the viral infections among blood donors, nature of blood donors whether replacement or voluntary, and the nature of care individual thalassemics receive.

TTIs such as HBV, HCV, and HIV are dreaded consequences of transfusions, as these can result in long-term morbidity and mortality. In India, it is mandatory to screen donated blood for anti-HIV 1 and 2 (since 1991), anti-HCV (since 2001), HBsAg, syphilis, and malaria.

TTIs can still occur even after regular screening for the markers for these infections, as found in different Indian and international studies.[8,9] This residual risk of acquiring a TTI from screened blood depends upon the sensitivity of the screening tests used, window-period of the virus, and other reasons, such as mutant strains.[10]

Hepatitis B infection was found in only one patient out of 126 patients (0.79%). HBV infection can be prevented in thalassemic patients, as very effective HBV vaccine is available. This may be the reason for low prevalence of hepatitis B infection as the patients are routinely vaccinated against HBV infection. Hence, all patients who require multiple transfusions should be vaccinated right from the beginning.

Nucleic acid testing (NAT) is widely recommended for the screening of donor blood. A study done by Makroo et al. showed that blood units negative for HIV, HBsAg, and HCV still have 1:1000-1:1500 chance of being positive when tested by NAT. The majority of the positivity was due to HBV virus, which underlines the need for HBV vaccination in thalassemic patients.[11] Now with the introduction of the fourth-generation ELISA test that detects p24 antigen along with antibodies, the window period can be reduced to 2 weeks, but NAT screening further shortens it to 2.93 days for HIV, to 10.24 days for HBV, and to 1.37 days for HCV.[12] In the study done by Malhotra et al. there was significant increase in the detection of seroreactivity with fourth-generation ELISA kits as compared to third-generation ones.[13]

In the present study, out of all cases positive for anti-HCV, majority (58.8%) had received more than 250 transfusions followed by those who had received transfusions between 100-250, which was statistically significant ($p<0.05$) (table-3). This may be due to the reason that they have been receiving transfusions before 2001, when screening for anti-HCV was routinely not done and it became mandatory thereafter. This finding is comparable to other studies.[4,6,7] In the study done by Mittal et al[14], 66.6% of the patients who had received more than 400 blood transfusions were seropositive for Anti-HCV. There is a reduction in the development of anti-HCV post 2001, but it has not been eliminated. All the cases of positive anti-HCV had received more than 100 transfusions, similar to other studies.[6,7] Thus, patients have more chances of developing anti-HCV with increase in number of transfusions.

No patient was positive for HIV. This may be due to stringent and regular screening of blood for HIV as per NACO guidelines.

CONCLUSION

Present study highlights higher prevalence of HCV in thallasemic patients for which they need to adopt better means for preventing TTI's. Measures which can be recommended for preventing TTI are: Better donor-screening strategies; the promotion of voluntary blood donation; and the implementation of newer technologies such as fourth-generation ELISA and/or NAT screening for HIV, HBV, and HCV, which reduces the window period and thus reduces exposure to these infections via blood transfusion. Also HBV vaccination must be done before starting the transfusion regimen or as soon as possible with frequent quantification of AntiHBsAg titres and booster doses if titres are found to be low.

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