Research Paper

Volume : 3 | Issue : 12 | December 2014 • ISSN No 2277 - 8179

A Retrospective Study for Prevalence of Transfusion-Transmitted Infections in Multiply Transfused Thalassemia Major Paediatric Patients

Medical Science

KEYWORDS : Hepatitis B, hepatitis C, Human immunodeficiency virus, β-thalassemia major, seroprevalence

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ABSTRACT

Objective:To study the rate of seropositivity to Hepatitis B and C and Human Immunodeficiency Virus (HIV) infections among children with β-thalassemia major receiving multiple transfusions in Ahmedabad, India, compared with healthy controls.Materials and Methods:The study was performed during 1st January 2013 to 31st December 2013 on multi-transfused children suffering with β-thalassemia major registered at the tertiary care center, Ahmedabad and investigated for the prevalence and development of transfusion-transmitted infections. Hepatitis B surface Antigen (HBsAg), anti-Hepatitis C Virus (HCV) Antibodies (Ab), and HIVAb were checked using a fourth-generation Enzyme-Linked Immunosorbent Assay (ELISA). Positive tests were confirmed by western blots. Healthy blood donors were used for the control group.Results:There were a total of 81 patients; of them 49(60.49%) were male and 32(39.51%) were female. one patient (1.23%) was positive for HBsAg, 13 (16.04%) were positive for anti-HCV, and one (1.23%) was positive for anti-HIV. Conclusion:It is concluded that HCV is the current major problem in multi-transfused children with thalassemia major and more careful pre-transfusion screening of blood for anti-HCV must be introduced in blood centers.

INTRODUCTION:

The Thalassemias are a group of congenital hemolytic anemia that is characterized by deficient synthesis of one or more globin subunits of the hemoglobin.Thalassemia is considered to be a quantitative hemoglobinopathy,since no structurally abnormal hemoglobin is synthesized. According to the chain whose synthesis is impaired, the thalassemia are designated as α, β, γ, δ, δβ, or εγδβ thalassemia. The β thalassemia is probably the most common inherited hemoglobin disorder in the Indian subcontinent, with an uneven distribution among the different populations.The basic defect in β thalassemia is a reduced or absent production of β globin chains with relative excess of α chains. Beta thalassemia major is a transfusion dependent severe anaemia requiring lifelong blood transfusions. Blood transfusion is double aged sword because thalessemia children at risk if the transfusion is inadequate but at the same time repeated blood transfusions are associated with hazards like iron overload and risk of transfusion transmitted infection.In the end thalessemic patient die either due to transfusions or due to lack of it.(1,2)

Conventional treatment of patients suffering from β thalassemia is regular blood transfusion support from early childhood. The current management of thalassemia includes regular transfusion program and chelation therapy. The rationale for this treatment started in 1960s and was modified in the following years to achieve progressively higher levels of hemoglobin, which corrects the anemia and prevents the ineffective erythropoiesis, increases oxygen delivery to tissues, promotes growth, and improves the general wellbeing.[1] Current guidelines recommend a pre-transfusion threshold not exceeding 9.5% g/dl, which seems to be associated with adequate marrow inhibition and a relatively low iron burden.[2,3]

Piomelli et al. have recommended a hypertransfusion regimen, with pre-transfusion hemoglobin level of 10 g/dl.[4] Blood transfusion exposes the patient to a number of risks, adverse events associated with transfusion, such as non-hemolytic febrile reactions, allergic reactions, delayed transfusion reactions, transfusion-related lung injury, graft-versus-host disease, red cell alloimmunization and transfusion of infectious agents including viruses, bacteria and parasites.[5,7]

Appropriate and regular red cell transfusion remains the main treatment of choice for a large number of patients with thalassemia major. These patients who are maintained on hypertransfusion regimen can develop various complications due to multiple transfusions, one of them being transfusion-associated infections. The transfusion-associated diseases are overcome by safe donor selection and, further, by application of better screening methods. This study was designed to determine the prevalence and incidence of Transfusion-Transmitted Infections (TTI) in multiply transfused thalassemia patients during the study period.

After the discovery of Hepatitis C virus in 1989,it has proved to be major cause of transfusion associated hepatitis in the world,other transfusion acquired disease being Hepatitis B,HIV,syphilis,malaria etc.Pretransfusion screening of blood is one of the cost effective way to prevent transfusion transmitted infections.Hepatitis B and HIV screening is being done in all blood banks in India since 1996.Screening for HCV was made mandatory from 1 june,2001.

MATERIAL AND METHODS:

The study was conducted among 81 beta-thalassemia major patients receiving regular blood transfusions atpediatric department in B.J. medical college,Ahmedabad located at Ahmedabad City,Gujarat state, India, from 1st January 2014 to 31th August 2014.

All confirmed beta-thalassemia major patients aged more than or equal to 6 month registered at paediatric department in B.J. medical college, Ahmedabad, and receiving blood transfusions regularly at the same institute were included in this study. After obtaining due permission from the authorities, the clinical data such as age, duration and number of blood transfusions, history of HBV vaccination were obtained from detailed interviewing of the patient and/or guardians through preformed questionnaires. Blood of the patients who had not been tested for theirHIV, HBsAg, and HCV status over the past 1 year, was sent for the same. The data thus obtained, including the laboratory results and the clinical examination results, were subsequently analyzed.

Data for antibodies to HCV was retrospectively reviewed for the period under study from the records of the Thalassemia Unit. Hepatitis B surface antigen, antibody to HIV and antibody to HCV is tested every six months for all thalassemic patients at our centre. For detection of Hepatitis C Virus (anti-HCV), Human Immunodeficiency Virus (anti-HIV) antibody, and Hepatitis B surface Antigen (HBsAg), the Enzyme Linked Immunosorbant Assays (ELISA) tests were done on the patients' serum.All the thalassemic and hemophilic children are registered are provided blood free of cost, which is cross-matched and transfused at our hospital

RESULT:

The prevalence of TTI was studied. There were a total of 81 patients; of them 49(60.49%) were male and 32(39.51%) were female. two patient (2.46%) was positive for HBsAg, 13 (16.04%) were positive for anti-HCV, and one (1.23%) was positive for anti-HIV.

Sex	No. of patient	Positive for HBsAg	Positive for HBcAg	Positive for anti-HIV
male	49	1	8	1
female	32	1	5	0

Relationship between Age and Number of Blood transfusions: The figure shows that with increase in age, the cumulative number of blood transfusion received will increase.

Relationship between positivity and Age: Incidence of Anti HCV Abseropositivityshows7 out of 13(53.84 %) children were having age more than 8 years.

Age of patient	Number of patient	Anti-HIV positive	Anti HBsAg positive	Anti HBcAg positive
0-2	15	01	00	01
2-5	17	00	00	02
5-8	20	00	02	03
8-11	25	00	00	05
11-14	4	00	00	02

Relationship between positivity and number of blood transfusions:8 out of 13 Anti HCV Ab positive children (61.53%) were transfused more than 50 units of blood.

DISCUSSION:

Beta-thalassemia major is one of major public health problems in India. The general incidence of thalassemia trait in India varies between 3 and 17%.[7] It is estimated that there are about 65,000-67,000 beta-thalassemia patients in India with around 9,000-10,000 cases being added every year.[8] The overall prevalence of beta thalassemia major in Gujarat State, Western India, is 7.48%.[1]

Patients with thalassemia major require repeated transfusions of blood exposing them to the risk of Transfusion-Transmitted Diseases (TTDs). The probability of acquiring TTDs is related to the probability of being exposed to the infected units of blood. This probability depends on the prevalence of carriers among the blood donors in the population and the number of units transfused. Thus, the infection rate of TTDs increase with age in subsequent years. The incidence of hepatitis and HIV infections in Indian pediatric patients with thalassemia is high due to high prevalence of hepatitis and HIV in the general population.[8,9]

Transfusion-transmitted infections such as Hepatitis B Virus (HBV), Hepatitis C Virus (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 2000), HBsAg, syphilis, and malaria. TTI can still occur from blood donations negative for markers for these infections as reported by various Indian investigators[6,10] and international studies. [11–13] This residual risk of TTI transmission from screened blood depends on the safety of donor population, sensitivity of the screening tests used, window-period donations, and other reasons such as mutant strains.[14]

Hepatitis C virus, which was discovered in 1989, is an enveloped virus of size 30-60 nm, and it gets transmitted through the parenteral route. Studies available from India give prevalence of markers for TTI in donors and recipients.[6,10–15] The prevalence of anti-HCV in multiple-transfused patients is confirmed to be high.[15,16] A three-years prospective study from India by Choudhury et al,[15] observed that anti-HCV prevalence in the same number of thalassemia major patients was 23%, 30.7%, and 35.9% each year, respectively.

Prevalence studies have found that common infections occurring in thalassemic patients are Hepatitis C (2.2%-44%), followed by Hepatitis B (1.2%-7.4%) and HIV (0%-9%).[6,10–12,15] Karimi et al,[12] found the prevalence of HCV to be 15.7%, Prati et al[13] found it to be 14.8%, and Singh et al[10] found a high prevalence of HCV (20%) in multiply transfused thalassemia major patients.

In the present study, out of 96 multiply transfused thalassemic patients, 24 (25%) were reactive for anti-HCV. An important finding in the present study, all anti-HCV–reactive patients were above the age of 8 years, which may be because of the HCV untested blood transfusion before June 2001. In the present study, a high prevalence of anti-HCV (25%) was reported probably because of HCV untested blood transfusion before 2001. Anti-HCV test has been made mandatory by the Government of India from June 2001.[15]

The prevalence of HBV is low in the US and Western Europe (0.1%-0.5%), while in South-East Asia and China, which are endemic areas, this is in the range of 5%-15%. Prevalence of HBV and HCV in blood donors in India is about 1%-5% and 1%, respectively. According to the Drugs and Cosmetic Act (1992), every blood unit has to be tested for HBsAg, anti-HIV I and II, VDRL, and malaria. HBsAg testing is mandatory according to the Act, but it can either be carried out by ELISA or Reverse Passive Hemagglutination Assay (RPHA).[15]

Hepatitis B is a special problem in blood transfusion services due to dependence on first-degree relative or paid blood donors and lack of non-remunerated repeat voluntary blood donors. Routine HBsAg screening in blood units does not eliminate the risk of HBV transmission. HBsAg test may be negative in the window phase of HBV infection, in the convalescence phase and also in HBV chronic infection, with very low level of viremia. Prevention of post-transfusion hepatitis starts with selection of non-remunerated voluntary blood donors. It has been observed that polyclonal antibody-based ELISA gives better sensitivity and provides better detection of mutants.[15] Hepatitis B Virus may occasionally be transmitted through transfusion of blood units that are HBsAg-negative but HBV DNA-positive. Many prevalence studies have found that the HBV infection occurring in multiply transfused thalassemic patients range from 0.53% to 7.4%.[6,10–12]

In the absence of treatment, the median time from HIV seroconversion to the onset of AIDS in transfused patients is about 7-11 years. Factors affecting progression include symptomatic primary infection, age at infection, and viral load. [6,10,12,17,18] The preventive measures include careful donor selection, laboratory testing, safe transfusion practice, and blood product sterilization.

CONCLUSION:

Out of 81 patient one patient (1.23%) was positive for HBsAg, 13 (16.04%) were positive for anti-HCV, and one (1.23%) was positive for anti-HIV.

So HCV is the current major problem in multi-transfused children with thalassemia major and more careful pre-transfusion screening of blood for anti-HCV must be introduced in our blood banks.

Another fact which may be responsible for high prevalence of HCV as compared to HBV is that no vaccine is available so far for protection against HCV.

Volume : 3 | Issue : 12 | December 2014 • ISSN No 2277 - 8179

Ideally all patients of thalassemia major should complete vaccination for Hepatitis B before starting transfusion or as soon as possible. Increased titre of Anti HBS antibody is protective against Hepatitis B viral infection.

Incidence of HIV positivity has decreased due to mandatory screening of all blood bags but the window periods can be further decreased by using improved technology like P24 Antigen detection or HIV viral RNA detection by RT-PCR.

Donor awareness program and providing a good questioner before transfusion can lead to self exclusion of high risk donors.

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