

Hepatitis C Virus Seropositivity in Repeatedly Transfused Thalassemia Major Patients

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Multiple transfusions in patients of thalassemia major who are conventionally treated by a regular transfusion regimen, are at a risk of developing Transfusion Transmitted Infections (TTIs), including HCV-hepatitis. Strict criteria of safe donor selection have to be adopted in order to minimize the risk of TTIs. The present study was conducted to evaluate the seropositivity of anti-HCV antibodies in multiply transfused thalassemia major patients. A total of 75 patients of thalassemia major who had received at least 10 transfusions were tested for anti-HCV antibodies, using third generation ELISA kits. Amongst these patients, 42% were seropositive for anti-HCV antibodies. This is a high prevalence rate and calls for a critical look into the prevailing transfusion practices and adoption of stricter donor selection criteria.

Key words: Anti-HCV antibodies; Thalassemia major; Safe blood transfusion.

Introduction

Thalassemia is an autosomal recessive disease prevalent in Pakistan. The carrier rate ranges between 4 and 5.5% in different regions and racial groups.^{1,2} At present, more than 150,000 thalassemia major patients exist in the country, and this number is on an increase, as little efforts are being made at any level to control this serious disease. The management of thalassemia major essentially comprises of regular "safe blood transfusion" and a life long iron-chelation therapy. Unfortunately, our patients, even those managed at relatively better management centers, are prone to develop both types of complication, i.e., those transmitted through blood transfusion (particularly hepatitis C) as well as sequelae of transfusion siderosis. Hepatitis B has a declining trend, probably as a result of regular pre-transfusion screening for HBsAg, use of hepatitis B vaccination and improved public awareness about the disease. HIV infection, fortunately, is uncommon in our setup.

Last decade has witnessed a tremendous increase in the sero-prevalence of hepatitis C amongst almost all the major cities of Pakistan. However, it has been observed that amongst blood donors belonging to different socioeconomic strata, this seroprevalence is variable; the figures are much lesser amongst young college students (0.7%) and non-remunerated donors

(1.3%) as compared to factory workers (11.8%).³ Furthermore, amongst the major Transfusion Transmitted Infection (TTI) markers in our service, the overall HCV sero-prevalence is high (4.1%).⁴ Usman et al screened 7955 military recruits at Abbottabad for HCV antibodies, and found a sero-prevalence of 4.3%.⁵ Rizvi et al (Karachi) observed a prevalence of HCV-antibodies amongst 560 apparently healthy blood donors as 1.8%.⁶ In another recently published study, the overall frequency of HCV antibodies amongst "well-selected blood donors" was 1.87%; it was 1.83% amongst first time, and 2.0% amongst second time donors.⁷

In case of hepatitis B, since an effective vaccine is available, immunization against this virus before transfusion management is started would effectively protect against transfusion transmitted hepatitis B. However, since no such vaccine is so far available against hepatitis C, the only effective protective measure against this virus is provision of HCV negative blood for transfusion. Therefore, screening of transfused blood for HCV is not only mandatory, but also it is essential to use the most sensitive screening methods with least possible false-negative results.

It is generally observed that in our setup, the HCV-positive thalasseemics are unfortunately not treated adequately for their hepatitis. Since these

children are usually also iron-overloaded, due to inadequate iron-chelation, their condition deteriorates rapidly.

The aim of this study was to look into the prevalence of HCV sero-positivity amongst multiply transfused thalassemia major patients in our setup.

Patients and Methods

This prospective study was conducted at the department of Pathology, Pakistan Institute of Medical Sciences, Islamabad, and Thalassemia Management Centre, Holy Family Hospital, Rawalpindi from July to September 2003.

A total of 75 cases of β -Thalassemia major registered for transfusion management at the aforementioned thalassemia clinics were randomly selected.

Inclusion Criteria: Known cases of β -Thalassemia major that had been transfused, as a part of their management, at least ten units of blood, irrespective of their age, sex, and history of jaundice were included in this study.

Exclusion Criteria: Patients who had been transfused less than 10 units of blood as a part of their management were not included in this study.

Clinical Features: A detailed clinical account was entered in a proforma, taking into account with emphasis: age; age at diagnosis; frequency of transfusion; history of jaundice; enlargement of liver & spleen; awareness about risk of developing transfusion transmitted hepatitis; whether transfusion blood was always screened for hepatitis for the best of parents knowledge; history of regular screening for hepatitis B & C and HIV infection, etc.

Collection of Blood Samples: About three ml of patient's blood sample was collected by a clean venepuncture. The blood was allowed to clot. Serum was separated and stored at -20°C till the test for HCV antibodies was performed in a batch.

Test for HCV antibodies was performed in duplicate for all the patients. The test was performed in batches of at least 10 cases, every time also running two negative and two positive controls, each in duplicate. A third generation ELISA kit was used for identification of HCV antibodies. The instrument used was Statfax ELISA Strip Reader.

Results

In a total of 75 patients of thalassemia major studied in this series, 48 were males and 27 females,

with a M: F ratio 1.77:1.

The age of the patients at the time of diagnosis ranged from 6m to 2 ½ yrs with a mean age of 1 year and 4 months.

The age at the time of this study ranged between 2 yrs 5m and 21 yrs with a mean age of 6.5 yrs.

The interval between successive transfusions varied between 7 days and to 5 weeks in different patients. It was learnt during questioning the parents that in 54 patients (72%), the frequency of transfusion had increased.

Three patients were found to have mild jaundice at the time of study. Ten patients had a history of jaundice in the past.

Hepatomegaly was observed in all the patients, and splenomegaly was noted in 73 (97%) of cases; in the remaining two patient, splenectomy had been performed for hypersplenism

Only 45.3% of patients were found to get their transfusions strictly from one of the thalassemia management centers. The remaining 54.7% kept on switching from one center to another in quest of blood without replacement. Parents of four patients claimed that the blood donation was always arranged from voluntary donors within the family and amongst friends. All these four patients were seronegative for anti-HCV antibodies.

All the parents were aware of the risk of transfusion-transmitted hepatitis; they were all satisfied that their child was being transfused with properly screened blood. All the centers providing transfusion care to the patients in our study are providing only screened blood (for hepatitis B and C).

Anti-HCV antibodies were detected in 32 (42%) of patients. These antibodies were already detected in 8 patients. Nineteen patients had never been tested before, and in 35 cases, test performed once in the past had shown seronegativity for these antibodies.

Discussion

Early and regular blood transfusion therapy in patients of β -thalassemia major decreases the complications of severe anemia and prolongs survival. It is particularly so in patients who are fortunate enough to receive an adequate, regular iron chelation therapy, and are therefore protected from organ damage by iron overload.⁸ However, if there is a breach in "safe blood transfusion", these patients are confronted by new clinical challenges, particularly in

the form of transfusion transmitted diseases, especially HCV, HBV and HIV infections.^{8, 9} Fortunately, HIV infection is still not a problem in our country, and HBV infection can be, to a great extent, prevented by a pre-transfusion immunization, HCV infection has gained importance particularly as one of the major complications in multiply transfused patients during the last decade. This is especially true for counties where HCV is more prevalent in general population and therefore also amongst blood donors. The prevalence rate of seropositivity increases with the number of transfusions.¹⁰ This post-transfusion hepatitis has significantly contributed to morbidity in thalassemia.⁸ It should be remembered that HCV hepatitis is more threatening than HBV hepatitis due to a greater risk of chronic liver disease.¹¹

As shown in table 1, the prevalence of HCV seropositivity in multiply transfused β -thalassemia patients has been observed to vary greatly from 11.1 to 63.8%.⁹⁻¹⁹ This extreme degree of variability depends on two major factors, i.e., the prevalence of HCV in the relevant population (and therefore also in the blood donors), and the practice of HCV antibody screening before the transfusion is instituted.

In our study, a high prevalence of HCV seropositivity (42%) was observed. Although our patients were usually transfused at the thalassemia

management centre of PIMS and Holy Family Hospital, where pre-transfusion screening of the transfused is regularly performed. However, it was learnt during interview of the patients' parents that in almost all instances, the patients did get transfused with blood from some other centers, where pre-transfusion HCV antibody screening was not guaranteed. Furthermore, the parents of about 60% of patients were not aware of the importance of HCV antibody screening of transfused blood. In many previous studies, the prevalence of HCV antibodies was observed to be reduced after the institution of a regular HCV screening before transfusion.¹⁰

In our setup, serious attempts have to be made to ensure a safe blood transfusion, so as to cut down the prevalence of HCV hepatitis in multiply transfused thalassemic patients. Education regarding transfusion transmitted infections, including HCV, HBV & HIV infections, is of prime importance. Further, in all the centres taking care of thalassemia management, uniform strict criteria for donor selection should be adopted. A serious consideration should be given to history of jaundice and drug addiction, etc in donors. While selecting donors, preference must be given to

Table 1: Comparison Of Our Findings With Some Previous Studies

Country	Year of Publication	Number of Patients Studied	HCV Sero-positivity Percentage	Reference Number
Bangladesh	2003	259	12.5	9
Jordan	2001	143	40.5	10
India	1992	54	11.1	11
Iran	2002	105	63.8	12
India	2002	50	30	13
Myanmar	2002		55.5	14
India	1993	72	16.7	15
Britain	1990	73	23.3	16
Iran	2001	466	15.7	17
Italy	1994	256	60	18
Pakistan	2004	60	35	19

Present Study	2004	75	42
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relatively younger donors without past history of Jaundice.³ Blood camps should be arranged by thalassemia management centres at colleges and other teaching institutions. The patients should be encouraged to stick to one thalassemia management centre, although it is understandable that provision of blood may not be prompt in every visit. The voluntary blood donor service which is presently rudimentary in our setup, can tremendously improve upon the ‘safe blood transfusion’.

Since the prevalence of HCV hepatitis is alarmingly increasing in our population, serious measures have to be undertaken to reduce the spread of HCV infection through awareness campaigns on war footing.

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