

Correlation of Hepatitis C with Multiple Blood Transfusions in Children of Thalassemia Major

MOBIN-UR-REHMAN¹, BASHIR ULLAH², FARIDA JAN³, TARIQ CHISHT⁴

¹Assistant Professor of Pediatrics, ²Assistant Professor of Medicine, ³Senior Registerar of Pediatrics, ⁴Associate Professor of Anatomy, Bolan Medical College, Quetta

Correspondence to Dr. Mobin-ur-Rehman, Department of Pediatrics, Bolan Medical Hospital, Quetta.
Email: mobin38@gmail.com

ABSTRACT

Objective: To assess the correlation of frequency of Hepatitis C (HCV) virus with multiple blood transfusions in patients of Thalassemia major (TM).

Material and methods: This study was conducted from at Thalassemia center, Bolan Medical Complex Hospital Quetta and was of six months duration.

Subjects and methods: One hundred and fifty patients of Thalassemia major (already diagnosed) who received two or more blood transfusions were included in this study. Blood sample from these 150 thalassemic patients was scrutinized for anti HCV antibodies by third generation ELISA technique.

Results: All 150 thalassaemia patients were in the age range of 6 months to 20 years. Younger patients aged 0-4 years required transfusion every 4.6 weeks while patients above 15 required every 2 weeks. Every TM patients received a mean of 167.64 ± 121.01 units of blood. A substantive number 45 (30%) were HCV positive. Direct correlation was found between anti HCV positivity and number of blood transfusions.

Conclusion: It is extremely important to sensitize the public regarding prevention of the disease Awareness of TM, family counseling and there is a need to move away from hospital based blood donation system to a community-based system.

Key words: Beta thalassaemia, Risk of HCV transmission, Multiple blood transfusion(s), Hepatitis C virus

INTRODUCTION

Human hepatitis C is an infectious disease affecting the liver, caused by the Hepatitis C Virus (HCV)¹. Although HCV is endemic worldwide, there is a large degree of geographic variability in its distribution. Countries with the highest reported prevalence rates are located in Africa and Asia; areas with lower prevalence include the industrialized nations in North America, northern and Western Europe, and Australia. Populous nations in the developed world with relatively low rates of HCV seroprevalence include Germany (0.6%), Canada (0.8%), France (1.1%), and Australia (1.1%). Low, but slightly higher seroprevalence rates have been reported in the USA (1.8%), Japan (1.5–2.3%) and Italy (2.2%)². In one Pakistani study conducted in district Mansehra it was found that 3.5% of the people are actively infected with HCV whereas 7% of the population in general, has the presence of antibodies against HCV in their blood³.

Blood transfusion has long been recognized as a risk factor for hepatitis c transmission⁴. HCV is responsible for the majority of cases of post- transfusion non-A, non-B hepatitis in patient with thalassaemia major². The risk of seroconversion for HCV was observed to be one in 1384 units of blood transfused by Lee et al⁵. Hemophiliac and thalassaemic patients treated with virus contaminated blood or blood derivatives frequently exhibit anti-HCV antibodies and signs of chronic hepatitis. In neighboring country Iran it was found that the HBsAg seropositivity and higher serum ferritin level were significantly associated with a higher prevalence of HCV⁶. Patients who were anti-HCV positive had a significantly higher mean number of blood transfusions and peak serum Alanine Transaminase level than anti-HCV-negative patients⁷.

PATIENTS AND METHODS

This descriptive study was conducted at Thalassemia Center Bolan Medical Complex Hospital, Quetta over a period of six months from September 2nd 2010 to February 2011. One hundred and fifty (150)

cases of diagnosed Thalassemia major patients were selected for this study by non-probability, purposive sampling technique. Diagnosed patients of Thalassemia major of both sexes who were above six months of age, who had received blood transfusions more than once were included this study. Those patients with Thalassemia major who were less than six months of age or were critically ill with co-morbid conditions were excluded from this study. One fifty patients who satisfied the inclusion criteria underwent a detailed clinical history and physical examination. Special attention was paid to source of blood, total number of blood transfusions received, age at the time of diagnosis and first transfusion given, family history of jaundice and brief drug history especially parental injections was asked. Physical examination performed with special attention paid to degree of anemia, jaundice and hepatosplenomegaly. After this an informed consent was taken from the parents/attendants of the patient before withdrawing blood. The sample of blood after being withdrawn aseptically was collected in two sterile bottles/tubes and Anti HCV antibodies were detected using ELISA kit was used (Cat No.HC-2408, Randox Laboratories Ltd, UK). Data analysis was performed using SPSS software version 10. Mean and standard deviation and percentages for age, sex and also sex ratios were reported.

RESULTS

A total of 150 transfusion dependent patients with thalassaemia major constituted the study population. Their age ranged from 9 months to 20 years with the mean age of 9.3 ± 4 years. Fifty patients were under the age of 9 years and only 8% above 15 years. There were 96 (64%) males, 54(36%) females with a male to female sex ratio of 1.8:1 (Table 1). The interval with which these patients required blood transfusion ranged from 1-10 weeks .The mean interval between two transfusions was 3.1 weeks. Every patient was exposed to 17 different donors/year. The requirement of blood transfusion was increasing proportionately with the increase in age of the patients (Figure 1). The patient's age group 0-4 years required transfusion after every 4.6 weeks, while patients above 15 years of age required blood after every 2 weeks. The total number of transfusion ranged from 6-636 units. All the patients received about 25147 transfusions. Every thalassemic patient received a mean 167.64 ± 121.01 units and in this way each patient was exposed to an average of 17 different donors. A total of forty-five (30%) patients were reactive to anti HCV (Table 2). Out of these, 14(26%) were females and 31 (32%) males. None was positive below 3 years of age or above 17 years of age. The maximum seropositive patients belonged to 14 years of age group. Eight patients were positive in this age group and 5 in each of 6 and 10-year groups and 4 in each of 8 and 12 years age groups. Three in each 5, 9, 11 and 16 years of age, 2 in each 4, 13 and 15-year age groups and a single case was positive in 7 years age group. Non-was positive in patient group who received <20 transfusions. Three patients were reactive to anti HCV, who had received 21-50 transfusions and all the remaining were from a group who received more than 50 transfusions. Statistically the increasing prevalence was significant.

Table 1: Age and sex-wise distribution of thalassemic patients

Age (years)	Male	Female	n=
0 – 4	10	6	16(11%)
5 – 9	29	20	59(39%)
10 – 14	39	24	63(43%)
> 15	8	4	12(8%)
Total	96	54	150(100%)

Table 2: Frequency of seropositivity of HCV according to age in thalassemia patients (n = 45)

Age (years)	n=	Percentage
3 – 5	5	11.2
6 – 10	18	40.0
11 – 15	19	42.2
16 – 19	3	6.6

Fig. Frequency of transfusion in patients with thalassemia major

DISCUSSION

Thalassemia is the commonest inherited disorder in Pakistan with the overall prevalence of 5%. The estimated rate of birth of affected infants is 1.3 per 1000 live births, and about 5250 infants with β-Thalassemia major are born annually. Married couples both consisting of two carriers have a twenty five percent chance that any child they have will be affected.⁸ In Pakistan the β-thalassemia is prevalent in all parts of the country and in all ethnic groups. Pathans have a slightly high prevalence rate 7.96% than Punjabi's 3.26%⁹.

Regular blood transfusion and iron chelation is the main stay of conservative therapy¹⁰. Patients who receive multiple transfusions are at a risk of acquiring post-transfusion infection especially viral hepatitis. Transmission of infectious diseases by the administration of blood, its components or derivatives, has been known since the beginning of transfusion. A number of viruses, parasites and bacteria can be transmitted by blood¹¹.

There were 96(64%) males and 54(36%) female patients in the present study. Male to female ratio was 1.8:1.0. The preponderance of males over females in the present study is difficult to explain. One possible reason is the fact that the people are more concerned with the health of male offspring and hence is more likely to seek medical care for them.

Hepatitis C virus (HCV) is one of the blood borne viruses with highest prevalence in TM patients. In Pakistan, 20.7% prevalence of anti-HCV in professional donor from Karachi was reported by Ahmed et al¹². In the present study thirty percent (45/150) multitransfused patients of thalassemia major were reactive for anti-HCV antibodies. Also a study conducted by Irshad M and Peter S from India, reported exactly the same values for positivity of anti-HCV antibodies in patients of TM receiving more than one transfusion¹³. A thirty percent frequency of HCV in the present study is strikingly lower than the 60% positivity reported by Bhatti et al in which they used particle agglutination test to screen the TM patients.¹¹ This difference may be due to difference in screening methodology because third generation ELISA is 10-100 times more sensitive and specific, compared to particle agglutination test. Higher figures are reported by Mollah et al¹⁴ from Bangladesh. The prevalence of hepatitis C virus infection is relatively low in childhood, with anti-HCV prevalence rates of 0.1-0.4% in the Western world.¹⁵ Twenty six percent (14/54) females and 32.5% (31/96) male patients showed reactivity to anti-HCV. The maximum anti-HCV antibodies positivity observed in TM patients was in the age group of 14 years. None was positive in patient group who had received < 20 transfusions. Anti-HCV positivity increased with the number of transfusion. Its positivity reached 41% in a group of patients who received >250 transfusions. The number of blood transfusions received by anti-HCV positive children was significantly higher than that by anti-HCV negative patients. This linear relationship had been demonstrated by el-Nanawy AA et al¹⁶. In addition, this study showed increase in anti-HCV positivity rate with increase in the age, because their

transfusion requirements increased with age, thus they were more prone to these infections. de Montalembert et al further supported these findings in a study conducted in France¹⁷.

CONCLUSION

Hepatitis C is fast becoming the major source of morbidity and mortality in patients with Thalassemia Major. The proper screening of blood is imperative to decrease this potentially preventable complication.

REFERENCES

1. Di Marco V. Chronic hepatitis C in children is a mild and curable liver disease. *Dig Liver Dis* [Internet]. 2011 Feb 23 [cited 2011 Mar 1]; Available from: <http://www.ncbi.nlm.nih.gov/pubmed/2135365>
2. Shepard CW, Finelli L, Alter MJ. Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis* 2005; 5: 558-67.
3. Ali A, Ahmad H, Ali I, Khan S, Zaidi G, Idrees M. Prevalence of active hepatitis c virus infection in district Mansehra Pakistan. *Virol J* 2010; 7: 334-5.
4. Qazi HA, Saleem K, Mujtaba I, Hashmi A, Soomro JA. Prevalence and factors associated with HCV (hepatitis C virus) seropositivity in islamabad, pakistan. *Acta Med Iran* 2010; 48: 394-8.
5. Lee WS, Teh CM, Chan LL. Risks of seroconversion of hepatitis B, hepatitis C and human immunodeficiency viruses in children with multitransfused thalassaemia major. *J Paediatr Child Health* 2005; 41: 265-8.
6. Mirmomen S, Alavian S, Hajarizadeh B, Kafaee J, YektaParast B, Zahedi M, et al. Epidemiology of hepatitis B, hepatitis C, and human immunodeficiency virus infecions in patients with beta-thalassemia in Iran: a multicenter study. *Arch Iran Med* 2006; 9: 319-23.
7. Ocak S, Kaya H, Cetin M, Gali E, Ozturk M. Seroprevalence of hepatitis B and hepatitis C in patients with thalassemia and sickle cell anemia in a long-term follow-up. *Arch Med Res* 2006; 37: 895-8.
8. Ahmed S, Saleem M, Modell B, Petrou M. Screening extended families for genetic hemoglobin disorders in Pakistan. *N Engl J Med* 2002; 347: 1162-8.
9. Khattak MF, Saleem M. Prevalence of heterozygous beta-thalassemia in northern areas of Pakistan. *J Pak Med Assoc* 1992; 42: 32-4.
10. Cazzola M, Borgna-Pignatti C, Locatelli F, Ponchio L, Beguin Y, De Stefano P. A moderate transfusion regimen may reduce iron loading in beta-thalassemia major without producing excessive expansion of erythropoiesis. *Transfusion* 1997; 37: 135-40.
11. Bhatti FA, Amin M, Saleem M. Prevalence of antibody to hepatitis C virus in Pakistani thalassaemics by particle agglutination test utilizing C 200 and C 22-3 viral antigen coated particles. *J Pak Med Assoc* 1995; 45: 269-71.
12. Shamsi T, Ahmed A, Taj Z, Vajid MA, Hassan F. Prevalence of hepatitis B, C and HIV virus infection among beta thalassaemia major patients. *J Pak Med Assoc* 1998; 48: 87-9.
13. Irshad M, Peter S. Spectrum of viral hepatitis in thalassemic children receiving multiple blood transfusions. *Indian J Gastroenterol* 2002; 21: 183-4.
14. Mollah AH, Nahar N, Siddique MA, Anwar KS, Hassan T, Azam MG. Common transfusion-transmitted infectious agents among thalassaemic children in Bangladesh. *J Health Popul Nutr* 2003; 21: 67-71.
15. Ruiz-Moreno M, Leal-Orozco A, Millán A. Hepatitis C virus infection in children. *J Hepatol* 1999; 31: 124-9.
16. el-Nanawy AA, el Azzouni OF, Soliman AT, Amer AE, Demian RS, el-Sayed HM. Prevalence of hepatitis-C antibody seropositivity in healthy Egyptian children and four high risk groups. *J Trop Pediatr* 1995; 41: 341-3.
17. deMontalembert M. Transfusion in patients with Hemoglobinopathies. *Transfus Clin Biol* 2000; 7: 553-8.