

PREVALENCE OF HEPATITIS C IN BETA THALASSAEMIA MAJOR

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ABSTRACT

Background: Thalassaemias is inherited as an autosomal recessive disorder. Due to repeated blood transfusions in thalassaemic children, hepatitis B, hepatitis C and HIV infection can occur in these patients. Hepatitis C virus infection is common in Pakistan. Multiple transfused patients represent a major risk group for hepatitis C acquirement. The aim of this study was to know the prevalence of hepatitis C in beta thalassaemia major children in our set up.

Material & Methods: This was a cross-sectional study of 2 years duration from January 2002 to December 2003, conducted at Children Hospital, Pakistan Institute of Medical Sciences Islamabad and Fatmid Foundation Peshawar. Children age 3 months to 12 years, with beta thalassaemia having regular blood transfusions at these two centers were enrolled. Complete history and physical examination was carried out in all the patients and blood samples collected for hepatitis C virus. The laboratory technique for analysis was simple manual method, confirmed by ELISA.

Results: During the study period, 180 beta thalassaemia major children were enrolled at the two sites. Out of these, 75 (41.7%) children were hepatitis C positive.

Conclusion: HCV infection is an important cause of viral infection among thalassaemic children with a prevalence of 41.7% in our study population..

Key words: Thalassaemia, Hepatitis C, Blood transfusion.

INTRODUCTION

Thalassaemias is inherited as an autosomal recessive disorder.¹ The probability of an offspring of heterozygous parents having the homozygous disorder, thalassaemia major is 25% in each pregnancy, while 50% are likely to have thalassaemia minor (Heterozygous) and 25% are expected to be normal in each pregnancy.¹ Beta-thalassaemia results from mutations resulting in diminished production of mRNA and decreased synthesis of structurally normal globin.²

Regular blood transfusions for patients of thalassaemia have improved the overall survival although these transfusions carry a definite risk of transmission of certain viruses.³

Due to repeated blood transfusions hepatitis B, C and HIV infection can occur. All these are transmitted by blood or blood products in 10% cases. Incubation period of hepatitis C is 7-9 weeks (range 2-24 weeks). Hepatitis C virus (HCV) is the most likely hepatitis virus to cause chronic liver infection. Chronic HCV progresses to cirrho-

sis in about half of the patients or 25% of all those initially infected. HCV infection is common in transfusion-dependent thalassaemia.⁴ HCV is the commonest cause of chronic viral hepatitis in the many developed countries and a significant cause of cirrhosis, hepatic failure, and hepatocellular carcinoma.^{5,6}

HCV is responsible for the majority of cases of post-transfusion non-A non-B hepatitis in patient with thalassaemia major.⁷ HCV seroprevalence and risk factors in north Iran were investigated in 105 thalassaemia sufferers, 93 haemodialysis patient and 5976 blood donors by second generation ELISA. The study showed that haemodialysis patients and thalassaemics were at higher risk of having HCV infection; the prevalence being 55.9% and 63.8% respectively in comparison to the prevalence of blood donors (0.5%).⁸ Multiple transfused patients represent a major risk group for HCV acquirement. Haemophilic and thalassaemic patients treated with virus contaminated blood or blood derivatives frequently exhibit anti-HCV antibodies and signs of chronic hepatitis.⁹⁻¹³

Although the incidence of transfusion-transmitted hepatitis has been dramatically reduced after introduction of hepatitis B vaccination for chronic transfusion recipients and the application of reliable screening of blood donors,¹⁴⁻¹⁸ thalassaemic patients may still develop liver dysfunction due to infection with blood born agents like HCV.

Patients affected from beta thalassaemia have a high prevalence of chronic liver disease, mainly a consequence of viral infections acquired through blood transfusion during past decades¹⁹⁻²¹

The purpose of the study was to find out the prevalence of HCV in Beta thalassaemia major patients.

MATERIALS AND METHODS

This was a cross-sectional study, conducted at Children Hospital, Pakistan Institute Medical Science, Islamabad and Fatmid Foundation, Peshawar. The duration of the study was two years, from January 2002 to December 2003. Children aged 3 months to 12 years with Beta thalassaemia major, confirmed on hemoglobin electrophoresis and on regular blood transfusion in both these centres were enrolled. Those children who had Sickle Cell anaemia or any other hemolytic anaemia were not included in this study.

All patients with aforementioned criteria were enrolled. Complete history and physical examination was carried out in all these patients and blood sample was collected for HCV. Samples were sent for analysis to the respective laboratories of the two centers. The laboratory technique for analysis was simple manual method, confirmed by ELISA. Our objective was assessed on structured proforma.

All the data was entered and Analysis was performed on the Statistical Package for Social Sciences (SPSS version 10.0).

RESULTS

During the study period, 180 children were enrolled at the two centres. Out of these, 75 (41.7%) were hepatitis C positive. The demographic characteristics are given in Table below.

Table: Demographic indicators of Hepatitis C positive children in Beta Thalassaemia major.
(n = 75)

Variable	Number	Percentage
Sex		
Male	36	48.0%
Female	39	52.0%
Age at enrollment (in years)		
Median	7	
Mean±SD	6.8 ± 3.6	
Age at the time of diagnosis of beta Thalassaemia major (in months)		
Median	9.0	
Mean±SD	9.6 ± 7.1	
Transfusion per month		
Median	2.0	
Mean±SD	2.1 ± 0.7	
One	10	13.3%
Two	52	69.3%
Three and more	13	17.4%
Place where transfusion managed		
Fatmid Foundation, Peshawar	26	34.6%
Children's Hospital, Islamabad	49	65.4%
Clinical Features		
Presence of pallor	75	100.0%
Presence of jaundice	34	45.3%
Presence of frontal bossing	72	96.0%
Presence of oedema feet	5	6.7%
Presence of ascites	Nil	0.00%
Presence of prominent zygomatic bone	71	94.7%
Presence of depressed nasal bridge	70	93.3%
Presence of Hepatomegaly		
Size of liver (cm)	74	98.7%
Median	5.0	
Mean±SD	5.8 ± 2.4	
Presence of splenomegaly		
Size of Spleen (cm)	74	98.7%
Median	6.0	
Mean±SD	5.6 ± 2.4	

DISCUSSION

In our study the prevalence of hepatitis C among thalassaemic children was 41.7%. This is a relatively high percentage keeping in mind that all the donated blood is regularly screened for HCV at all thalassaemic centers in Pakistan.

In different parts of the world the prevalence of HCV infection in thalassaemic patients is different. In India it is 16.7%,²² and in Malaysia 22.4%.²³ In another study the prevalence of hepatitis C was 23.8% in thalassaemic patients.²⁴ There are many reasons for low prevalence, including the awareness about hepatitis C and other blood born diseases.

In Italy the prevalence of hepatitis C in thalassaemic patients was 47.0%,²⁵ and in Iran 63.8%.²⁶ This is much higher than that of our study.

In a study in Rawalpindi region of Pakistan, the prevalence of hepatitis C in thalassaemic children was 60.0%.²⁷ Another study from Karachi showed the prevalence rate of 20.5% in thalassaemic patients.²⁸

There is a great variation of the prevalence rate of HCV in thalassaemic patients among different parts of the world. In all these countries the donor's blood is routinely screened for HCV. It is a known fact that the hepatitis C infection is most probably related to thalassaemic patients' treatment.²⁹ Thalassaemic patients may acquire hepatitis C through the administration of HCV infected blood collected during the donor window period. This is one reason in thalassaemic children because the risk due to drug abuse and sexual activity are reasonably low in them.

In our study the mean age of thalassaemic children was 6.8 years. The mean age of diagnosis of beta thalassaemia in these children was 9.6 months. In another study the mean age of hepatitis C in thalassaemic patients was 14.3±3.0 years.²⁹ It is higher than in our study. This difference is due to the fact that we considered the paediatric age group only.

In our study the majority of children were diagnosed as a case of thalassaemia before their first birthday. Our results showed that among thalassaemic children with hepatitis C 52.0% were females. Similarly in another study out of 28 thalassaemia multitransfused patients half (14) of them were female.²⁹

Our study showed that the mean number of blood transfusions per month to thalassaemic children with HCV was 2.1. This is a high rate as these children receive almost 24 blood transfusions a year. High rate of transfusions can produce many complications in these patients. A study showed

the comparison of number of transfusions in thalassaemic patients with HCV positive and negative status. It was observed that the number of blood transfusions received by anti-HCV positive thalassaemia patients was significantly higher than that of anti-HCV negative thalassaemic patients.²⁴

CONCLUSION

Despite screening of blood donors, HCV infection remains an important cause of viral infection among thalassaemic children with a prevalence of 41.7% in our study population.. Immediate steps should be taken to reduce it.

REFERENCES

1. Haneef SM, Maqbool S, Arif AM. In: Textbook of Paediatrics. Pak Paed Assoc 2000; pp: 652-57.
2. Lee GR, Bithell TC, et al. Wintrobe's Clinical Hematology beta- thalassaemia 1993; 1: 1106-17.
3. Nelson WE, Behrman RE, Kliegman RM, Avin AM. In: Nelson's TextBook of Pediatrics. 16th Ed. Pp: 1401-4.
4. Li CK, Chan PK, Ling SC, Ha SY. Br J Haematol 2002; 117: 755-58.
5. Adrian G and John KO. Iron and response to treatment of Hepatitis C. Am J Gastroenterol 2002; 97: 788-90.
6. Jamal R, Fadzillah G, Zulkifli, Yasmin M. Seroprevalence of hepatitis B, Hepatitis C, CMV and HIV in multiple transfused thalassaemia patients: Results from thalassaemia day care center in Malaysia. Southeast Asian J Trop Med Public Health 1998; 29: 792-94.
7. Spiliopoulous L, Repanti M, Katinakis, et al. Response to interferon alfa-2b therapy in multi transfused children with beta thalassaemia and chronic Hepatitis C. Hepatogastroenterology 1999; 46: 2515-20.
8. Ansar MM, Kooloobandi A. Prevalence of hepatitis C virus infection in thalassaemia and haemodialysis patients in North Iran-Rasht. J Virol Hepatol 2002; 9: 309-14.
9. Antipa C, Ruta S and Ernescu C. Serological profile assessment of the infection with hepatitis C Virus (HCV) in haemophiliac and thalassaemic patients. Rom J Virol 1996; 47: 3-11.
10. Telfer PT, Garson JA, Whitby K, et al. Combination therapy with interferon alpha and ribavirin for chronic hepatitis C virus infection in thalassaemic patients. Br J Haematol 1997; 98: 850-55.
11. Di Marco V, Lo Iacono O, Almasio P, et al. Long-term efficacy of alpha-interferon in beta-thalassaemics with chronic hepatitis C. Br J Haematol 1997; 97: 904-07.

12. Donohue SM, Wonke B, Hoffbrand AV et al. Alpha interferon in the treatment of chronic hepatitis C infection in thalassaemia major. *Br J Haematol* 1993; 83: 491-97.
13. S Fernando, SDD Fernando, MHR Sberiff, Vitarana UT. Antibodies to hepatitis C virus in patients who have had multiple transfusions in Sri Lanka. *Southeast Asian J Trop Med Public Health* 1998; 29: 792-94.
14. Aach RD, Stevens CE, Hollinger FB. Hepatitis C virus infection in post-transfusion hepatitis-an analysis with first- and second generation assays. *N Engl J Med* 1991; 325: 1325.
15. Donahue JG, Munoz A, Ness PM, Brown DE, Yawn DH, McAllister HA, Reitz BA, Nelson KE. The declining risk of post-transfusion (Letter). *N Engl J Med* 1992; 327: 369.
16. Nelson KE, Donahue JG, Stambolis V. Post-transfusion hepatitis C virus infection (Letter). *N Engl J Med* 1992; 327: 1601.
17. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The retrovirus Epidemiology Donor Study. The risk of transfusion-transmitted viral infections. *N Engl J Med* 1996; 334: 1685.
18. Blajchman MA, Bull SB, Feinman-SVTI. Post-transfusion hepatitis: Impact of non-A, non-B hepatitis surrogate tests. *Lancet* 1995; 345: 21.
19. Zurlo MF, De Stefano P, Borgna-Pignatti C, Di Palma A, Piga A, Melvendi C, Di Gregorio F, Burattini MG, Terzoli S. Survival and causes of death in thalassaemia major. *Lancet* 1989; 2: 27.
20. Rebulli P, Mozzi F, Contino G, Locatelli E, Sirchia G. Antibody to hepatitis C virus in 1305 Italian multiple transfused thalassaemia: Comparison of first and second generation tests. *Tranfus Med* 1992; 2: 69.
21. Olivieri NF, Brittenham GM. Iron-chelating therapy and the treatment of thalassaemia. *Blood* 1997; 89: 739.
22. Agarwal MB, Malkan GH, Bhave AA, Vishwanathan C, Billa V, Dube SR, Bajan K, Rajadhyaksha GC, Shah SH. Antibody to hepatitis C virus in multi-transfused thalassaemia; Indian experience. *Br J Haematol* 1993; 83: 491-97.
23. Jamal R, Fadzillah G, Zulkifli SZ, Yasmin M. Seroprevalence of hepatitis B, hepatitis C, CMV and HIV in multiply transfused thalassaemia patients: results from a thalassaemia day care center in Malaysia. *Eur J Clin Microbiol Infect Dis* 1999; 18: 709-15.
24. Laosombat V, Pornpatkul M, Wongchanchailert M, Worachat K, Wiriyasatienku A. The prevalence of hepatitis C virus in thalassaemic patients in the south of Thailand. *Southeast Asia J Trop Med Public Health* 1997; 28: 149-53.
25. Cacopardo B, Russo R, Fatuzzo F, Cosentino S, Lombardo T, LaRosa R, Celesia BM, Nigro L, Frontini V, Nunnari A. HCV and HBV infection among multi-transfused thalassaemia from eastern Sicily. *Ann Trop Med Parasitol* 2002; 96: 197-202.
26. Ansar MM, Kooloobandi A. Prevalence of hepatitis C virus infection in thalassaemia and haemodialysis patients in North Iran-Rasht. *J Virol Hepatol* 2002; 9: 390-92.
27. 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.
28. Akhtar S, Moatter T, Azam SI, Rahbar MH, Adil S. Prevalence and risk factors for interfamilial transmission of hepatitis C virus in Karachi, Pakistan. *Baillieres Clin Haematol* 1998; 11: 147-62.
29. Parti D, Zanella A, Farma E, Mattei CD, Bosoni P. A multicentre prospective study on the risk of acquiring liver disease in anti-hepatitis C virus negative patients affected from homozygous beta thalassaemia. *Blood* 1998; 9: 3460-64.

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