FREQUENCY OF HEPATITIS B AND HEPATITIS C IN MULTI- TRANSFUSED BETA THALASSEMIA MAJOR PATIENTS

Muhammad Mahmood Iqbal, Shamama Hassan, Shahid Aziz

Military Hospital Rawalpindi

ABSTRACT

Objective: To determine the frequency of hepatitis B and C virus infection among children with beta thalassemia major registered at Military Hospital Rawalpindi.

Study Design: Descriptive study

Place and Duration of Study: The study was carried out at Military Hospital Rawalpindi, from 1st September 2008 to 31st August 2009.

Patients and Methods: Children attending Thalassemia Centre Military Hospital Rawalpindi for regular blood transfusion were registered. They belonged to different ethnic groups and came from different parts of the country. Their demographic data was recorded, detailed history taken and physical examination was carried out. Their serum samples were tested for hepatitis B surface antigen and anti HCV antibody assay with third generation commercial ELISA method.

Results: During the study, 141 patients of beta thalassemia major were screened. Out of them 50 patients (35.5 % ,95% confidence interval 27.8-43.5) were found hepatitis C virus antibody positive and 1 patient (0.7 %) hepatitis B surface antigen positive. One patient (0.7%) had both hepatitis B and C virus infection. Mean age of hepatitis C infected patients was 10.4+3.85 years (range 2-16 years). Mean age of uninfected patients was 6.1 + 3.59 years. (p value 0.000)

In addition, the results indicate that higher prevalence of anti-HCV was significantly associated with longer duration of transfusion (p value <0.003).

Conclusion: In spite of the fact that screened blood is used for transfusions, still a large number of patients have been found infected with hepatitis C. Therefore more accurate techniques are required for screening of blood to prevent transfusion associated transmission.

Key words: Prevalence, Hepatitis B and C, Thalassemia Major

INTRODUCTION

The combination of regular blood transfusion and chelation therapy has improved the overall survival of patients of thalassemia major, thus transforming thalassemia from a rapidly fatal disease of childhood to a chronic illness compatible with a prolonged life[1,2]. On the other hand, frequent blood transfusions and the chronic nature of the disease have contributed to a new spectrum of complications[3,4]. Liver disease ranks second as a cause of death among patients of thalassemia major[5]. Thalassemia patients on being long term transfusion therapy continue to be at high risk of acquiring transfusion associated infections. In a developing country like Pakistan due to lack of facilities / resources for universal and effective screening of blood donors for hepatitis B and hepatitis C markers, blood transfusion is major source of hepatitis B and C transmission[6]. Hepatitis C and hepatitis B infection are one of the major public health problems of Pakistan. A weighted average of hepatitis B antigen prevalence among healthy adults (blood donors and non-donors) was 2.4% (range 1.4-11.0%) and for hepatitis C antibody was 3.0% (range 0.3-31.9%). Rates in the high-risk subgroups were far higher[7,8].

Although the incidence of transfusion-transmitted hepatitis has been dramatically reduced after introduction of hepatitis B vaccination and the application of reliable screening of blood donors, patients of thalassemia major may still develop liver dysfunction due to infection with other blood born agents[9-12]. Thalassemic patients have a high prevalence of chronic liver disease mainly a consequence of viral infections acquired through blood transfusion[13,14]. HCV is

Correspondence: Brig Muhammad Mahmood Iqbal, Classified Child Specialist, Military Hospital Rawalpindi
Email: mi_chishti@hotmail.com
Received: 23 Jan 2010; Accepted: 10 April 2009

responsible for majority of cases of post-transfusion hepatitis in thalassemic patients[15]. The manifestations of hepatitis C are variable; with an asymptomatic chronic HCV infection at one end of the scenario to chronic hepatitis, advanced cirrhosis and hepatocellular carcinoma at the other. In children with thalassemia, there is excessive iron load in liver and HCV infection has been shown to have a potentiating effect on hepatic fibrogenesis[16]. HCV infection and iron overload are independent but mutually reinforcing risk factors for the progression of fibrosis and development of cirrhosis[17].

The purpose of the study was to find out the prevalence of Hepatitis C and B virus infection in beta thalassemia major patients in a facility where they are being transfused screened blood.

PATIENTS AND METHODS

This study was carried out at Thalassemia Centre Military Hospital Rawalpindi from 1st September 2008 to 31st August 2009. Patients attending Thalassemia Centre with confirmed diagnosis of beta thalassemia major were registered. Their demographic data was recorded and detailed history taken and physical examination was carried out. Demographic data such as age, gender, social class, age at diagnosis, number of transfusions per month and the centres from where transfusions were done was also recorded. Parents of the children were also asked whether they knew about the hazard of transmission of viral hepatitis through blood transfusion. Whole blood samples were collected and sent to Department of Pathology Army Medical College Rawalpindi for screening of hepatitis B and C viruses.

Laboratory assays: All sera were screened for anti-HCV and HBsAg with third-generation commercial ELISA, Diamate Anti-HCV USA and Diamate HBsAg, USA.

Frequency and the corresponding 95% confidence interval were calculated with SPSS version 10.0. Data comparison was done using the Student's t-test. The difference was considered significant if p value was< 0.05.

RESULTS

One hundred and forty one thalassemia major patients were enrolled during the study period. There were 82 (58.2%) males and 59 females (41.8%). Forty-nine (34.8%) patients were HCV positive and one (0.7 %) was hepatitis B surface antigen positive. (Table 1) One (0.7%) patient was found positive for both hepatitis B and C virus infection. As the number of hepatitis B virus infected patients was quite low (n=2 1.4%), therefore further analysis was carried out only for HCV infected 50 patients. To study different factors of two group were compared with HCV infected patients and the other one of HCV uninfected patients. Among HCV infected patients 31 (62%) were male and 19 (38%) were females. Mean $\pm$ SD age of hepatitis C infected patients was 10.4$\pm$3.85 years (range 2-16 years). Mean age of uninfected patients was 6.1 $\pm$ 3.59 years. (p value 0.000) (Table)

Majority of HCV infected patients 36 (72.0%) belonged to lower middle class (monthly income between Rs. 10000.00-15,000.00). Most of the infected patients (n=27 54%) were of urban origin. For infected patients average age at which the transfusions started was 5.4 ($\pm$2.16) months. It was less than that for the uninfected patients which was 8.5 ($\pm$8.11) months. The results also indicate that the frequency of anti HCV was significantly associated with longer duration of transfusion ($p<0.003$). Majority of HCV seropositive patients (n=29, 58%) were between 11- 16 years age group. Infected patients had 1.68+0.65 transfusions per month. Uninfected patients had 1.26$\pm$0.44 transfusions per month ($p<0.05$). Twenty seven patients (54.0%) received two to three transfusions per month. Twenty one of them (77.8%) were amongst 11-16 years age group. Majority of children received blood from various Armed Forces Hospitals/ Transfusion Facilities having adequate facilities for mandatory screening of blood.

Question was also asked regarding parent's knowledge of the risk of virus transmission through blood. It turned out that 32(22.7%) were unaware of the fact while109 (77.3%) were aware of the risk of transmission. Of those unaware of the fact, majority belonged to poor

families (78.6%) and also belonged to rural areas (78.6%).

Table: 1 Characteristics of HCV positive and negative thalassemic patients.

Factors	No. of patients (n=141)	HCV antibody positive (n=50)	HCV antibody negative (n=91)
Gender			
Male	82(58.2%)	31 (62%)	51 (56.0%)
Female	59(41.8%)	19 (38%)	40 (44.0%)
Mean age (years)	7.64±4.21	10.4±3.85	6.1±3.59

DISCUSSION

Thalassemia major (beta-thalassemia) affects a significant segment of the population in Pakistan. There are more than 70,000 people with thalassemia in Pakistan and 6000 children with thalassemia are born annually[18]. Thalassemia carries gene frequency of 5-8% amongst our population. There are 8-10 million carriers of ß-thalassemia genes in the country[19].

Patients of thalassemia major being on long term transfusion therapy continue to be at high risk of acquiring hepatitis B and C virus infection1. HCV is a common cause of post transfusion hepatitis. Chronic hepatitis follows acute hepatitis C in 60 to 70% of cases, progression to cirrhosis occurs in about 10 -20% of patients with chronic hepatitis C over a period of 20-30 years and hepatocellular carcinoma in 3-5%[20].

Prevalence of hepatitis C in patients of thalassemia major varies in different studies. Our study showed that the prevalence of HCV infection in thalassemics is 35.5% which is consistent with results of other studies carried out in Pakistan. In a study carried out in Karachi seroprevalence of anti HCV antibodies among patients of thalassemia major was 34.8%[21] and another study carried out in Islamabad and Peshawar revealed HCV prevalence of 41.7%[22]. There is great variation of the prevalence rate of anti HCV among thalassemic patients of different parts of the world. A recent report from Khuzestan province, Iran showed prevalence of HCV in thalassemia patients of about 28.1%[23]. In India it was 16.7%,[24] and 22.4% in Malaysia[25]. In another study the prevalence of hepatitis C was 23.8% in thalassemia major patients in Thailand[26]. In Italy, the prevalence of hepatitis C in thalassemic patients was 47.0%[27].Variation in prevalence may be due to difference in prevalence of hepatitis C in general population and different assay methods used in detecting HCV.

In patients of thalassemia major seroprevalence of hepatitis B has been quite low as compared to hepatitis C virus. In our study 1.4% patients were HBsAg positive. This is consistent with results of another study in Pakistan where hepatitis B seroprevalence was 3.9%[28]. In another study carried out in NWFP Province HBsAg prevalence in thalassemia patients was 8.4%[29]. Low prevalence of hepatitis B seromarkers may be due to prior vaccination of thalassemics against hepatitis B, better screening assays and low prevalence of HBV as compared to HCV in our setup.

The mean age (SD) of HCV seropositive patients was 10.4±3.85 years while that for Hepatitis B surface antigen positive patients was 10.5±1.4 years. Thirty one patients with anti HCV (62%) were male while 19 (38%) were female. In other studies carried out in Pakistan mean age for anti HCV was 6.8 years[22] and 11.9±4.6 years[8]. This difference may be due to the fact that patients of different pediatric age groups were selected in different studies. Majority of HCV seropositive patients (n29, 59.2%) were between 11- 16 years age group. Twenty seven patients (55.1%) received two to three transfusions per month. Twenty one of them (77.8%) were amongst 11-16 years age group. Thus increased number of transfusion makes children more vulnerable to HCV infection.

Majority of patients included in our study were transfused blood from the facilities where blood was effectively and comprehensively screened for hepatitis B and C viruses. Thalassemic patients may acquire hepatitis C through the administration of HCV-infected blood collected during the donor window period[30]. In some immunosuppressed patients the anti-HCV assay appears negative due to

their disease pattern and/or due to treatment but the patient is actually infected with HCV. Moreover, frequent nosocomial exposure, is an additional risk factor for HCV transmission[31].

Both iron overload and HCV infection lead through different mechanisms to hepatocellular necrosis, fibrosis and cirrhosis. HCV infection and iron overload are independent but mutually reinforcing risk factors for the progression of fibrosis and development of cirrhosis. 10-year probability of progression of fibrosis reached 80% in patients with severe iron overload and HCV infection, whereas in patients with good control of iron overload, the rate of such progression appeared insignificant in HCV-negative patients[32].

CONCLUSION

It is important to consider that, in spite of the systematic screening of blood donors, a significant proportion of recipient develop hepatitis C virus infection. This finding demonstrates that more efforts should be made to improve blood transfusion safety. It is therefore imperative that highly sensitive sero-assays be used in screening donors. Simpler measures such as enforced general asepsis rules, careful disinfection and equipment sterilization should be followed. Awareness should be made regarding complications of transfusion and effect of efficient chelation.

REFERENCES

1. Agarwal MB. Advances in management of thalassemia (Editorial). Indian Pediatrics 2004; 41:989-92.
2. Fazal-ur-Rahman Khan. Thalassemia: Still a challenge.(Editorial) Gomal J Medl Sci 2006; 4: 47.
3. Borgne-Pignatti C, Cappellini MD, De Stefano P, Del Vecchio GC, Forni GL, Gamberini MR, et al. Survival and complications in thalassemia. Ann N Y Acad Sci 2005: 1054: 40-47.
4. Olivieri NF, Nathan DG, MacMillan JC, Wayne AS, Liu PP, McGee A, et al. Survival in medically treated patients with homozygous beta thalassemia. New Eng J Med 1994; 331: 574-8.
5. DanieleP,Alberto Z,Elena F,Claudia DM et al, A multicenter prospective study on the risk of acquiring liver disease in anti-Hepatitis C virus negative patients affected from Homozygous B-Thalassemia. Blood 1998; 92:3460-64
6. Luby SP, Niaz O, Siddique S, Fischer Hoch S. Patient's perceptions blood transfusion risk in Karachi, Pakistan Int J Infect Dis 2001; 6: 732-8
7. Khokhar N, Gill ML,Malik G. General seroprevalance of hepatitis C and Hepatitis B virus infection in population. J Coll Physicians Surg Pakistan 2004; 14:534-6
8. Ali SA, Donahue RM, Qureshi H,Vermund SH. Hepatitis B and hepatitis C in Pakistan: prevalence and risk factors. Int J Infect Dis.2009; 13:9-19
9. Donahue JG, Munoz A, Ness PM, Brown DE, Yawn DH, McAllister HA etal.The declining risk of post-transfusion hepatitis (Letter). N Engl J Med 1992; 327: 369.
10. Nelson KE, Donahue JG, Stambolis V. Post-transfusion hepatitis C virus infection (Letter). N Engl J Med 1992; 327: 1601
11. 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
12. Blajchman MA, Bull SB, Feinman-SVTI. Post transfusion hepatitis: Impact of non-A, non-B hepatitis surrogate tests. Lancet 1995; 345: 21.
13. Zurlo MF, De Stefano P, Borgna-Pignatti C, Di Palma A, Piga A, Melvendi C et al. Survival and causes of death in thalassaemia major. Lancet 1989; 2: 27.
14. Olivieri NF, Brittenham GM. Iron-chelating therapy and the treatment of thalassaemia. Blood 1997; 89: 739
15. Spiliopoulous L, Repanti M, Katinakis, et al. Response to interferon alfa-2b therapy in multi transfused children with beta thalassaemia and chronic Hepatitis C. Hepatogastroenterology1999; 46: 2515-20.
16. Malik S, Syed S, Ahmed N. Complications in transfusion–dependent patients of ß-thalassemia major. Pak J Med Sci 2009; 25:678-682.
17. Angelucci E, Pilo F. Treatment of hepatitis c in patients with thalassemia, Hematologica, 2008; 93: 1121-23
18. Cooleys anemia Foundation 2009. available from: http://www.thalassemia.org
19. Satwani H, Raza J, Alam M, Kidwai A. Endocrinal complications in thalassemias: Frequency and association with ferritin levels. Pak Ped J 2005; 29: 113-19.
20. Dienstag JL, Isselbacher KJ. Acute viral hepatitis and chronic hepatitis. In:Anthony S.Fauci, Dennis L. Casper, Dan L. Longo, Eugene Braunwald, Stephon L. Hauser, Jo Larry Jameson et al, eds. Harrison's principles of internal medicine. Mc Graw-Hill, USA, 2005: 1822-50.
21. Akhtar S, Moattar T. Hepatitis C virus infection in Polytransfused Thalassemic children in Pakistan (letter) Ind Ped 2004;41: 1072
22. Hussain H, Iqbal R, Khan M,Bushra I,Sabina A,Fayaz KB etal, Prevalence of hepatitis C in beta Thalassemia major. Gomal J Med Sci ;2008 :6 ;87-90.
23. Ghafourian BM, Assareh ZMA, Zandian KM, Haghirizadeh RM. Prevalence of Hepatitis C virus (HCV) among Thalassemia Patients in Khuzestan Province, Southwest Iran. Pak J Med Sci 2009; 25:113-117.
24. Agarwal MB, Malkan GH, Bhave AA,Vishwanathan C, Billa V, Dube SR et al. Antibody to hepatitis C virus in multi-transfused thalassaemia; Indian experience. Br J Haematol 1993; 83:491-97.
25. 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 Dis1999; 18: 709–15.
26. Laosombat V, Pornpatkul M, WongchanchailertM, Worachat K, Wiriyasatienku A. The prevalenceof hepatitis C virus in thalassaemic patientsin the south of Thailand. Southeast Asia JTrop Med Public Health 1997; 28: 149-53.
27. 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.
28. Muhammad FKB, Mumtaz H, Liaqat A, Mufti Zw. Frequency of hepatitis Bvirus in regularly blood transfused beta Thalassemia Major patients. Pak Paed J 2009; 33: 153-6
29. Mukhtar AS, Muhammad TK, Zahoor U, Yasmeen A. Prevalence of hepatitic B and hepatitis C virus infection in multi- transfused Thalassemia major patients in North West Frontier Province. Pak J Med Sci 2006; 21: 282-3
30. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ TheRetrovirus Epidemiology Donor Study: The risk of transfusion transmitted viral infections. N Engl J Med ;1996:334:1685
31. Prati D, Capelli C, Silvani C, De Mattei C, Bosoni P, Pappalet Pappalettera et al. The incidence and risk factors of community-acquired hepatitis C in a cohort of Italian blood donors. Hepatology.1997; 25:702
32. Emanuele A, Federica P. Treatment of hepatitis c in patients with thalassemia. Hematologica. 2008; 93: 1121-3