

## Frequency of Hepatitis C in B-Thalassemia major patients

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**Objectives:** To determine the frequency of hepatitis C virus infection in children with  $\beta$ -thalassemia major at our institution.

**Methodology:** This descriptive cross sectional study was conducted at Military Hospital, Rawalpindi, Pakistan from October 11, 2009 to April 10, 2010. A total 95 patients of  $\beta$ -thalassemia major were included in the study. They were screened for presence of Anti-HCV antibodies by 3<sup>rd</sup> generation ELISA technique.

**Results:** Out of total 95 patients, there were 60% (n=57) male and 40% (n=38) female patients. 42.1 % (n=40) were found to have anti HCV

positive while 57.9% (n=55) patients were anti HCV negative. Mean age of anti-HCV positive patients was 10.4 $\pm$ 3.54 years and mean age of anti-HCV negative patients was 8.2 $\pm$ 3.12 year.

**Conclusion:** The frequency of HCV infection in our patients with  $\beta$ -thalassemia major receiving multiple transfusions was very high. There is urgent need to ensure the universal availability of screened blood and introduce more effective screening methods. (Rawal Med J 2013;38: 328-331).

**Key words:** Hepatitis C Antibodies, thalassemia, blood transfusion.

### INTRODUCTION

Thalassemias are genetic disorders of globin chain production.<sup>1</sup> The estimated carrier rate of  $\beta$ -thalassemia is 5-7% in Pakistan<sup>2</sup> and due to culture of cousin marriages the numbers of such patients is increasing. In  $\beta$ -thalassemia major (BTM) there is severe anemia requiring regular blood transfusions and hence exposing the patients to transfusion-associated diseases<sup>1,3</sup> After the discovery of Hepatitis C Virus (HCV) in 1989, it has proved to be the major cause of transfusion-associated hepatitis,<sup>4,5</sup> and an important cause of death in thalassemic children.<sup>1</sup> Given that the current HCV treatment is costly and leads to a successful outcome in only about 50% of the patients,<sup>6</sup> prevention is surely the most effective policy.

In our region, the prevalence of anti-HCV antibodies in the multitransfused  $\beta$ -thalassemics has been variously reported to range from 19.3-43.5%.<sup>3,7</sup> Pakistani patients and their parents are largely unaware of the importance of screening for blood products<sup>8</sup> and facilities for effective screening of blood for HCV and other pathogens are limited to few larger cities. The prevalence of anti-HCV antibodies in the general Pakistani population has been variously reported to range from 1.7-5.3%.<sup>8,9</sup> HCV infection adds to morbidity and mortality in  $\beta$ -

thalassemic children and is a preventable disease. Limited data is available regarding HCV infection in our thalassemic population. The purpose of this study was to determine the burden of HCV infection in thalassemic children reporting to our facility.

### METHODOLOGY

This descriptive cross sectional study was conducted on out-patient basis at the Pediatrics Department, Military Hospital, Rawalpindi, Pakistan, a tertiary care Army funded hospital, from October 11, 2009 to April 10, 2010. It included 95 diagnosed cases of  $\beta$ -thalassemia major of both genders between the ages of 4 and 18 years who had received at least five blood transfusions. Non probability convenience sampling was used. Any thalassemic child known to be anti-HCV antibodies positive before starting blood transfusions, any thalassemic child born to anti-HCV antibody positive mother and any thalassemic child with past history intravenous drug abuse involving syringe sharing were excluded from the study.

Every child was assigned a serial number. Their demographic data including age, gender, number of transfusions was recorded. The blood samples were collected at under strict aseptic conditions and were analyzed at Armed Forces Institute of Pathology,

Rawalpindi, by 3<sup>rd</sup> generation ELISA technique (ETI-AB-HCVK-4, DiaSorin, Italy). Data was analyzed in SPSS version 17.

## RESULTS

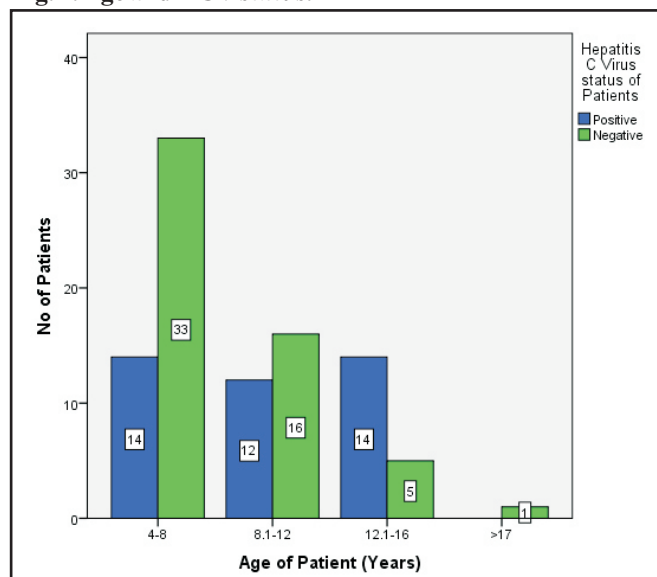
Out of 95 patients, 57 (60%) were male and 38 (40%) were female. Out of 95 patients, 40 (42.1%) had anti HCV positive and 55 (57.9%) were anti HCV negative (Table 1).

**Table 1. Demographic characteristics of study population.**

	Number (N=95)	Anti-HCV positive (N=40)	Anti-HCV negative (N=55)
<b>Gender</b>			
Male	57 (60%)	27 (67.5%)	30 (54.5%)
Female	38 (40%)	13 (32.5%)	25 (45.5%)
<b>Mean age±SD (Years)</b>	9.12±3.46	10.4±3.54	8.12 ±3.12

Out of 95 patients, 47 (49.5%) were between 4-8 years. Out of these 47, 14 (29.8%) were HCV positive. Only patient of more than 16.1 years category was found to be HCV negative (Fig. 1).

**Fig. 1. Age and HCV status.**



## DISCUSSION

Beta thalassemia is the most common single gene disorder in Pakistan with a gene frequency of 5-8% and about 8-10 million carriers in the country.<sup>11</sup> Due

to unawareness regarding the disease and ongoing culture of cousin marriages, the numbers of patients with BTM are increasing in Pakistan. Over the past three decades, regular blood transfusions and iron chelation has significantly improved the quality of life and transformed thalassaemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life.<sup>12,13</sup> However, with the dramatically improved survival of patients with BTM, care providers face new clinical scenarios and new challenges associated with the longer life and aging of these patients. One of such challenges is the management of liver disease in thalassaemics patients. Liver disease has long been recognized as an important cause of morbidity and mortality in patients with thalassemia.<sup>14</sup> This is due to combination of iron over load causing liver damage and transfusion transmitted hepatitis C and B.

While rigorous donor screening and testing procedures have dramatically reduced transmission of HCV via blood products, there are still many countries in which standards of blood product management do not adequately protect chronically transfused patients from this complication. HCV infection remains a significant problem for patients with thalassemia major in Pakistan, as there is high prevalence of hepatitis C infection in Pakistani blood donors.<sup>15,16</sup> In Pakistan, the facilities for universal and effective screening of blood donors for HCV markers are not available, thus making blood transmission a major source HCV infection. In 2000, Luby et al<sup>17</sup> reported that only 23% of the blood banks screened for HCV while 29% of them were storing blood outside the WHO recommended temperature.

In our study, 42 % of thalassaemics were HCV positive. Prevalance of hepatitis C in patients of thalassemia major varies in different studies. Hussain et al reported a seroprevalance of anti HCV antibody among multitransfused thalassaemics to be 41.70%, which was comparable to our results.<sup>18</sup> Other reports 57%<sup>19</sup> and 36%.<sup>20</sup>

There is great variation of anti-HCV antibody prevalence among thalassaemic patients in different parts of the world. Mirmomen et al found that 19.3% of 732 Iranian, multitransfused thalassaemics were anti-HCV positive.<sup>3</sup> A study from India reported a

seroprevalence of 43.65%.<sup>7</sup> A very high rate of 76% was reported in a recent study of 125 multitransfused thalassemic Egyptian patients.<sup>21</sup> Anti-HCV antibody in multitransfused thalassemics of Gujarat state of India was found to be 18%.<sup>22</sup> In Turkey, where better screening facilities and protocol exist, 4.4% of thalassemics were found to be positive.<sup>23</sup> The variation of results in different studies might be due to different methods of blood screening, different age group of patients selected and variation of blood screening protocols in different parts of the world. The prevalence is less in countries with better blood screening system in place.

In our study, mean age of anti-HCV positive thalassemics was significantly greater than anti HCV negative thalassemics (10.4±3.54 vs 8.12 ±3.12 years, p=0.01). The HCV prevalence was highest in age category 12.1-16 years. In this age group, 73.7 % patients were anti-HCV positive as compared with 29.8% belonging to 4-8 years category, thus showing a clear association between advancing age and risk of acquiring HCV infection. This might be because of the fact that the total numbers of blood transfusions received by older thalassemics are more than younger patients. Moreover, frequency of transfusions received by older thalassemics is more compared with younger ones. These results are comparable to other studies done in our country.<sup>18,20</sup>

Most of our patients received transfusions from blood banks, which routinely screen blood for anti-HCV antibodies. Despite screening, high prevalence of anti-HCV antibody may be multifactorial. One of such factors may be transfusion during window period of HCV infection. Commonly used screening methods ELISA 2 and ELISA 3 have a window period of 82 and 70 days respectively.<sup>24</sup> Thus, these screening methods are not able to detect HCV infection during window period making the blood recipient susceptible to infection. Other factor can be absence of HCV antibodies in some patients even outside the window period. For example, in immunocompromised individuals (HIV infection, patients on dialysis, and transplant recipients) anti-HCV antibody may not be detectable despite the

presence of HCV infection. One of the other possibilities is getting transfusions from local facilities in hometowns and small cities where blood screening is not done or methods with low sensitivity and specificity are used resulting in more chances of transmission of HCV. Blood screening using the viral antigen and nucleic acid amplification tests (NAT) can reduce the window period of HCV infections.<sup>25</sup>

## CONCLUSION

The frequency of hepatitis C virus infection in children with  $\beta$  thalassemia major receiving multiple transfusions at Military Hospital, Rawalpindi was very high. The mean age of anti-HCV positive thalassemics was significantly greater than anti HCV negative thalassemics thus showing a clear association between advancing age and total numbers of blood transfusions received by older thalassemics. We also recommend implementation and adherence to strict blood screening protocols.

### Author contributions:

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**Conflict of Interest:** None declared.  
Rec. Date: Apr 16, 2013 Accept Date: September 17, 2013

## REFERENCES

1. Rund D, Rachmilewitz E. Beta-thalassemia. *N Engl J Med* 2005;353:1135-46.
2. Ansari SH, Shamsi TS, Ashraf M, Borhany M, Farzana T, Khan MT, et al. Molecular epidemiology of  $\beta$ -thalassemia in Pakistan: far reaching implications. *Int J Mol Epidemiol Genet* 2011;2: 403-8.
3. Mirmomen S, Alavian SM, Hajarizadeh B, Kafae J, Yektaparast B. Epidemiology of hepatitis B, hepatitis C, and human immunodeficiency virus infections in patients with beta-thalassemia in Iran: a multicenter study. *Arch Iran Med* 2006;9:319-23.
4. 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.
5. Sy T, Jamal M. Epidemiology of Hepatitis C Virus (HCV) Infection. *Int J Med Sci* 2006;3:41-6.

6. Webster DP, Klenerman P, Collier J, Jeffery KJ. Development of novel treatments for hepatitis C. *Lancet Infect Dis* 2009;9:108-17.
7. Mathur M, Wanjari K, Turbadkar D. Seroprevalence of HIV, hepatitis C and hepatitis B in multitransfused thalassemics. *Indian J Med Microbiol* 2008;26:205-6.
8. Arif F, Fayyaz J, Hamid A. Awareness among parents of children with thalassemia major. *J Pak Med Assoc* 2008;58:621-4.
9. Butt T, Amin MS. Seroprevalence of hepatitis B and C infections among young adult males in Pakistan. *East Mediterr Health J* 2008;14:791-7.
10. Khokhar N, Gill ML, Malik GJ. General seroprevalence of hepatitis C and hepatitis B virus infections in population. *J Coll Physicians Surg Pak* 2004;14:534-6.
11. Satwani H, Raza J, Alam M, Kidwai A. Endocrinal complications in thalassemias: Frequency and association with ferritin levels. *Pak Ped J* 2005;29:113-9.
12. Agarwal MB. Advances in management of thalassemia. *Indian J Pediatr* 2009;76: 177-84.
13. Borgna-Pignatti C, Rugolotto S, De Stefano P, Zhao H, Cappellini MD. Survival and complications in patients with thalassemia major treated with transfusion and deferoxamine. *Haematologica* 2004;89:1187-93.
14. Di Marco V, Capra M, Gagliardotto F, Borsellino Z, Cabibi D. Liver disease in chelated transfusion-dependent thalassemics: the role of iron overload and chronic hepatitis C. *Haematologica* 2008;93:1243-46.
15. Sultan F, Mehmood T, Mahmood MT. Infectious pathogens in volunteer and replacement blood donors in Pakistan: a ten-year experience. *Int J Infect Dis* 2007;11:407-12.
16. Khattak MN, Akhtar S, Mahmud S, Roshan TM. Factors influencing Hepatitis C virus sero-prevalence among blood donors in north west Pakistan. *J Public Health Policy* 2008;29:207-25.
17. Luby S, Khanani R, Zia M, Vellani Z, Ali M. Evaluation of blood bank practices in Karachi, Pakistan, and the government's response. *J Pak Med Assoc* 2006;56:25-30.
18. Hussain H, Iqbal R, Khan MH, Iftikhar B, Aziz S. Prevalence of hepatitis C in Beta thalassaemia major. *Gomal J Med Sci* 2008;6:87-90.
19. Shah SMA, Khan MT, Zahour Ullah, Ashfaq NY. Prevalence of hepatitis B and hepatitis C virus infection in multitransfused thalassaemia major patients in North West Frontier Province. *Pak J Med Sci* 2005;21:281-4.
20. Muhammad J, Hussain M, Khan MA. Frequency of Hepatitis B and Hepatitis C infection in Thalassaemic children. *Pak Pediatr J* 2003;27:161-4.
21. El-Shanshory MR, Kabbash IA, Soliman HH, Nagy HM, Abdou SH. Prevalence of hepatitis C infection among children with  $\beta$ -thalassaemia major in Mid Delta, Egypt: a single centre study. *Trans R Soc Trop Med Hyg* 2013;107:224-8.
22. Bhavsar H, Patel K, Vegad M, Madan M, Pandey A, Asthana A, et al. Prevalence of HIV, Hepatitis B and Hepatitis C infection in Thalassaemia major patients in tertiary care hospital, Gujarat. *NJIRM* 2011;2:47-51.
23. Ocak S, Kaya H, Cetin 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.
24. Tobler LH, Stramer SL, Lee SR. Impact of HCV 3.0 EIA relative to HCV 2.0 EIA on blood-donor screening. *Transfusion* 2003;43:1452-9.
25. Kuhns MC, Busch MP. New strategies for blood donor screening for hepatitis B virus: Nucleic acid testing versus immunoassay methods. *Mole Diagnost Ther* 2006;10:77-91.