

Prevalence of Hepatitis B and Hepatitis C in Transfusion Dependent Thalassemia Patients

Iftikhar Ahmed, Shahid Iqbal and Aida Waheed

ABSTRACT

Objective: The objective of this study was to determine the prevalence of transfusion transmitted diseases such as viral hepatitis B and C in thalassemic patients.

Study Design: Descriptive / cross section study

Place and Duration of Study: This study was conducted at the Department of Pediatrics, Sheikh Khalifa Bin Zayed Teaching Hospital, Rawalakot AJK (Teaching Hospital of Poonch Medical College, Rawalakot from November 2016 to May 2017).

Materials and Methods: 55 thalassemic patients were screened for transfusion transmitted hepatitis B and C virus using electro chimiluminescence using auto analyzer elecsys Cobas E 411 as well as PCR techniques where possible. The outcome i.e., hepatitis B and C infection was stratified by age, parity and duration of transfusion.

Results: The prevalence of transfusion transmitted hepatitis C was 30.91% in our study and it had a statistically significant association with the age and duration of blood transfusion in thalassemic patients. Hepatitis B was not positive in any patient.

Conclusion: High prevalence of transfusion transmitted hepatitis C in thalassemic patients despite adoption of donor blood screening protocols needs to be addressed urgently to determine the factors responsible for this complication of transfusion therapy.

Key Words: Thalassemia, Transfusion, Viral Hepatitis, Cirrhosis liver, Chelation, Hepatitis C

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INTRODUCTION

Thalassemia, an autosomal-recessive disorder, is an important cause of severe anemia in children and young adults. Incidence of thalassemia is particularly high in a geographical area extending from South East Asia to Middle East affecting Burma and Indian subcontinent as well.¹ The disease burden of thalassemia in Pakistan is very high and according to recent estimates, every year about five thousand infants homozygous for thalassemia are born.² The thalassemic patients are dependent on regular blood transfusions throughout their life for survival and even though regular blood transfusions better the survival of thalassemic patients as a whole, they are exposed to a significant risk of transfusion associated infections, particularly blood-borne viral infections.³

Thalassemic patients who have received multiple blood transfusions are more likely to develop post-transfusion viral hepatitis such as Hepatitis B and Hepatitis C.⁴ Among the two, Hepatitis C is the leading reason for post-transfusion hepatitis in this patient population and it contributes to the morbidity and mortality associated with thalassemia owing to its complications in the long-term such as cirrhosis of liver and hepatocellular cancer.^{5,6} Hepatitis C poses a major evolving health issue in the third world for the general population as a result of inadequate policies for Hepatitis C prevention and infection control.⁷ It has been estimated that Hepatitis C is responsible for up to 90% of transfusion associated infections in thalassemic patients.⁸ Even though Hepatitis C is a widely prevalent public health problem across the world.⁹ and is known to affect more than 200 million worldwide with a prevalence rate varying from 0.2%-40%.^{10,11} The prevalence of hepatitis B is much more than that of Hepatitis C. It affects more than two billion people worldwide and is responsible for more than one million deaths annually.¹² A significant number of patients (more than twenty one million) diagnosed with Hepatitis C reside in the eastern Mediterranean region.¹³ The global prevalence of Hepatitis B and Hepatitis C in thalassemic patients in terms of Hepatitis B surface antigen positivity (HbsAg+) and anti-

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Hepatitis C antibodies (Anti HCV) varies between 0.3%-5.7% and 4.4%-85.4% respectively.¹⁴

A number of risk factors have been found to be associated with acquisition of Hepatitis C and hepatitis B infection in thalassemic patients. These include increased age^{3,15}, duration of transfusion^{3,15}, parity¹ and HbsAg Seropositivity³. A recently published study from Egypt identified at least ten transfusions per year and age more than 10 years in addition to co-infection with Hepatitis B to be significantly associated with the risk of acquiring Hepatitis C infection.¹⁶

To reduce the risk of transmission of infections associated with transfusions, the donor blood is screened for common pathogens such as Hepatitis B, Hepatitis C and HIV. In view of lack of studies as well as data from this region and a huge variation in the reported prevalence of Hepatitis C in thalassemic patients from Pakistan, we decided to determine the prevalence of viral hepatitis B and C and the risk factors associated with the transmission of Hepatitis C in thalassemic patients registered with our department. We thought that the resulting information could be used to revise the current management strategies in place.

MATERIALS AND METHODS

This descriptive cross sectional study was conducted at the Department of Pediatrics, Sheikh Khalifa Bin Zayed Teaching Hospital, Rawalakot AJK (Teaching Hospital of Poonch Medical College, Rawalakot from November 2016 to May 2017. Fifty five thalassemic patients are registered with our department and they were enrolled in the study after obtaining an informed consent. Patients aged at least two years who were being transfused for thalassemia were enrolled in the study. They were assured of confidentiality and privacy. The patients receive regular blood transfusions as well as chelation therapy in our center. Three cc blood was drawn from antecubital vein of each patients under strict aseptic conditions and was sent to laboratory for HbsAg and anti HCV antibody levels by electro chemiluminescence using auto analyzer Elycsys Cobas E 411 . The patients who tested positive for anti-HCV by device method were contacted again and blood was drawn again for both qualitative and quantitative polymerase chain reactions to measure HCV viral DNA levels. Patients whose HCV was confirmed by PCR were then referred to a gastroenterologist for further management. The data was recorded by the investigators themselves. The data was entered into and analyzed using SPSS 16. Mean±SD were calculated for numerical variables while frequencies and percentages were calculated for categorical variables. The outcome i.e., hepatitis C infection was stratified by age, parity and duration of transfusion. Post stratification chi-square test was applied and a p value < 0.05 was taken to be significant.

RESULTS

This study enrolled fifty five thalassemic patients with a mean±SD age of 9.16±6.36 years and a range of 3-- 30 years. The mean duration of transfusion was 8.02±5.45 years. There were thirty (54.55%) males and twenty-five (45.45%) females in the study cohort. The frequency of hepatitis C positivity was 41.82% (n=23) initially which later dropped to 30.91% (n=17) after PCR assays. No patient was found to have HbsAg positivity. When the outcome i.e., Hepatitis C was stratified by age, parity and duration of transfusions a statistically significant association was found with age of the patients and duration of transfusion (p <0.05). Older thalassemic patients were more likely to acquire Hepatitis C. Similarly, those with a long duration of blood transfusion (i.e. more than 9 years) were also exposed to a risk of acquiring hepatitis C.

Table No.1: Cross tabulation of age and prevalence of hepatitis C in study population

Hepatitis C	Age of patients		Total	P value
	Upto 10 years	More than 10 years		
Present	6.00	11.00	17.00	0.001
Absent	31.00	7.00	38.00	
Total	37.00	18.00	55.00	

Table No.2: Cross tabulation of duration of treatment and prevalence of hepatitis C in study population

Hepatitis C	Age of patients		Total	P value
	Upto 9 years	More than 9 years		
Present	6.00	11.00	17.00	0.001
Absent	31.00	7.00	38.00	
Total	37.00	18.00	55.00	

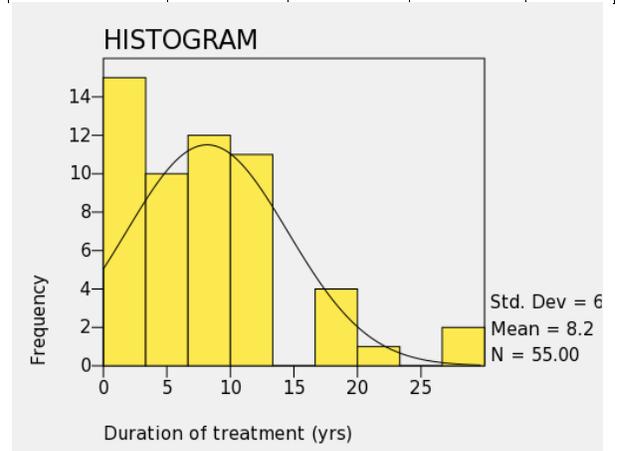


Figure No.1: Duration of treatment of study population

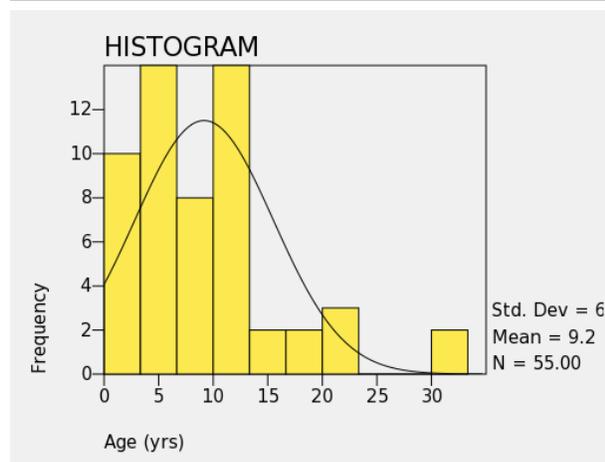


Figure No.2: Age of study participants

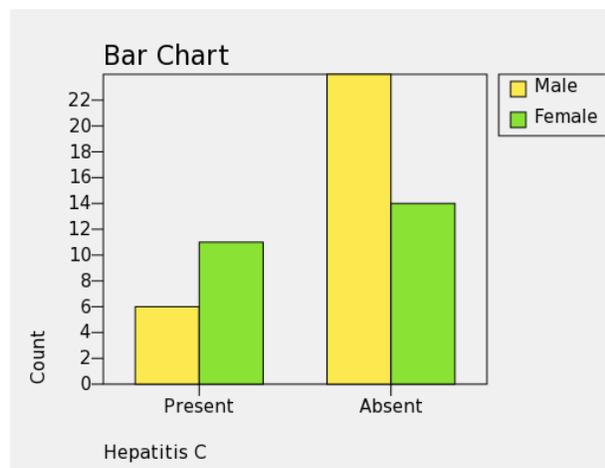


Figure No.3: prevalence of hepatitis C according to the gender of study population

DISCUSSION

Among the single-gene autosomal disorders, β -thalassemia is one of the commonest disorders. β -thalassemia is the commonest form of thalassemia and is known to affect more than 150 million people across 60 countries.¹⁷ Regular and timely blood transfusion is a necessary component of thalassemia management to ensure survival and prevention of complications arising from severe anemia in these patients. However, these patients are exposed to a lifetime risk of acquiring transfusion associated infections, particularly HIV, Hepatitis C and Hepatitis B.¹⁸

The objective of this study was to determine the prevalence of hbsAg and anti-HCV antibodies in thalassemic patients from rawalakot AJK region. β -thalassemia major was the common form of thalassemia in this study and was present in 96.3% of patients. The rest had β -thalassemia intermedia. Similar prevalence rates have been reported from this region: 96% and 4% for β -thalassemia major and β -thalassemia intermedia respectively from Rawalpindi¹, 93% and 7% for β -

thalassemia major and β -thalassemia intermedia respectively from Faisalabad¹⁷ and 87% and 13% respectively for β -thalassemia major and β -thalassemia intermedia from India.¹⁹ The prevalence of Hepatitis C was 30.91% in this study which, even though, is quite high but is similar to other reports from different regions of Pakistan.^{1,20,21}

Though the majority of patients in this study was male (n=30; 54.55%), the number of affected females was almost twice that of affected males (11 vs 6). This is interesting since the opposite of this trend has been observed elsewhere in studies from Pakistan.^{1,8,14} In this study, the mean serum ferritin level was found to be more in affected females than in the affected males however, this was found to be statistically insignificant ($p > 0.05$). Though this fact can be explained by the number of affected females as well as the difference in age of affected males and females where females, by virtue of their increased age had received more transfusions than the males. The increased serum ferritin levels also suggested the state of compliance with chelation therapy which, considering the socioeconomic status is not affordable for everyone all the time.

In our study, majority of patients belonged to first parity followed by third and second parity. Similar findings have been reported by Shah and colleagues who reported that more than half of their patients (56.7%) belonged to first parity. 38.3% of their patients belonged to third parity and only 5 % belonged to second parity.²² However, A number of studies have reported second parity to be most common among Pakistani thalassemic patients.^{1,17}

In addition to risk factors for HCV sero-positivity mentioned above, increased serum ferritin, transfusion at an early age have also been identified as risk factors for acquiring HCV infection in thalassemic patients.¹ However, we found that increasing age and duration of transfusion treatment were significantly associated with the risk of acquiring HCV infection.

Despite the fact that screening procedures for blood transfusions have been adopted in Pakistan and have been in place for decades now, increased prevalence of Hepatitis C in multi-transfused thalassemic patients is a worrying scenario. This is a serious complication of transfusion therapy for thalassemic patients and needs to be addressed on war-footing. Public health policy planning and implementations should focus on this problem and guidelines need to be developed for management of β -thalassemia in Pakistan that should also address the prevention of blood-borne infections in this population.

CONCLUSION

High prevalence of transfusion transmitted hepatitis C in thalassemic patients despite adoption of donor blood screening protocols needs to be addressed urgently to

determine the factors responsible for this complication of transfusion therapy.

Author's Contribution:

Concept & Design of Study: Iftikhar Ahmed
 Drafting: Shahid Iqbal
 Data Analysis: Aida Waheed
 Revisiting Critically: Iftikhar Ahmed, Shahid Iqbal
 Final Approval of version: Iftikhar Ahmed

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

- Din G, Malik S, Ali I, Ahmed S, Dasti JI. Prevalence of hepatitis C virus infection among thalassemia patients: a perspective from a multi-ethnic population of Pakistan. *Asian Pac J Trop Med* [Internet]. 2014 [cited 2018 Jan 3];7((Suppl 1)):S127–33. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1995764514602182>.
- Ansari SH, Shamsi TS, Ashraf M, Bohray M, Farzana T, Khan MT, et al. Molecular epidemiology of β -thalassemia in Pakistan: far reaching implications. *Int J Mol Epidemiol Genet* 2011;2(4):403–8.
- Mansour AK, Aly RM, Abdelrazek SY, Elghannam DM, Abdelaziz SM, Shahine DA, et al. Prevalence of HBV and HCV infection among multi-transfused Egyptian thalassemic patients. *Hematol Oncol Stem Cell Ther* [Internet]. 2012 [cited 2018 Jan 3];5(1):54–9. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1658387612500063>
- El-Faramawy A, El-Rashidy O, Tawfik P, Hussein G. Transfusion transmitted hepatitis: Where do we stand now? A one center study in upper Egypt. *Hep Mon* 2012;12:286–91.
- Ataei B, Hashemipour M, Kassaian N, Hassannejad R, Nokhodian Z, Adibi P. Prevalence of anti HCV infection in patients with Beta-thalassemia in Isfahan-Iran. *Int J Prev Med* 2012;3:S118-23.
- Yousefi M, Dehesh M, Ebadi M, Dehghan A. The Prevalence of Hepatitis C Virus Infection in Patients With Thalassemia in Zabol City of Iran. *Int J Infect* 2017;4(1):e37009.
- Rezvan H, Abolghassemi H, Kafiabad S. Transfusion-transmitted infections among multi transfused patients in Iran: A review. *Transfus Med* 2007;17:425–33.
- Ansari SH, Shamsi TS, Khan MT, Perveen K, Farzana T, Erum S, et al. Seropositivity of Hepatitis C, Hepatitis B and HIV in Chronically Transfused $\beta\beta$ -Thalassaemia Major Patients. *J Coll Physicians Surg Pak* 2012;22(9):610–1.
- El-Beshlawy A, Youssry I. Prevention of Hemoglobinopathies in Egypt. *Hemoglobin* [Internet]. 2009 [cited 2018 Jan 3];33(sup1):S14–20. Available from: <http://www.tandfonline.com/doi/full/10.3109/03630260903346395>
- Brown RS, Gaglio PJ. Scope of worldwide hepatitis C problem. *Liver Transpl* [Internet]. 2003 [cited 2018 Jan 3];9(11):S10–3. Available from: <http://doi.wiley.com/10.1053/jlts.2003.50244>
- Alavian SM. Hepatitis C infection in Iran; A review article. *Iran J Clin Infect Dis* 2009;4(1):47–59.
- Alavian SM. Ministry of Health in Iran is serious about controlling hepatitis B. *Hepat Mon* 2007;7(1):3–5.
- Ramia S, Eid-Fares J. Distribution of hepatitis C virus genotypes in the Middle East. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis* 2006;10(4):272–7.
- Riaz H, Riaz T, Ullah F, Aziz S, Khan MU, Pervaiz R, et al. Assessment of the seroprevalence of viral hepatitis B, viral hepatitis C and HIV in multitransfused thalassaemia major patients in Karachi, Pakistan. *Trop Doct* 2011;41(1):23–5.
- Boroujerdnia MG, Zadegan MAA, Zandian KM, Rodan MH. Prevalence of hepatitis-C virus (HCV) among thalassemia patients in Khuzestan Province, Southwest Iran. *Pak J Med Sci* 2009;25(1):113–7.
- Atwa ZT, Abdel Wahed WY. Transfusion transmitted infections in frequently transfused thalassemic children living in Fayoum Governorate, Egypt: Current prevalence and risk factors. *J Infect Public Health* [Internet]. 2017 [cited 2018 Jan 3];10(6):870–4. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1876034117300904>
- Qurat-ul-Ain LA, Hassan M, Rana SM, Jabeen F. Prevalence of β -thalassemic patients associated with consanguinity and anti-HCV-antibody positivity—a cross sectional study. *Pak J Zool* 2011;43(1):29–36.
- 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;67–71.
- Mishra AK, Tiwari A. Iron overload in beta thalassaemia major and intermedia patients. *Maedica* 2013;8(4):328.
- Younus M, Hassan K, Ikram N, Naseem L, Zaheer HA, Khan MF. Hepatitis C virus seropositivity in repeatedly transfused thalassemia major patients. *Int J Pathol* 2004;2(1):20–3.
- Hussain H, Iqbal R, Khan MH, Iftikhar B, Aziz S, Burki FK, et al. Prevalence of hepatitis C in beta thalassaemia major. *Gomal J Med Sci* 2004;6(2).
- Shah S, Khan MT, Ullah Z. Hepatitis-B and Hepatitis-C virus infection in multi-transfused thalassemia Major patients. *Pak J Med Sci* 2005; 21(3):281.