

Original Research Article

Seroprevalance of hepatitis-c infection in multi-transfused thalassemic children: study from a West Indian tertiary care center

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ABSTRACT

Background: To study the prevalence of hepatitis-C virus infection in multi-transfused thalassemic children and to correlate these patients with age, number of transfusion, serum ferritin levels and transaminases levels.

Methods: This study was conducted in the Department of Pediatrics of a Teaching Institute of Rajasthan. It was a hospital based cross sectional study, conducted over a period of 12 months (April 2016- March 2017). Blood sample for Ant-HCV antibody detection was taken at time of follow-up visit in the subspeciality clinic. These samples were processed in central laboratory for hep-C antibody, serum ferritin and transaminases levels. Anti-HCV antibody detection was done by BI-DOT machine. HCV RNA PCR was done to access viral load in all positive cases.

Results: A total of 300 patients were enrolled in the study. There were 219 (73%) males and 81 (27%) females. The mean age of the study group was 7.59 ± 3.6 years (range 1.5-18years). At the time of our study 277 (92.4%) cases were on one or the other chelating agent whereas 23 (7.6%) cases were not taking any kind of chelation therapy. Out of 300 patients, 72(24%) cases tested positive for anti HCV antibody. Out of 72 patients only 36(12%) patients had detectable viral load in RNA PCR. Mean age of the HCV positive cases (9.58 ± 3.28) years was higher as compared to HCV negative cases (6.98 ± 3.54). Maximum HCV positivity 20/38 (52.6%) was seen in 12-18 year age group; followed by 33/76 (43.4%) in 9-12yr age group. Significant association was observed between advancing age and prevalence of hepatitis C in thalassemia major patients ($p=0.002$). The number of blood transfusions received by anti-HCV positive children (Avg. Transfusion 185 ± 98.40 ml/kg/year) was significantly higher than that by anti-HCV negative patients (Avg. Transfusion 102.8 ± 71.20) (p value < 0.001). Maximum HCV positive cases 33 (45.83%) had total transfusions > 200 in a year followed by 15 (20.83%) cases with 151-200 transfusions ($p < 0.001$).

Conclusions: Despite ELISA screening of blood donors, our study demonstrated high (24%) prevalence of transfusion transmitted hepatitis-C virus in thalassemic children which increases with increasing number of transfusions, it also correlates with rising serum ferritin level and SGPT level.

Keywords: Hepatitis-C, HCV, Thalassemia, Transfusion transmitted infections

INTRODUCTION

Thalassemia is an autosomal recessive hemoglobinopathy disorder.^{1,2} Absent production of β chain results in

excessive production of α -globin chains, which precipitate in red cell precursors resulting in intra-medullary destruction and hence ineffective erythropoiesis. Ineffective erythropoiesis leads to anemia and tissue hypoxia requiring regular blood transfusion.

It is a major health problem, causing much morbidity, early mortality and a great deal of misery for a family both financially and emotionally. Blood transfusion is absolute necessity as a treatment modality for these patients. This prevents growth impairment, organ damage, bone deformities and allowing normal activity and good quality of life.

Among the undesirable complications arising from transfusion, transfusion transmitted infections (TTIs) such as HIV, hepatitis B (Hep B), hepatitis C (Hep C) and syphilis (caused by *Treponemapallidum* subsp. *pallidum*) are the most significant ones.³ In an Italian multicenter study, infections were the second cause of death after heart failure in thalassemia.⁴

The probability of acquiring TTIs is related to the probability of being exposed to the infected units of blood which in turn depends on the prevalence of the donors in the population and the number of units transfused. Hep C, newly emerging, has become a major cause of chronic hepatic diseases and also hepatic malignancy.

A survey of blood transfusion practices noted that testing for TTIs is not good enough and badly managed in most blood banks, both private and government, all over India.⁵ Prevalence studies have found that common infections occurring in thalassemic patients are Hepatitis C (2.2%-44%), followed by Hepatitis B (1.2%-7.4%) and HIV (0%-9%).⁶ There is a paucity of studies of prevalence of hepatitis C in multi-transfused thalassemic patients in this region, and thus we conducted this study.

METHODS

The study was conducted in the department of pediatrics, SPMCHI, S.M.S Medical College, Jaipur from April 2016 to March 2017. It was a hospital based cross sectional study.

Inclusion criteria

- Beta thalassemia major patients
- Age group 18 months to 18 years
- Patients who have received ≥ 8 blood transfusions

Exclusion criteria

- Those suffering from other hemoglobinopathies.
- Patients who had been given (administered) less than eight blood transfusions, as part of their management were not included in this study.

An informed consent by the guardians or parents of the patients was taken after which 300 thalassemia patients were included in the study. On admission, particulars of the patient (name, age, sex, religion, residence, etc.) were noted in a pre-designed proforma. A complete detailed history was taken regarding age of diagnosis, age of first transfusion, average number of transfusion in a month and during last year, family history, if any so as to ascertain the pedigree. A thorough anthropometric examination was done with regards to height, weight, head circumference, mid arm circumference and body mass index of the patient. Blood sample for Ant-HCV antibody detection was taken at time of follow-up visit to the subspecialty clinic. These samples were processed in central laboratory. Anti-HCV antibody detection done by BI-DOT (J Mitra and Co. Pvt. Ltd.) machine. HCV RNA PCR was done to access viral load in all positive cases.

RESULTS

A total of 300 patients were enrolled in the study. There were 219 (73%) males and 81 (27%) females with an overall male to female ratio of 2.73:1. The mean age of the study group was 7.59 ± 3.6 years (range 1.5-18years). Most common clinical manifestation was anemia (100% cases), followed by hepatomegaly (90.2%) and splenomegaly (81.05%).

Table 1: Association of age with anti-HCV positivity in beta thalassemia major cases.

age subgroups	Total beta thalassemia cases (n=300)		Anti HCV positive (N=72)		HCV RNA positive (N=36)		Chi square test
	No. of cases	%	No. of cases	% of HCV + cases in subgroup	No. of cases	% of HCV RNA positive cases in subgroup	P value LS
1.5 to <3	28	9.33	0	0	0	0	17.079 at 4 DF; P=0.002 HS
3 to <6	86	28.66	8	9.30	4	4.6	
6 to <9	72	24	11	15.2	6	8.3	
9 to <12	76	25.33	33	43.4	12	15.7	
12 to 18	38	12.66	20	52.6	14	34.2	
Total	300	100	72	24	36	50	

At the time of present study 277 (92.4%) cases were on one or the other chelating agent whereas 23 (7.6%) cases were not taking any kind of chelation therapy. Out of 300 patients, 72 (24%) cases tested positive for anti HCV antibody. Out of 72 patients only 36 (12%) patients had detectable viral load in RNA PCR. Mean age of the HCV positive cases (9.58±3.28) years was higher as compared to HCV negative cases (6.98±3.54). Maximum HCV positivity 20/38 (52.6%) was seen in 12-18 year age group; followed by 33/76 (43.4%) in 9-12yr age group (Table 1). Significant association was observed between advancing age and prevalence of hepatitis C in thalassemia major patients (p=0.002).

Table 2: Association of no. of blood transfusions with anti HCV positivity among beta thalassemia major patients.

No. of blood transfusions	Total cases (n=300)	Anti HCV positive (N=72)	HCV RNA Positive (N=33)	Chi square test
	Number (%)	Number (%)	Number (%)	
8 to 50	28 (9.33)	3 (10.7)	2 (6.06)	P value LS 21.757 at 4DF p<0.001
51 to 100	58 (19.33)	9 (15.5)	3 (9.09)	
101 to 150	64 (21.33)	12 (18.75)	6 (18.2)	
151 to 200	56 (18.66)	15 (26.78)	6 (18.2)	
>200	94 (31.33)	33 (35.10)	19 (48.48)	
Total	300	72	36	

Table 3: Association of serum ferritin and ALT with anti HCV positivity among the beta thalassemia cases.

	Serum ferritin			ALT		
	N	Mean	SD	N	Mean	SD
Anti HCV positive	72	3167.1	1814.3	72	123.63	31.27
HCV RNA positive	33	2840.96	1535.79	33	151.29	38.37
Anti HCV negative	228	1814.2	1030.4	228	53.43	12.31

The number of blood transfusions received by anti-HCV positive children (Avg Transfusion 185±98.40 ml/kg/year) was significantly higher than that by anti-HCV negative patients (Avg Transfusion 102.8±71.20) (Table 2) (p value <0.001). Maximum HCV positive cases 33 (45.83%) had total transfusions >200 in a year followed by 15 (20.83%) cases with 151-200 transfusions (p<0.001). Average serum Ferritin of HCV positive cases was higher as compared to HCV negative cases (3167.15±1814.3 vs. 1814.2±1030.4 ng/ml (p<0.001).

Mean serum SGPT of HCV positive cases was significantly higher than HCV negative cases (96.36.3±85.14 IU/dl compared to 48.41±31.34 IU/dl (p<0.001).

DISCUSSION

In the present study, 300 thalassemic patients were enrolled. Male to female ratio was 2.73:1. There was male preponderance which can be explained by the fact that parents are more concerned about the health of male children and seek admission for them as compared to female children. 90% cases had hepatosplenomegaly that can be explained due to extramedullary hematopoiesis.

Transmission of hepatitis C through blood transfusion can be explained because of four reasons:

- Marker negative window phase donations
- Immune variant viral strains
- Persistent antibody-negative
- Procedural testing errors

With every unit of blood, there is 1% chance of transfusion associated problems including TTI.⁷ Over the last couple of decades, the risk of TTI has declined dramatically in high income developed nations, but it is not the same for the developing countries. Total 72 patients (24%) tested positive for anti-HCV.

Studies of Anti-HCV antibody in thalassemia major children in India by various authors shows a prevalence ranging from 7.8% to 60%.⁸⁻⁹ In present study high prevalence of hepatitis C may be because of lack of natural machine in our set up. In present study the mean age of the HCV positive cases was higher than HCV negative case (p=0.002). With age the number of blood transfusions received increases and so does the risk of acquiring Transfusion Transmitted Infection (TTI). Marwah et al supported this observation through his study.⁹

The number of blood transfusions received by HCV positive group in the study population was significantly higher than that by HCV negative group (p<0.001). The risk of acquiring HCV increases with increased number of transfusions as supported by Bhavsar et al.¹⁰

Ferritin of HCV positive cases was significantly higher as compared to that of HCV negative cases (p<0.001). Similar results were seen in the studies conducted by Grewal et al who reported higher serum ferritin in Anti-HCV positive patients due to higher number of blood transfusions.¹¹

Serum SGOT, SGPT, were significantly higher in HCV positive cases in comparison to HCV negative group and so these parameters can be used as a surrogate marker of HCV.¹²

CONCLUSION

Despite ELISA screening of blood donors, present study demonstrated high (24%) prevalence of transfusion transmitted hepatitis-C virus in thalassemic children which increases with increasing number of transfusions, it also correlates with rising serum ferritin level and SGPT level. Limitations in the screening tests include false negative results and the problems associated with the window period, needs to be addressed. Though not 100% effective, NAT narrows the infectious window period.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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