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Original Article

Burden of Hepatitis C Virus Infection in Multitransfused Beta-Thalassemia Major Patients

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ABSTRACT

Background: β-Thalassemia major is a common inherited disorder characterized by reduced or absent β-globin chain production, often requiring lifelong blood transfusions for survival. Iron overload is a known complication of repeated transfusions but little is discussed about increase in transfusion-transmitted infections, particularly hepatitis C virus (HCV). Despite improved donor screening, HCV remains prevalent among multi-transfused thalassemia patients, with reported rates of 7.8–60% in India.

Aim: To find out the association of hepatitis C infection with various factors like number of transfusions, inter-transfusion interval, splenectomy, lowest/Average haemoglobin level, alanine transaminase (ALT), aspartate transaminase (AST) and serum ferritin.

Methodology: This hospital-based cross-sectional observational study was conducted in the Department of Paediatrics, Sir Padampat Mother and Child Health Institute, S.M.S. Medical College, Jaipur (Tertiary care Public hospital) from April 2012 to March 2013. A total of 153 β-thalassemia major patients aged 18 months–18 years who had received more than 8 blood transfusions were included. Clinical details, transfusion history, and investigations including Complete blood count (CBC), Liver enzymes (AST/ALT), serum ferritin, HBsAg, anti-HIV, and anti-HCV antibodies were recorded. Anti-HCV antibodies were detected using the HCV BI-DOT test.

Result: Out of 153 β-thalassemia major patients, 36 (23.53%) were anti-HCV positive. A higher mean number of blood transfusions (185 ± 98.4) was associated with seropositivity compared to seronegative patients (102.8 ± 71.2). HCV prevalence increased significantly with increasing transfusions frequency ($p<0.001$) and shorter inter-transfusion intervals. $p=0.000$). Mean AST, ALT, and serum ferritin levels were significantly higher in seropositive patients ($p<0.001$). No significant association was observed with haemoglobin levels or splenectomy status.

Conclusion: Multi transfusion in β-thalassemia major patients is significantly associated with HCV seropositivity along with shorter transfusion intervals. More sensitive screening like NAT and improved blood safety is warranted to help reduce infection burden.

Keywords*: Hepatitis C, thalassemia major, transfusion transmitted infection, splenectomy, alanine transaminase, aspartate transaminase, ferritin.*

INTRODUCTION

Beta-thalassemia major is a severe inherited haemoglobin disorder requiring lifelong regular packed red blood cell transfusions. While transfusion therapy has significantly improved survival, repeated exposure to donor blood places these

children at high risk for transfusion-transmitted infections (TTIs), particularly hepatitis C virus (HCV) infection, which remains a major global health concern [1,2].

HCV in multi-transfused thalassemia patients has high propensity to progress to chronic hepatitis, hepatic fibrosis, cirrhosis, and hepatocellular carcinoma. The risk persists despite routine donor screening because blood donated during the serological window period may escape detection by conventional ELISA-based methods. This issue is more pronounced in developing countries where universal nucleic acid testing (NAT) is not uniformly implemented across blood banks.

The burden of HCV in transfusion-dependent thalassemia patients varies widely across regions. In Western India, Mishra et al. reported anti-HCV seroprevalence of 51.1% among 196 multi-transfused beta-thalassemia patients, with HCV RNA positivity in 33.7%, highlighting ongoing occult transmission risk despite serological screening[3]. In Egypt, one of the highest prevalence settings, Mansour et al. demonstrated markedly elevated HCV positivity among multitransfused thalassemic patients, reflecting persistent transfusion-associated viral exposure [4]. Similarly, data from Oman showed that HCV prevalence among homozygous beta-thalassemia patients remained substantial, although a decline was observed after the introduction of improved screening assays and PCR-based testing[5].

Indian studies continue to demonstrate a significant HCV burden in thalassemia cohorts. The recent six-year molecular epidemiological study from Eastern India by Dutta et al. reported HCV RNA positivity in 598 of 917 (65.21%) seroreactive multitransfused β-thalassemia patients, with genotype 3a predominance[2]. The authors also observed increased vulnerability among male patients from rural and economically disadvantaged populations, emphasizing the interplay of healthcare access and transfusion safety. Most importantly, the study strongly advocated the urgent implementation of NAT-based donor screening to reduce residual transmission risk.

Given the lifelong transfusion dependence of beta-thalassemia major patients and the serious long-term hepatic consequences of HCV infection, determining the seroprevalence of hepatitis C in this vulnerable group is essential. Such data help assess the effectiveness of current blood safety measures, identify gaps in transfusion practices, and guide policies for early diagnosis, antiviral therapy, and improved donor screening protocols. Due to limited regional data on transfusion-associated HCV infection in β-thalassemia major patients, the present study was conducted to determine its prevalence in our clinical setting.

MATERIAL AND METHODS

This hospital based cross sectional observational study was conducted in the regional referral center and medical college in Rajasthan, India. Department of Paediatrics, Sir Padampat Mother and Child Health Institute, S.M.S Medical College Jaipur between April 2012 to March 2013. This study included 153 Thalassemia major patients of age group 18 months to 18 years who received more than 8 blood transfusions. Those suffering from thalassemia intermedia, alpha thalassemia and other hemoglobinopathies were excluded. Patients who have received less than 8 blood transfusions and with successful bone marrow transplant were also excluded. Cases were studied with relevant history, detailed clinical examination and investigations including CBC, AST, ALT, Serum ferritin, Anti-HCV antibody, HBs antigen, Anti-HIV 1, 2 antibodies.

Thalassemia major patient confirmed by hemoglobin electrophoresis were included in the study after applying predefined inclusion and exclusion criteria. Written informed consent was obtained from parents or guardians. Investigations including complete blood count, SGOT, SGPT, serum ferritin, HBsAg, anti-HIV 1 & 2, and anti-HCV were performed. Blood samples were evaluated for detection of hepatitis C virus antibodies using the HCV BI-DOT test. Children below 18 months were excluded due to the possibility of passive transfer of maternal hepatitis C antibodies, which may persist up to 12–18 months of age.

Statistical analysis was done using computer software (Microsoft excel SPSS 20 and primer). Quantitative values were expressed as mean and standard deviations and qualitative data were expressed in proportions and percentage. For qualitative analysis chi-square test and for quantitative analysis student's T test was performed for comparing means of groups for investigation. Significance level for tests was determined as 95% ($P< 0.05$).

RESULT AND OBSERVATION

The mean age of the study population was 7.59 ± 3.6 years, and the age at diagnosis ranged from 2.5 to 48 months with a mean of 14.62 ± 8.02 months. Males constituted 73.2% of the study population with a male-to-female ratio of 2.73:1. Similar male predominance has been reported in other Indian studies, possibly reflecting healthcare-seeking behavior and sociocultural factors influencing access to treatment.

The most common clinical manifestations observed were **anaemia (100%)**, **hepatomegaly (90.2%)**, and **splenomegaly (81.05%)**, which are typical clinical findings in thalassemia major due to chronic haemolysis, extra medullary haematopoiesis, and iron overload. The **mean pre-transfusion haemoglobin level was 7.3 ± 1.35 g/dl**, which is

comparable with previous studies in multitransfused thalassemia patients. The mean levels of **AST (62.69 ± 60 IU/L)** and **ALT (59.7 ± 59.7 IU/L)** were elevated, reflecting possible hepatic involvement related to iron overload or viral infections.

Demographic characteristics of the study population (n = 153)

Variable	Category	HCV Positive	HCV Negative	n (%)
Age group (years)	1.5 to <3	0(0)	14(100)	14 (9.2)
	3 to <6	5(10.2)	44(89.8)	49 (32.0)
	6 to <9	9(30)	21(70)	30 (19.6)
	9 to <12	11(23)	37(77)	48 (31.4)
	12 to 18	11(91.6)	1(8.3)	12 (7.8)
	Total	**36**	**117**	**153 (100.0)**
Sex	Male	30(83.3)	82(70)	112 (73.2)
	Female	6(16.6)	35(30)	41 (26.8)
	Total	**36**	**117**	**153 (100.0)**

A total of 153 thalassemia patients were studied. Most were aged 3–<6 years (32.0%), followed by 9–<12 years (31.4%), with 83.0% between 3 and 12 years; mean age was 7.59 ± 3.6 years. Seropositivity was rarely seen in < 3 years and 91% after 12 years.

Table 2. Prevalence of transfusion transmitted infections in beta thalassemia major patients

Transfusion transmitted infections	Anti-HCV	HbsAg	Anti-HIV
Negative	117 (76.47%)	147 (96.08%)	152 (99.35%)
Positive	36 (23.53%)	6 (3.92%)	1 (0.65%)
Total cases	153 (100%)	153 (100%)	153 (100%)

Among transfusion transmitted infections HCV has the highest prevalence with 23.53% being positive for anti-HCV, 3.92% were HbsAg positive and only 0.65%) were positive for anti-HIV.

Table 3. Association of number of blood transfusions with anti-hcv positivity among beta thalassemia major patients

NUMBER OF BLOOD TRANSFUSIONS	Total Cases (n=153)	Anti HCV Negative (n=115)		Anti HCV Positive (n=36)		Chi SquareTest
	Number	Number	Percentage %	Number	Percentage %	P value LS
8 to 50	36	33	91.66	3	8.3	21.757 at 4DF P<.001 HS
51 to 100	29	26	89.65	3	10.34	
101 to 150	32	26	81.25	6	18.75	
151 to 200	22	13	59.09	9	40.9	
>200	32	17	53.125	15	46.8	
Total	153	115		36	23.53	

Seropositivity increased with the number of transfusions, showing a significant association with hepatitis C prevalence ($p<0.001$). It increased from 8.3% in < 50 transfusion to 46.8% in > 200 transfusion. Seropositive patients had a higher mean number of transfusions (185 ± 98.4) than seronegative patients (102.8 ± 71.2).

Table 4. Association of inter-transfusion interval with anti-hcv positivity among beta thalassemia major patients

Intertransfusion interval (days)	Total Cases(n=153)	Anti HCV Positive (n=36)		Chi SquareTest
	Number	Number	Prevalence %	P value LS
0 to7	1	1	100.00	49.725 at 3 DF; P = 0.000 Hs
8 to14	21	17	80.95	
15 to21	122	18	14.75	
22 to 28	9	0	0	
Total	**153**	**36**	**23.53**	

In, intertransfusion groups of 0 to 7 days, 8 to 14 days, 15 to 21 days and 22 to 28 days seroprevalence was 100% (1/1), 80.95% (17/21), 14.75% (18/122) and 0% (0/9) respectively.

Table 5. Association of splenectomy with anti-hcv positivity among the beta thalassemia cases

Splenectomy	Total cases	Anti-HCV Positive	Percentage %	Chi Square Test
Not done	141	29	20.57	3.15 at 1DF; P = 0.07 NS
Done	12	7	58.33	
Total	**153**	**36**	23.53	

A non-statiscally significant association was seen with anti-HCV positivity and splenectomy. 58.33% (7/12) of splenectomised patients were anti-HCV positive compared to 20.57% (29/141) of non- splenectomised. (p=0.07)

Table 6. Association of hemoglobin with anti-hcv positivity among the beta thalassemia cases

Parameter	Anti-HCV Status	N	Mean	SD	P value (LS)
AST (IU/L)	Positive	36	92.78	87.81	<0.001 HS
	Negative	117	53.43	44.89	
ALT (IU/L)	Positive	36	96.36	85.14	<0.001 HS
	Negative	117	48.41	31.34	
Haemoglobin (g/dl)	Positive	36	7.24	1.33	0.36
	Negative	117	7.46	1.18	
Serum Ferritin (ng/ml)	Positive	36	3167.1	1814.3	<0.001 HS
	Negative	117	1814.2	1030.4	

Mean difference in AST, ALT and Ferritin levels were significantly higher in anti-HCV Positive cases. but no significant association was observed for Haemoglobin.

DISCUSSION:

Our cross-sectional study evaluated the prevalence of HCV infection and its associated factors among 153 multi-transfused β-thalassemia major patients. The anti-HCV seroprevalence of 23.53% observed in our study is comparable to recent Indian studies conducted in tertiary care settings, which have reported prevalence rates ranging from approximately 18% to 30% among multitransfused thalassemia patients [6,7]. However, lower or variable prevalence has also been reported across different regions of India depending on screening practices and transfusion safety measures [8–10].

International studies have also shown wide variability in prevalence among multitransfused thalassemia patients, ranging from 8% to 69% [11]. Reported rates include 42% in Pakistan, 35% in the United States, and up to 69% in Egypt [11–14]. These differences may be attributed to variations in blood donor screening practices, availability of nucleic acid testing, and transfusion safety protocols. Potential sources of infection include window-period donations, immune-variant viral strains, antibody-negative carriers, and procedural testing errors [15].

A significant association between increasing age and anti-HCV positivity and number of blood transfusions was also observed. The mean age (9.58 ± 3.28 years) and mean number of transfusions (185 ± 98.4) were higher than those of seronegative patients (6.98 ± 3.54 years and 102.8 ± 71.2, respectively). This finding is consistent with recent evidence suggesting that cumulative exposure to blood transfusions significantly increases the risk of acquiring transfusion-transmitted infections, including HCV [16].

The intertransfusion interval also showed a significant association with HCV infection ($p = 0.000$), with shorter intervals linked to higher seropositivity, likely due to increased annual exposure to donor blood. However, variability in this association has been reported in the literature, with some studies not demonstrating a significant correlation [17].

Although a higher proportion of splenectomized patients were anti-HCV positive (58.33%) compared to non-splenectomized patients (20.57%), this difference was not statistically significant ($p = 0.07$). Similar observations have been reported in earlier and recent studies evaluating complications and comorbidities in thalassemia patients [18].

Elevated biochemical parameters were observed, with significantly higher AST and ALT levels in anti-HCV positive patients ($p < 0.001$), indicating hepatic involvement, consistent with previous reports on the natural history and progression of hepatitis C infection [19]. Hemoglobin levels, however, showed no significant association with HCV positivity ($p = 0.36$). In contrast, serum ferritin levels were significantly higher in seropositive patients (3167.1 ± 1814.3 ng/ml) compared to seronegative patients (1814.2 ± 1030.4 ng/ml) ($p < 0.001$). Elevated ferritin likely reflects iron overload and higher transfusion requirements, both of which may indirectly increase the risk of transfusion-transmitted infections [20].

CONCLUSION:

This study highlights a substantial prevalence of hepatitis C virus infection (23.53%) among multi-transfused β-thalassemia major patients, despite routine donor screening using ELISA. The persistence of HCV infection suggests limitations in

conventional serological screening, particularly during the diagnostic window period and due to occasional false-negative results. Implementation of more sensitive screening strategies such as **nucleic acid amplification testing (NAT) or combined antigen–antibody assays may significantly reduce transfusion-transmitted HCV infections.**

A significant association was observed between **shorter intertransfusion intervals and HCV seropositivity**, indicating that increased exposure to donor blood increases the risk of infection. Strategies aimed at reducing donor exposure, such as administering larger packed red cell aliquots when clinically feasible, along with strengthening blood safety protocols, may help decrease the burden of HCV infection among thalassemia patients.

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