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Quick Response Code:

Website: www.ajts.org
DOI: 10.4103/ajts.AJTS_74_18

# Transfusion-transmitted infections, its risk factors and impact on quality of life: An epidemiological study among $\beta$ -thalassemia major children

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Submitted: 16-06-2018  
Accepted: 05-06-2019  
Published: 26-05-2022

## Abstract:

**BACKGROUND:** Multi-transfused thalassaemic children are at higher risk of acquiring transfusion-transmitted infections (TTIs). There are limited data available on TTIs among thalassaemic children, especially on its impact on their quality of life (QoL).

**AIM:** The aim of this study is to find out the proportion of multi-transfused  $\beta$ -thalassemia major ( $\beta$ -TM) children suffering from TTIs, its risk factors and impact on QoL.

**METHODS:** This was a hospital-based, analytical observational study, cross-sectional in design, conducted among 328  $\beta$ -TM children and their caregivers attending thalassaemia day care unit of a medical college during May 2015–April 2016, with a structured schedule. Data were analyzed with appropriate statistical methods using the Statistical Package for the Social Sciences.

**RESULTS:** Two-fifth (39.9%) of them were found to have TTIs with hepatitis C being the most common (34.5%), followed by hepatitis B (4.5%) and human immunodeficiency virus (1.8%). In the multivariable model, place of residence (adjusted odds ratio [AOR] – 2.23 [1.19–4.17]), per capita monthly family income (AOR – 1.84 [1.10–3.07]), and blood transfusion frequency (AOR – 1.19 [1.10–1.29]) were significant predictors of TTIs adjusted with their age, age at diagnosis, last pretransfusional hemoglobin level, size of spleen, and caregivers knowledge regarding the disease. The study participants with TTIs had a lower QoL compared to others as there were significant differences in between the total QoL scores ( $[49.9 \pm 15.6$  vs.  $57.4 \pm 15.5]$ ,  $P \leq 0.001$ ) and its various domains.

**CONCLUSION:** There was high burden of TTIs among multi-transfused  $\beta$ -TM children and it has significant negative impact on their quality of lives.

## Keywords:

Blood transfusion frequency, quality of life, transfusion-transmitted infections

## Introduction

$\beta$ -thalassemias are one of the common autosomal recessive single-gene inherited hemoglobin disorder in the world, affecting nearly 200 million.<sup>[1,2]</sup> Indian subcontinent being known hotspot for thalassemias, has an uneven distribution of the disease among different endogenous populations.<sup>[2,3]</sup> In

India, nearly 12,000 infants born every year with the major form of the disease (10% of global burden) with half of these patients die before reaching adulthood. A large proportion of these early deaths are contributed due to the complications of the disease.<sup>[4,5]</sup>

Right from the onset of the diagnosis, a thalassaemic child has to receive frequent blood transfusions, iron chelation,

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**How to cite this article:** Biswas B, Naskar NN, Basu K, Dasgupta A, Basu R, Paul B. Transfusion-transmitted infections, its risk factors and impact on quality of life: An epidemiological study among  $\beta$ -thalassemia major children. Asian J Transfus Sci 2022;16:99-105.

splenectomy, etc., in order to maintain vitality.<sup>[1,6]</sup> These frequent blood transfusions, iron chelation, and surgical interventions (i.e., splenectomy) increase the risk of various transfusion-transmitted infections (TTIs) among them with hepatitis C, hepatitis B, and human immunodeficiency virus (HIV) being the most common of all the TTIs.<sup>[7,8]</sup> There may be other contributory factors such as place of residence, per capita income of the family, and foremost the caregivers knowledge regarding the disease which may facilitate high-risk behavior (i.e., transfusion from private blood banks having poor laboratory practices) for the acquisition of TTIs.<sup>[9,10]</sup> These TTIs not only complicates therapeutic management of these patients but also has a significant impact on their quality of lives too.<sup>[9-12]</sup>

There are limited data available on TTIs among multi-transfused thalassemic children, especially in the eastern part of India. Those existed only focused on the proportion of TTIs giving less importance to its risk factors and impact on the quality of life (QoL). Thus, this study was an attempt to find out the proportion of multi-transfused  $\beta$ -TM children suffering from TTIs, its risk factors, and impact on their QoL.

## Methods

This study was a hospital-based, analytical observational study, cross-sectional in design conducted in thalassemia day care unit of a medical college of West Bengal, situated in the eastern part of India, from May 2015 to April 2016. In the present study, 328  $\beta$ -TM children and their accompanying caregivers participated. The data were collected with a structured schedule by face-to-face interview method of the caregiver of the thalassemic children. The schedule consisted of sociodemographic (age, sex, and place of residence), socioeconomic (per capita monthly family income), clinico-therapeutic (TTIs, age at diagnosis, transfusion frequency, last pretransfusal hemoglobin level, spleen status, and iron chelation status), caregivers knowledge regarding the disease and Peds4QL for assessing QoL of thalassemic children. Patients medical records were also reviewed for some of the clinico-therapeutic data (i.e., TTIs, last pretransfusal hemoglobin level, whether splenectomized and iron chelation status). At first, the schedule was drawn up in English, followed by a translation in the local language (Bengali). The schedule was pretested among 30 study participants. Later on, these 30 study participants were not included in the study. After making necessary modifications based on results of the pretesting, the final schedule was prepared and used for the study. In the final schedule, knowledge questionnaire comprised knowledge of the cause of the disease, premarital counseling, antenatal screening, and treatment modalities of the disease. Scores of individual

items of the knowledge questionnaire are depicted in Table 1.

$\beta$ -TM children who had at least received one blood transfusion in the previous year and attended thalassemia day care unit along with a caregiver during the study and consented to participate were included in the study. On the other hand, those who were critically ill were excluded from the study. One day in a week was allotted for data collection. On an average thalassemia unit, the outpatient department serves 15–20 patients on a single day. An interview took on an average of 15–20 min. Thus, on an average, eight parents could be interviewed on a single day. There were a total of 917 patients (thalassemic children) registered with the thalassemia unit at the beginning of the study. During the study, 349 patients accompanied by at least a caregiver could be approached in 41 (excluding public holidays) data collection days of which 328 consented and participated in the study which was 35.7% of registered patients with a response rate of 93.9%. Only one caregiver per patient was conveniently chosen for the study. Before each interview study participants were asked if they were interviewed before, to prevent duplication.

**Table 1: Distribution of caregivers of study participants according to their knowledge regarding the disease (n=328)**

Variable	Frequency (%)	Score
Do you know how this disease is caused		
Yes	189 (57.6)	-
No	139 (42.4)	
Cause of thalassemia as specified by the caregiver		
Correct knowledge (genetic)	156 (47.6)	1
Incorrect knowledge (destiny/contact with other thalassemic)	33 (10.0)	0
Don't know	139 (42.4)	0
Have you ever heard about premarital counselling		
Yes	172 (52.4)	1
No	156 (47.6)	0
Have you ever heard about antenatal screening		
Yes	167 (50.9)	1
No	161 (49.1)	0
Do you know about treatment of thalassemia		
Yes	303 (92.4)	-
No	25 (7.6)	
Treatment modalities as specified by the caregiver*		
Only blood transfusion	54 (16.5)	1
Only iron chelation	0 (0.0)	1
Both blood transfusion and iron chelation	249 (75.9)	2
Splenectomy	63 (19.2)	1
Bone marrow transplantation	9 (2.7)	1
Do not know	25 (7.6)	0

\*Multiple responses

Operational definitions used in the study are listed next.

### Transfusion-transmitted infections

Those who were reported to be hepatitis B surface antigen (HBsAg) using HEPALISA by J. Mitra and Co. Pvt. Ltd. (sensitivity: 100.0% and specificity: 100.0% by the WHO), anti-hepatitis C virus (HCV) using HCV Microlisa 3<sup>rd</sup> generation by J. Mitra and Co. Pvt. Ltd. (sensitivity: 100.0% and specificity: 97.4% by the WHO) and anti-HIV-1/HIV-2 using Microlisa HIV by J. Mitra and Co. Pvt. Ltd. (sensitivity: 100.0% and specificity: 100.0% by the WHO) positive in serological tests as per their medical records were considered as hepatitis B, hepatitis C, and HIV positive, respectively.

### Caregiver

In the present study, any adult first-degree relative who accompanied the thalassemic child during a visit to the thalassemia unit of the hospital and currently living with and taking care of the patient was considered as a caregiver.

### Caregivers' knowledge regarding the disease

It was calculated by the addition of scores they received for each knowledge item where higher score indicated a higher level of knowledge. The minimum and maximum attainable score were 0 and 7, respectively. Meanwhile, the minimum and maximum attained score was the same as attainable scores.

### Splenomegaly

It was estimated by palpation of the abdomen of the patient in lying down position and expressed in centimeters.

### Quality of life score

Items of the Peds4QL scale were reverse scored and linearly transformed to a 0–100 scale as follows: 0 = 100, 1 = 75, 2 = 50, 3 = 25, and 4 = 0. Scores were obtained by summing of the items over the number of items answered. In this way, scores of each domain (physical, emotional, social, and school) and the total score was obtained where higher the score more favorable QoL was.<sup>[13]</sup>

### Ethical issues

Ethical clearance of respective Institutional Ethics Committees was taken before conducting the study. Informed written consent of accompanying caregiver and assent of the child were taken before their participation. During data collection, their confidentiality was assured.

### Statistical analysis

Data were analyzed using IBM SPSS (Chicago, USA) (version 16). For determining sociodemographic, socioeconomic, clinico-therapeutic, and caregivers

knowledge regarding the disease-related risk factors and TTIs, first univariate analysis was performed using logistic regression to ascertain the one is to one relationship between various attributes and TTIs. Only those variables which were found to be significant in univariate analysis were entered into multivariable logistic regression model by forced entry method. The strength of associations was assessed by odds ratio at 95% of confidence interval. For assessing the impact of TTIs on the study participants total QoL and its various domains independent samples "t" test was used. Statistical significance for all analyses was set at  $P < 0.05$ .

## Results

Of 328 study participants, 39.9% were suffering from TTIs, of which 34.5% were anti-HCV positive, while 4.3% and 1.8% were HBsAg and anti-HIV positive, respectively [Figure 1].

Table 1 shows knowledge of caregivers regarding different aspects of thalassemia. The attained knowledge score had the mean  $\pm$  standard deviation (SD) of  $3.4 \pm 1.5$  and median (interquartile range) of 4 (2–5).

Most of the study participants were aged between 11 and 12 years (37.2%) with range (5–12 years). There was almost equal representation of both the sexes. Most of the study participants were diagnosed as thalassemic within the 7<sup>th</sup> year of their lives (56.5%) with a mean age at the diagnosis of 20.25 months. Three-fifth (61.3%) of them had a palpable spleen while the palpable size of spleen ranged from 1 cm to 8 cm. Majority of the study participants were receiving blood transfusion once or less than once a month (63.7%), while for most of the patients, pretransfusional hemoglobin level was between 5.3 and 5.9 g/dl (35.4%). Most of them were taking iron chelators for the past 13–24 months (20.6%) with a mean  $\pm$  SD,  $35.6 \pm 20.2$  months [Table 2].

In univariate logistic regression analysis, their age, place of residence, per capita monthly family income,

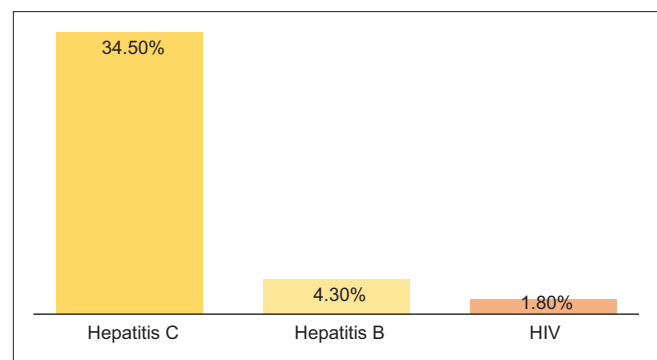


Figure 1: Bar chart showing the prevalence of various transfusion-transmitted infections among study participants ( $n = 328$ )

age at diagnosis, blood transfusion frequency, last pretransfusional hemoglobin level, size of spleen, and caregivers knowledge regarding the disease were significant predictors of TTIs. In the multivariable logistic regression model, place of residence (adjusted odds ratio [AOR] – 2.23 [1.19–4.17]), per capita monthly family income (AOR – 1.84 [1.10–3.07]), and blood transfusion frequency (AOR – 1.19 [1.10–1.29]) were

significant predictors of TTIs adjusted with their age, age at diagnosis, last pretransfusional hemoglobin level, size of spleen, and caregivers knowledge regarding the disease. Independent variables in the model were explaining 28.8% variability of TTIs of the study participants with predictive accuracy rate of 73.5%. In the multivariable logistic regression model, insignificant Hosmer Lemeshow test ( $P = 0.401$ ) indicated model fit [Table 3].

**Table 2: Background characteristics of the study participants (n=328)**

Variable	n (%) / mean ± SD
Age in completed years	8.0 ± 2.3
Sex	
Male	177 (54.0)
Female	151 (46.0)
Place of residence	
Urban	91 (27.7)
Rural	237 (72.3)
Per capita monthly family income in rupees	1643.4 ± 883.0
Number of blood transfusion received last year	11.6 ± 4.9
Last pretransfusional Hb level (g/dl)	5.51 ± 0.82
Undergone splenectomy	
Yes	83 (25.3)
No	245 (74.7)
Size of the spleen (cm)	3.94 ± 2.64
Iron chelators were taken	
Yes	306 (93.3)
No	22 (6.7)

Hb=Hemoglobin

Study participants with TTIs had a lower QoL compared to others as there were significant differences in between the total QoL scores ( $49.9 \pm 15.6$  vs.  $57.4 \pm 15.5$ ),  $P \leq 0.001$ ) and its various domains [Table 4].

## Discussion

The study was a facility-based cross-sectional study to find out the proportion of multi-transfused  $\beta$ -TM children suffering from TTIs, its risk factors, and impact on their QoL. Table 5 shows the burden of TTIs as reported by various studies and the current study. In our study, 34.5% of study participants were anti-HCV positive which was concurrent to findings of Mittal *et al.*<sup>[14]</sup> (35.5%) and Mahmoud *et al.*<sup>[15]</sup> (37.1%). There were studies which reported more<sup>[9,21]</sup> and vice versa<sup>[10,16-20,22-25]</sup> compared to our study. Of 328 study participants, 4.3% were HBsAg positive similar to Modi *et al.*<sup>[17]</sup> (4.5%), Biswas *et al.*<sup>[16]</sup> (5.0%), and Atwa and Abdel Wahed<sup>[10]</sup> (5.0%).

**Table 3: Univariate and multivariable logistic regression analysis showing determinants of transfusion-transmitted infections of the study participants (n=328)**

Variables	Transfusion-transmitted infections Yes (n=131; 39.9%), n (%)	OR (95% CI)	P	AOR (95% CI)	P
Age in completed years: Increasing	-	1.11 (1.01-1.23)	0.035	0.98 (0.87-1.10)	0.708
Sex					
Male	77 (43.5)	1.38 (0.88-2.16)	0.154	-	-
Female	54 (35.8)	Reference			
Place of residence					
Rural	109 (46.0)	2.67 (1.55-4.60)	0.000	2.23 (1.19-4.17)	0.012
Urban	22 (24.2)	Reference		Reference	
PCMI (INR) (median 1408)					
>1408	75 (45.7)	1.62 (1.04-2.53)	0.033	1.84 (1.10-3.07)	0.020
≤ 1408	56 (34.1)	Reference		Reference	
Age at diagnosis in completed months	-	0.97 (0.96-0.98)	0.000	0.99 (0.97-1.00)	0.147
Blood transfusion frequency in the previous year	-	1.22 (1.15-1.29)	0.000	1.19 (1.10-1.29)	0.000
Last pretransfusional Hb level (g/dl)	-	0.65 (0.49-0.86)	0.000	1.04 (0.72-1.51)	0.824
Undergone splenectomy					
Yes	33 (39.8)	0.99 (0.59-1.64)	0.969	-	-
No	98 (40.0)	Reference			
Size of the spleen (cm): Increasing	-	1.20 (1.10-1.29)	0.000	0.99 (0.88-1.10)	0.816
Iron chelators were taken					
Yes	127 (41.5)	3.19 (1.05-9.65)	0.097	1.52 (0.45-5.13)	0.502
No	4 (18.2)	Reference		Reference	
Caregivers knowledge regarding the disease					
Increasing	-	0.76 (0.65-0.88)	0.000	0.84 (0.71-1.00)	0.055

PCMI=Per capita monthly income, INR=Indian rupees, OR=Odds ratio, CI=Confidence interval, AOR=Adjusted odds ratio, Hb=Hemoglobin



**Table 4: Impact of transfusion-transmitted infections on quality of life of the study participants (n=328)**

Variable	Physical domain	Emotional domain	Social domain	School domain	Total QoL score
TTI					
Yes	45.7±20.8	54.8±14.8	57.6±24.2	44.0±31.1	49.9±15.6
No	53.0±19.5	61.0±14.5	66.3±23.7	52.1±30.7	57.4±15.5
P <sup>#</sup>	0.001	<0.001	0.001	0.021	<0.001

<sup>#</sup>Independent samples t-test. TTI=Transfusion-transmitted infection, QoL=Quality of life

**Table 5: Burden of transfusion-transmitted infections reported by various studies and current study**

Studies	Country	Year	Hepatitis C (%)	Hepatitis B (%)	HIV (%)
Present study	India	2017	34.5	4.3	1.8
Mittal <i>et al.</i> <sup>[14]</sup>	India	2017	35.5	2.4	-
Atwa and Abdel Wahed <sup>[10]</sup>	Egypt	2017	20.7	5.0	0.0
Mahmoud <i>et al.</i> <sup>[15]</sup>	Egypt	2016	37.1	4.1	0.0
Biswas <i>et al.</i> <sup>[16]</sup>	India	2016	25.0	5.0	15.0
Din <i>et al.</i> <sup>[9]</sup>	India	2016	49.0	3.2	-
Modi <i>et al.</i> <sup>[17]</sup>	India	2016	20.4	4.5	3.2
Kiani <i>et al.</i> <sup>[18]</sup>	Pakistan	2016	25.3	3.0	0.5
Patel <i>et al.</i> <sup>[19]</sup>	India	2016	3.9	2.2	2.2
Ayoub <i>et al.</i> <sup>[20]</sup>	UAE	2013	6.5	-	-
Mansour <i>et al.</i> <sup>[21]</sup>	Egypt	2012	40.5	44.0	-
Vidja <i>et al.</i> <sup>[22]</sup>	India	2011	2.0	2.0	3.0
Pemde <i>et al.</i> <sup>[23]</sup>	India	2011	3.2	7.0	6.3
Surapolchai <i>et al.</i> <sup>[24]</sup>	Thailand	2010	1.3	-	-
Bhavsar <i>et al.</i> <sup>[25]</sup>	India	2008	18.0	6.0	9.0

HIV=Human immunodeficiency virus

In the study, 1.8% of the study participants were HIV positive; it had similarities with the findings of Patel *et al.*<sup>[19]</sup> (2.2%). There were studies which reported more<sup>[9,21]</sup> and vice versa<sup>[18,20,22-25]</sup> compared to our study. As per the WHO all blood donations should be screened for evidence of infection prior to the release of the blood and its components for clinical or manufacturing use. Screening of all blood donations should be mandatory for HIV, hepatitis B and C, and syphilis.<sup>[26]</sup> India being a part of the initiative and having a similar policy<sup>[27]</sup> given the high proportion of the TTIs in the study participants is just unacceptable. In the context, the researcher expresses his doubt regarding the quality of screening of collected blood being provided to these children.

In our study with increase in age chances of TTIs also increased which was similar to the findings of Atwa and Abdel Wahed,<sup>[10]</sup> Mahmoud *et al.*,<sup>[15]</sup> Mansour *et al.*,<sup>[21]</sup> and Kiani *et al.*,<sup>[18]</sup> but unlike the findings of Din *et al.*<sup>[9]</sup> and Mittal *et al.*<sup>[14]</sup> which failed to show any such association. Similarly, we also found that with the increase in age at the diagnosis the chances of getting TTI also reduces which was in concordance with the findings of Atwa and Abdel Wahed<sup>[10]</sup> and Mahmoud *et al.*<sup>[15]</sup> which reported that with the increase in the duration of illness chances of TTIs increases. In our study, those who resided in a rural area had higher per capita monthly family income and whose caregivers had less knowledge regarding the disease had higher chances of acquiring TTIs. Money without knowledge may be

fatal at times. Those caregivers who belonged to a rural area, had higher per capita monthly family income, did not know about the disease tends to give their children blood transfusions from private sources in addition to the government sources with the hope of improvement of the health status of their children. In the context, researcher express his doubt on the quality of screening tests these private blood sources use which, in turn, further increases chances of TTI acquisition in children who receives it. These findings were unlike findings of Atwa and Abdel Wahed,<sup>[10]</sup> and Din *et al.*<sup>[9]</sup> which failed to demonstrate any such findings. The variability of findings may be due to their small sample sizes compared to us. This variation could be also due to the low incidence of TTIs in their blood donor population as compared to ours. In the present study, those who were receiving more frequent blood transfusions had lower last pre transfusional hemoglobin level and had more spleen size are at more risk of acquiring TTIs. All these prestated clinico-therapeutic attributes indicate the severity of the disease in thalassemic children. Those who had more severe form of the disease tend to receive more blood transfusions likely to have low pre transfusional hemoglobin level and more spleen size. Frequent blood transfusions increase the risk of TTI transmission. This was in concordance with the findings of Atwa and Abdel Wahed,<sup>[10]</sup> Mansour *et al.*,<sup>[21]</sup> Bhavsar *et al.*<sup>[25]</sup> and Mittal *et al.*<sup>[14]</sup> which found out the frequency of blood transfusion as an important determinant of TTIs. However, there are contrary evidence too, reported by

Mahmoud *et al.*<sup>[15]</sup> and Biswas *et al.*<sup>[16]</sup> The variability of findings may be due to their small sample sizes compared to us.

In the present study, those who had TTIs had a lower QoL compared to others as there were significant differences in between the total QoL scores and its various domains. This was similar to the findings of Dhirar *et al.*<sup>[11]</sup> and Klaassen *et al.*<sup>[12]</sup> which found the presence of comorbidity impairs QoL. This may be because the additional burden of TTIs over thalassemia significantly affects the QoL of children with the disease.

In strengths, it was one of the fewer studies exploring the proportion of thalassemic children suffering from TTIs and its risk factors, impact on QoL with considerably large sample size than prior studies.

The significant limitations of the study were its cross-sectional design, self-reported data, etc. There may be under or over reporting, and chances of social desirability bias cannot be overlooked. Definitive knowledge of caregivers regarding TTIs was not explored rather than their knowledge regarding the disease was taken as a proxy indicator of their knowledge regarding TTIs. Data related to TTI prevalence among blood donors, percentage of replacement donation, and whether nucleic acid amplification test (NAT) testing used for definitive screening of blood to be transfused were not addressed in the study. As this was a cross-sectional study, so the incidence of new infections during the study period could not be estimated. In the present study, effect of TTIs on QoL of the study participants was only explored ignoring the other contributory factors of QoL (i.e., multiple blood transfusion, iron overload, low hemoglobin levels, etc.).

## Conclusion

There was a high burden of TTIs among multi-transfused  $\beta$ -TM children as almost two-fifths of them were suffering from TTIs. Those who had TTIs had significantly lower QoL scores than others; thus, TTIs had a negative impact on their quality of lives. In India, it is mandatory to screen donated blood for the TTIs based on five parameters (hepatitis B, hepatitis C, HIV, syphilis, and malaria) still such high prevalence of TTIs in the present study indicates need of more sensitive tests for blood screening (i.e., NAT) to make donated blood more safe for transfusion. Further, this will help to curb this problem and to offer thalassemic children a better QoL.

## Acknowledgment

The authors want to express their gratitude toward all the study participants for their participation and co-operation during the study.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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