

## **Transfusion Transmitted Infections in Multiple Transfused Thalassemia Patients in Rahim Yar Khan**

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### ABSTRACT

**OBJECTIVES:** To assess the frequency of transfusion transmitted infections in frequently transfused beta thalassemia patients & to determine the association of transfusion transmitted infections with age, gender and number of blood transfusions.

**METHODOLOGY:** This cross-sectional study was performed from June to December 2018 on 350 samples of diagnosed patients of Beta Thalassaemia Major and Beta Thalassaemia Intermedia by Convenient Sampling technique registered at Centre for Thalassaemia Care, Sheikh Zayed Hospital, Rahim Yar Khan receiving repeated blood transfusions. The cases were distributed into three separate age groups, i.e., <10 years, 11-20 years and more than 20 years. Screening of HBsAg, Anti-HCV, Anti-HIV, Malarial Antigen and Anti treponema pallidum was done through Immunochromatographic technique (ICT).

**RESULTS:** There were 225(64.3%) males and 125(35.7%) females. 274(78.3%) were in <10 years, 70(20%) in 11-20 years and 6(1.7%) in 21-30 years' age groups respectively. HCV, HBV, HIV and MP were seen in 34.8%, 5.1%, 1.1% and 6% respectively. No case of syphilis was detected. The patients with >200 transfusions developed 9% more infections than the patients getting transfusions < 200. All the obtained data was inserted and studied in SPSS version 20.

**CONCLUSION:** This study flourished that the most frequent infection among beta thalassemia patients was HCV followed by Malaria, HBV and HIV. The risk of transmission of Transfusion Transmitted Infections is directly proportional to the number of transfusions. All blood banks and transfusion centers have to implement mandatory screening of blood against the TTIs.

**KEYWORDS:** Thalassaemia, Transfusion Transmitted Infections (TTIs), Frequency.

**INTRODUCTION**

The thalassaemic syndrome is a heterogeneous group of disorganized hemoglobin resulting from decreased or absent production of globin (alpha or beta) chains of hemoglobin. Thalassaemia is predominantly due to the excessive rupture of the red blood cells leading to chronic anemia which is mainly due to intramedullary and extramedullary hemolysis<sup>1</sup>. Depending upon the severity Thalassaemia disorder is categorized in Thalassaemia Major needs frequent blood transfusions and Thalassaemia Intermedia needing seldom transfusions. Thalassaemia carriers are the individuals who have Thalassaemia gene but are otherwise healthy.  $\beta$ -Thalassaemia is a major problem in Pakistan, with a carrier rate of 5 to 8% that is due lack of awareness about Thalassaemia which results an estimated 9 million beta-thalassaemia carriers (with carrier rate 5-7%) producing more than 5,000 children with transfusion-dependent thalassaemia (TBD) every year in Pakistan, which is estimated about 1,00,000 Thalassaemia cases in Pakistan, representing 5% of the world's total cases<sup>2</sup>. In northern Pakistan, the prevalence of beta thalassaemia in the Pakhtoon population is 7.96% and that of Punjabis is 3.26%. This is mainly due to the community and traditional system and the greater frequency of weddings among cousins<sup>3</sup>.

To cope with severe anemia which occurs within a few months or during the first two years of life in thalassaemia major patient, regular blood transfusions is needed<sup>4</sup> Transfusion of blood and its components is a ransom and is also mortally dangerous when the practice of "safe blood transfusion" is not observed. Such patients have to face new clinical challenges, mainly transfusion-transmitted infections (TTIs), particularly HCV (hepatitis C), HBV (viral hepatitis B), HIV infection and syphilis. The probability of problems related to transfusion per unit of blood is 1%, including transfusion-transmissible diseases. Although there are many possibilities of transmission for infectious diseases, the blood transfusion is a simple and important way. In Pakistan, a nation of about 1.8 billion people, the blood volume required for transfusion is about 1.5 million pints per year, 60% of what is demanded by the private sector and 40% by the government sector<sup>5</sup>.

The prevalence of TTIs in India is 1.8-4%, 0.4-1.09%, 0.2-1% and 0.05-0.9% for HBV, HCV, HIV and syphilis respectively<sup>6</sup>. Worldwide, 4.4% to 85.4% patients with thalassaemia are positive for antibodies to hepatitis C. The rate of HCV infection in hemodialysis and thalassaemic patients is high as 25%. The frequency of hepatitis C in thalassaemia patients of Iranian population was noted 13.6%<sup>7</sup>. Although improvements in the blood screening system from 1980 to 1990 resulted in reduce risk of transmission of blood borne diseases but hepatitis C remains a significant problem for thalassaemia patients. The patients infected with HCV infection are usually asymptomatic (70% to 90% of cases); however, most people develop a chronic infection with a virus (70-80%). After a time interval between 20 and 30 years, an average of 10 to 20% develops liver cirrhosis or Carcinoma liver<sup>8</sup>. While the incidence of hepatitis B infection is significantly reduced because of vaccination against hepatitis B, however its transmission through blood transfusions or blood products is considered as an epidemiological influence in parts of sub-Saharan Africa.

In the absence of intervention, 15% of patients with chronic HBV infection will develop cirrhosis, advanced liver disease and hepatocellular carcinoma. Overall, 0.3% to 5.7% of patients with thalassaemia are positive for hepatitis B surface antigen (HBsAg).

Another problem in transfusion of unsafe blood is the transmission of Syphilis. In recent years, it has been estimated that 26,000 donations were canceled each year because of positive serological

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tests for syphilis. If the individual is already infected with syphilis, there are high chances that patient may get the human immunodeficiency virus (HIV)<sup>9</sup>. The incidence and prevalence of HIV infection are independently correlated with the diversity of blood exposures. According to data from 2007-2008, it is conservatively estimated that the threat of HIV infection from blood transfusion is one in 1.5 million<sup>10</sup>.

For the 50% of the world's population, malaria remains a risk factor. Malaria can be transferred by transfusion of blood and placenta. Patients with thalassemia are exposed to malaria because they are regularly infused with red blood cells. It is reported that the coexistence of thalassemia and malaria parasite protects hosts infected with only *Plasmodium falciparum*<sup>11</sup>. In endemic countries, the prevalence of parasitemia in blood donors is increased and the incidence of transfusion-related malaria (TRM) is much higher; systematic reviews in sub-Saharan Africa indicate an average parasitemia of 10.2% in blood donors<sup>12</sup>.

Consistent blood transfusions and chelation therapy have improved the survival of patients with thalassemia major in the last 4 decades but there is a risk of infections concomitant with transmission of blood borne viruses. Every year, about 81 million blood bags are donated worldwide and of these, more than 18 million pints of blood are not accurately screened<sup>13</sup>.

In developing countries where blood safety standards are poor blood transfusion transmitted infections are common. Considering this dilemma this study was planned to discover the frequency of Transmitted transfusion infections in thalassemia patients and to see its associations with age, gender and number of blood transfusions.

## **METHODOLOGY**

This cross-sectional study was performed on Three hundred and fifty samples of diagnosed thalassemic patients included by Convenient Sampling technique at Pathology laboratory & Center for Thalassemia Care at Sheikh Zayed Hospital, Rahim Yar Khan., during the period commencing from June 2018 to December 2018.

The diagnosed Beta thalassemia patients registered at thalassemia center, Sheikh Zayed Hospital, RYK receiving repeated blood transfusions bearing all age groups without gender discrimination were included. Thalassemia Patients using Hydroxyurea who need seldom blood transfusions were excluded & rejected from the study.

The data was gathered by using a pretested Questionnaire. The variables included in questionnaire were demographic variables (Name, Age, Sex and Address), diagnosis, HBsAg, HCV, HIV, Syphilis, Malaria, and the history of blood transfusions (age of first transfusion and frequency of transfusion). Under strict aseptic measures 5 ml blood sample was collected in two vacutainers the EDTA vacutainer for malarial parasite and Gel vacutainer for HBsAg, Anti-HCV, Anti-HIV and Anti treponema pallidum tests.

HBV, HCV and HIV were screened using Rapid Immunochromatographic (ICT) technique [ICTs technique was used due to these are rapid, easy to perform and interpret, save time and effort, and compare favorably to other tests]. For the qualitative recognition of antibodies specific to HCV, HCV SD BIOLINE kits were used (immunochromatographic technique). Tri line human immunodeficiency virus Rapid Test Device is qualitative test which was used for detection of antibodies against HIV -1, HIV-2. The rapid TP (treponema pallidum/syphilis) test was used for the detection of treponema pallidum antibody (IgM and IgG) and malaria was screened by ICT technique using SD rapid test device. All investigations were done in the same laboratory.

All the obtained information was coded and data was inserted and studied in SPSS version 20. All the entries were double checked for any possible keyboard error. Frequency and percentage were calculated for HBV, HCV, HIV, Syphilis and Malaria.

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### RESULTS

Three hundred and fifty subjects were studied amongst them majority of the subjects included were males 225(64.3%) and 125 (35.7%) patients were females. From that 149(43%) subjects were infected and 201(57%) were safe from transfusion transmitted infections.

**TABLE I: FREQUENCY OF TRANSFUSION TRANSMITTED INFECTIONS (n=350)**

TTIs	Frequency	Percentage
HCV	122	34.8%
HBV	18	5.1%
HIV	4	1.1%
Malaria	21	6%
Syphilis	0	0

Table shows that majority of patients 122(34.8%) were infected with HCV.

**TABLE II: RELATION OF PATIENTS AGE AND GENDER WITH TRANSFUSION TRANSMITTED INFECTIONS (n=350)**

Age group (years)	TTIs (n = 149)	Without TTIs (n=201)	P value
< 10	113(75.8%)	161(80.1%)	0.18
11-20	35(23.5%)	35(17.4%)	
21-30	1(0.07%)	5(2.5%)	
<b>Gender</b>			0.47
<b>Male</b>	99(64.4%)	126(62.7%)	
<b>Female</b>	50(33.6%)	75(37.3%)	

Table shows that 149(42.6%) were infected with TTIs, with high proportion 99(64.4%) of male cases. Age group less than 10 years had the highest proportion of TTIs 113(75.8%).

[Frequent blood transfusions in these patients increase their risk of acquiring TTIs compared to the other age groups]

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**TABLE III: FREQUENCY OF THALASSEMIA MAJOR AND INTERMEDIA PATIENTS ACCORDING TO TRANSFUSION TRANSMITTED INFECTIONS (n=350)**

TTIs	Frequency		P value
	Thalassemia Major(n=326)	Thalassemia Intermedia (n=24)	
HCV	118 (36.2%)	4 (16.7%)	0.05
HBV	16 (4.9%)	2(8.3%)	0.4
HIV	4 (1.2%)	0	0.5
Malaria	20 (6.1%)	1(4.2%)	0.6
Co-Infection (HBV+HCV) 3.4% of overall infections	5 (1.5%)	0	0.5
Co-Infection (HBV+ Malaria) 2.0% of overall infections	3 (0.9%)	0	0.6
Co-Infection (HCV+ Malaria) 5.4%of overall infections	8 (2.4%)	0	0.4
Syphilis	0	0	0

Table shows that majority of Thalassemia major patients 118(36.2%) were suffering from HCV whereas, only 4(16.7%) cases of Thalassemia intermedia had HCV, this differentiation was statistically significant (P=0.05). The least number of Thalassemia major patients 3(0.9%) had co-infection of HBV/Malaria.

**TABLE IV: FREQUENCY OF STUDY SUBJECTS IN RELATION TO NUMBER OF TRANSFUSIONS AND OVERALL INFECTIONS**

Number of transfusions	Frequency of study subjects	Percentage	Overall infections
<100	127	36.3%	40%
100-200	118	33.7%	40%
200 and above	105	30.0%	49%
<b>Total</b>	<b>350</b>	<b>100%</b>	

Table shows that 127(36.3%) patients had number of transfusions less than 100 and show that high frequency of infections (49%) were seen in patients with number of transfusions > 200.

**DISCUSSION**

Blood transfusion is a lifesaving process however it is an additionally noteworthy mode of transmission of infections in developing countries. Transfusion related infections are one of the serious complications in patients who receive multiple blood transfusions. The goal of this study was to evaluate the frequency of infections as Human Immune Deficiency Virus (HIV), Hepatitis C virus (HCV), Hepatitis B virus (HBV), Malaria and Syphilis appearing in thalassemia patients and its correlation with age, gender and number of blood transfusions. A total of 350 multi-transfused thalassemia patients including 225 (64%) males and 125 (36%) females were recruited during the study period.

This study indicated major prevalence of males 225 (64.3%) than females 125 (36%). Many other researchers have also shown male predominance in their studies in thalassemia children. However, in contrast to these studies and our results, another study conducted in Iran reported more female cases, (56.64%) than males which were (43.36%). In present study, most of the patients (78.3%) were in the age group of less than 10 years. The same results were found in a study conducted in India showed that proportion of children were high in age group 6-11 years<sup>14</sup>. In conjunction to the age and existence of TTIs, it is found that there was no significant difference between age and prevalence of TTIs ( $P > 0.05$ ). Majority of patients (93.1%) included in our study had thalassemia major and only 6.8% were cases of Thalassemia intermedia. A study conducted in Gujarat also showed similar differences in the patients<sup>15</sup>.

The frequency of TTIs like HCV, Malaria, HBV and HIV in present study was 34.9%, 6%, 5.1% and 1.1% respectively. The noteworthy outcome of our study was high frequency of HCV (34.9%) in thalassemia patients. The outcomes of present analysis are very close to other studies, a study conducted in Iran reported 36.25% for anti-HCV antibodies,<sup>16</sup> 35.54% and 30% cases reported in India. Result of present study showed higher frequency of HCV (34.9%) as compared to a study conducted in Mosul which showed frequency of HCV (17%)<sup>17</sup> and 19.3% in Iran<sup>18</sup>. The frequency was lower than those reported in Pakistan (55.7%),<sup>14</sup> and (46%) in Ibn-Al Balady Thalassemia Center, Baghdad<sup>19</sup>.

A local study in Karachi showed that 5% cases were positive for Hepatitis B surface antigen which was same to our study in which 5.1% were positive for HBsAg. There were other studies which supported our results; 6% reported in Gujrat and 5% was reported in Egypt<sup>20</sup>.

However, there were studies in which HBV prevalence was less than present study. These studies were conducted in Pakistan (2.68%)<sup>21</sup> and Kolkata (1.75%)<sup>22</sup>, while there were other studies in which prevalence of HBV was greater than our study. A Study conducted in India indicated high prevalence of HBV (34.4%)<sup>23</sup>.

The Present study shows a very high frequency of HCV (34.9%) as compared to HBV (5.1%) infection in thalassemia Major children<sup>24</sup> and this difference was Statistically Significant ( $P = 0.05$ ). Alike results were found in study conducted in India in which HBV (3.38%) frequency was lower than HCV (24.64%)<sup>25</sup>.

The prevalence of HIV in present study found to be 1.1%. There were some studies which were comparable our results. A Study conducted in India reported 1.04%<sup>24</sup> and Study in Pakistan reported 0.11% cases of HIV<sup>26</sup>. Studies from India have reported that HIV sero-positivity varies from 0 to% 9.3 in multi transfused thalassemia children. In this study the prevalence of malaria was 6%. Study conducted in Pakistan reported 1.20% and 0.8% cases of malaria and syphilis respectively<sup>27</sup>, in present study we reported zero positive cases for syphilis. A study conducted in Peshawar also reported zero positive cases of syphilis<sup>28</sup>. However, study conducted in Lahore

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reported 0.39% malaria which is much lesser than present study. Some other studies conducted in Pakistan stated 0.43% and 2.08% cases which are different than our results<sup>29</sup>.

In this study we also found that five (1.4%) of thalassemia patients had co-infection of HCV and HBV. The co-infection frequency of HCV/MP, HCV/HBV, HBV /MP was 2.3%, 1.4%, and 0.9% respectively. A study conducted in Lahore also found co-infections with frequency of 0.1% and 0.009% for HCV/HBV and HCV/MP respectively<sup>30</sup>. Our study also revealed that frequency of transfusion transmitted infections increases with the increasing number of transfusions. The group of transfusion with 200 and above transfusions had highest number of transfusion transmitted infection (TTI). However, this dissimilarity was not statistically significant ( $P > 0.05$ ). A study carried out in India also supported our results<sup>31</sup>.

Instead of profound screening of blood before transfusion, blood transfusion consequences and TTIs are more predominant in Thalassemic patients than common population. In the improvement of quality assured blood screening techniques to guarantee the screening for TTIs is a necessary element of blood safety. Though, this has been compromised in undeniable conditions where poor quality screening procedures have risen in transmission of TTIs to the patients; predominantly in multi transfused thalassemia patients which are not admitted in the hospital and visit various centers for transfusion depending on availability of blood. It is significant to mention here that blood safety also depends on its supplier, and as advocated by the WHO the safest source is the consistent voluntary non- reimbursed donors from low threat populations, nowadays advanced screening procedures are exploited to ensure harmless blood transfusion<sup>32</sup>.

The strength of the study was that from cases of Thalassemia registered in Thalassemia Center, Rahim Yar khan many of them come for transfusion on regular basis. There are fewer researches on this topic. There were no ethical issues related to this study.

The weakness of the study was that as it was cross sectional study so there was no follow up of patients and convenient sampling was used due to lack of time and financial problems. It is the weakest sampling technique.

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### CONCLUSION

This study showed that the most frequent infection transmitted through blood was HCV (34.8%) [ICT results for blood donor screening are acceptable just like Elisa due to its comparable sensitivity and specificity with Elisa. it can be used in blood banks with limited facilities because it is rapid and cost effective. Reference: Zameer M, Shazad F, Saeed M, Aziz S, Nazish and Hussain S. Comparison Between Elisa and ICT Techniques for The Detection of Anti Hcv Antibody Among Blood Donors. Biomedica. 2016; 32(4): 281-4.] followed by Malaria (6%). However, the frequency of HBV and HIV was quite low. Even subsequent introduction of sensitive screening tests, TTIs are more in patients than overall population.

These high infections are noted due to lack of knowledge to general population of these infections, so it can be reduced by educating the general population by massive awareness programs, routine immunization for infants and high-risk individuals to stop the spread of these alarming diseases and also other preventive measures which should be carried out in order to avoid development of this infection can be by proper pre-transfusion screening of donated blood by ELISA, Polymerase chain reaction or nucleic acid amplification techniques for these viruses in the blood banks and transfusion centers, Practicing safe sex , Avoiding sharing razors , syringes, tooth brushes, nail clippers, or needles, when getting a manicure, a tattoo, or having any body part pierced.

**Ethical Permission:** Shaikh Zayed Medical College/Hospital, Rahim Yar Khan, Letter No: 285/IRB/SZMC/SZH, Dated: 02-08-2018.

**Conflict of interest:** There is no conflict of interest.

**Funding:** There was no Grant or other financial support for this project.

### AUTHOR CONTRIBUTIONS

Ghafoor B: Main idea & research design

Memon FA: Data analysis & review of literature

Saleem M: Critical review

Shabbir R: Data & sample collection

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