

Assessment of the Infectious Status of Transmissible Transfusion Infections (Hepatitis B and C) among β -Thalassemia Major Patients of Karachi; A Multicenter Study by SBTA (Sindh Blood Transfusion Authority)

HIRA AFREEN¹, MEHREEN SHEIKH², DUR E NAZ JAMAL³, HOOMA OUROOJ BUTT⁴, MAEESA WADOOD⁵, AZIZ ALI⁶

¹Monitoring officer, FCPS Gynecologist, Sindh Blood Transfusion Authority

²Monitoring officer, FCPS Radiologist, Sindh Blood Transfusion Authority

³MSC in Health Policy management, Director Sindh Blood Transfusion Authority

⁴Monitoring Officer, Diploma In Family Medicine, Sindh Blood Transfusion Authority

⁵Associate Professor, Baqai institute of Hematology, Baqai Medical University, Executive Medical Director, Muhammadi institute of Hematology, Oncology and Welfare Foundation

⁶Post graduate Trainee in anesthesiology, Ruth K Pfau Civil Hospital Karachi

Corresponding author: Hira Afreen, Email: dr.afreen86@gmail.com

ABSTRACT

Background: Transfusion-transmitted infections such as Hepatitis B and C are a great health concern to blood safety as they are associated with significant morbidity and mortality. Multi-transfused patients like Beta Thalassemia Major patients are particularly vulnerable to the fatal consequences of these blood-borne diseases. Early diagnosis and prompt treatment will improve the quality of life of these patients.

Objective: The study was intended to determine the prevalence of HBV and HCV, using Real-time Quantitative Polymerase Chain Reaction among registered Beta Thalassemia Major patients in various thalassemia centers of Karachi.

Method: six month cross-sectional study was conducted in Karachi following the ethical approval of the Sindh blood transfusion authority (SBTA). A total of 328 multi-transfused Beta Thalassemia Major patients were enrolled in the study from eight different facility centers in Karachi. The. All patients were screened for Hepatitis B surface antigen (HBsAg) and Anti-Hepatitis C antibodies (HCV) using enzyme-linked immunosorbent assay (ELISA). HCV RNA was detected of all reactive anti HCV samples and HBV DNA of HbsAg reactive samples using real time PCR.

Results: Out of 328 study participants, 282 showed serological reactive initially for Anti HCV antibodies and 52 patients were reactive for Hepatitis B Surface Antigen (HBsAg). Among the HCV positive screened females 82 have positive PCR results, while 95 males have positive PCR result. Among the HBV positive screened females 18 have positive PCR results, while 10 males have positive PCR result.

Practical Implication: this study will help to determine the prevalence of HCV, HBV in thalassemia patients.

Conclusion: This study concluded that hepatitis Cis the most common transfusion-transmitted infection (TTIs) among transfusion-dependent β -thalassemia major patients.

Keywords: transfusion-transmitted infection, HCV, HBV, Thalassemia

INTRODUCTION

Blood transfusion is a life-saving measure in treating patients with hemolytic anemias. β -thalassemia is one of the most common single-gene hemoglobin disorders worldwide, with a prevalence of 1.5 % [1]. Annually, 50,000 to 60,000 children are born with β -thalassemia Major [2]. The highest prevalence is documented in the natives of the Mediterranean region, Africa, the Indian subcontinent, and the Middle Eastern population [35]. The reported carrier rate of β -thalassemia gene in the Pakistani population is about 5 – 7% leading to a high burden of the disease in Pakistan. It is stated that about 5000 to 9000 β -thalassemia children are added to the pool of Thalassemia patients every year in Pakistan.

β -thalassemia Major is characterized by defective β globin genes resulting in impaired production of beta-globin chains. This leads to ineffective erythropoiesis and premature hemolysis of the red blood cell. Therefore, patients with β -thalassemia major present in early infancy with severe chronic anemia, failure to thrive, splenomegaly, and skeletal abnormalities. Conventionally, they are treated with regular blood transfusion followed by iron chelation therapy for their survival. But lifelong transfusion leads to an increased risk of Transfusion-Transmitted infections like Hepatitis B, Hepatitis C, Human immunodeficiency virus (HIV) infection, and Syphilis among them [6]. Various studies have reported a higher prevalence of hepatitis B and C among β -thalassemia major patients [7]. As Pakistan is a developing nation with scarcity of resources, post-transfusion hepatitis among thalassemia patients is a great point of concern for healthcare authorities [9]. Therefore, this multicenter research study was conducted by Sindh Blood Transfusion Authority to determine the prevalence of transfusion-transmitted infections among β -thalassemia patients of Karachi using Real-time quantitative PCR.

SBTA functions to control the collection, examination, processing, storage, release, distribution, and transfusion of human blood and blood components in order to preserve public health and prevent the transmission of illnesses via transfusion. Section 3 of the Sindh Safe Blood Transfusion Bill created the Sindh Blood Transfusion Authority. The Sindh Safe Blood Transfusion Bill, 2017, which received the Governor of Sindh's assent on November 30 and was approved by the Provincial Assembly of Sindh on November 6 is now published as an Act of the Sindh Legislature.

METHODOLOGY

A cross-sectional study was conducted in Karachi for a period of 6 months from May to October 2022, 328 registered transfusion-dependent β thalassemia major patients were included in the study as per the selection and rejection criteria from eight different centers of Karachi; highly reputed well trained and maintained, Informed consent was taken from all study participants and their guardians. A detailed history inquired from each patient regarding the frequency of blood transfusion, family history, previous exposure to HBV, HCV & HIV infections, and vaccination history for Hepatitis B. The Sindh blood transfusion authority (SBTA) ERC gave approval to the study's methodology and moral implications. Serological testing of HBV and HCV was performed using enzyme-linked immunosorbent assay (ELISA) following the manufacturer's guidelines. As a confirmatory test Real-time quantitative PCR was performed of positive ELISA patients, to determine the viral load All calibrations and controls were run for accurate results. The data was tabulated on Microsoft Excel Version 10 and data analysis was processed on SPSS version 26. Descriptive analysis was done to calculate the mean, standard deviation, and frequency.

The p-value of <0.05 was considered to be statistically significant in group comparison.

RESULTS

Out of 328 study participants, 177 (54%) were males and 152 (46%) were females. The mean age of the selected patients was 12.83±10 (Table 1). HCV was the most prevalent infection affecting 282 patients (86%) with 151 males and 129 females. Hepatitis B infection was observed in 52 patients; 29 males and 26 females. Co-infection with HCV and HBV was detected in 6 patients (1.8%) (Table 2). Among the HCV positive screened females 82 have positive PCR results, while 95 males have positive PCR result. Among the HBV positive screened females 18 have positive PCR results, while 10 males have positive PCR result. Table 3 and Figure 1 show facility center-wise distribution of

the participants having HCV and HBV infection screening as well as PCR confirmatory viral load mean± S. D. It was evaluated that HCV infection is frequently seen among multi-transfused thalassemic patients in most of the thalassemia care providers except for the center 5 which had all the patients with HBV infection. No significant difference (p=0.69) was observed in HCV and HBV infection in the facility center-wise distribution. Table 4 and Figure 2 show the age group-wise distribution of the participants having HCV and HBV infections. Maximum participants in the present study fall in the age group of 2-12 years, followed by the age group of 13-23 years. All the age groups have a maximum number of individuals infected with HCV. No significant difference (p=0.184) was observed in HCV and HBV distribution age group-wise.

Table 1: Clinical and demographic data of the patients

Gender		Age				HCV Infection		HBV Infection		HCV and HBV
Male	Female	Mean	S. D	Min	Max	Yes	No	Yes	No	
177 (54%)	152(46%)	12.83	10	2	55	282 (86%)	46(14%)	52 (16%)	276(84%)	6 (1.8%)

Table 2: Gender-wise distribution of HCV and HBV in thalassemia patients

Screening	Female (n=152)	Male (n=177)	PCR	Female (n=152)	Male (n=177)
HCV	129	151	HCV	82	95
HBV	26	29	HBV	18	10

Table 3: Facility-wise distribution of HCV and HBV in thalassemia patient

Facility center	Screening		Viral load	
	HCV	HBV	HCV	HBV
Center 1 (N=4)	4	0	1964±1847.7	-
Center 2 (N=3)	3	3	22396.3±21568.86	8198±11504.97
Center 3 (N=37)	37	1	206,508±370870.69	35,621
Center 4 (N=154)	153	3	879608.94±1499029.07	1140168±796423.39
Center 5 (N=41)	0	41	-	273676±528801.98
Center 6 (N=32)	29	3	984735.40±2008742.15	1,128,173±1285962.8
Center 7 (N=21)	21	0	1,067,440±1076708.98	-
Center 8 (N=36)	35	1	755477±994852.96	510890.22±1425699.10

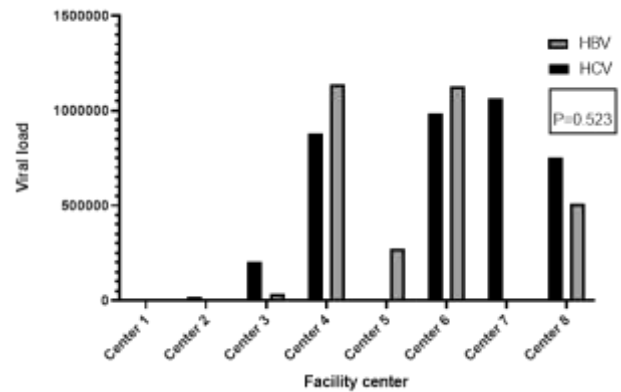


Figure 2: HCV and HBV Distribution obtained through confirmatory PCR test in different facility centers. T-test was used to determine the significance. P value ≤0.05 was considered significant.

Table 4: Age-wise distribution of HCV and HBV in thalassemia patients

Age Groups	HCV	HBV
2-12 years (n=142)	142	3
13-23 years (n=60)	60	6
24-24 years (n=8)	5	3
35-45 years (n=9)	9	0
46-55 years (n=5)	5	0

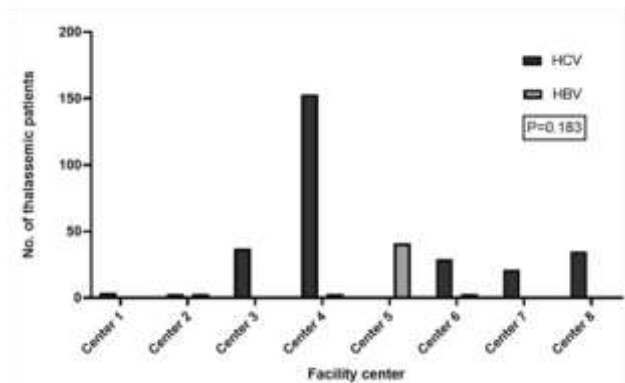


Figure 1: HCV and HBV Distribution obtained through rapid screening test in different facility centers. T-test was used to determine the significance. P value ≤0.05 was considered significant.

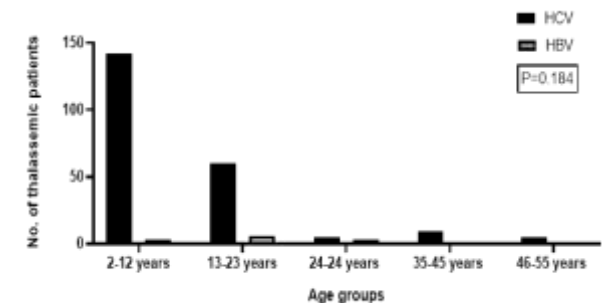


Figure 3: HCV and HBV Distribution in different age groups. T-test was used to determine the significance. P value ≤0.05 was considered significant.

DISCUSSION

β -thalassemia Major is one of the most common inherited hemoglobin disorders in Pakistan. Thalassemia major patients are transfusion dependent and require repeated blood transfusions which makes them vulnerable to acquiring blood-borne infection. Post-transfusion hepatitis B and C are frequently reported among β -thalassemia major patients of Pakistan due to the increased prevalence of Hepatitis B and C in the population, inadequate donor screening procedures, lack of awareness, and malpractices in health care setups. TTIs have been a significant concern for patients with β -thalassemia in poorer nations [11]. The rationale of this study was to determine the prevalence of HBV and HCV viral illnesses in multi-transfused thalassemia patients to have an early diagnosis and prompt treatment.

The average age of patients with β -thalassemia in the current study was 12.83 ± 10 years. The average age of the study participants was comparable to other studies conducted in Pakistan i.e., 11.5 ± 5.2 years by Alavi et al [12], 8.5 ± 6.42 years by Ansari et al. [13], and 10.1 ± 6.4 years by Ahmed Kiani R et al. [14]. Our study revealed that male children were more commonly affected by post-transfusion hepatitis i.e., 54% as compared to females 46%. A similar conclusion was drawn by Mirmomen et al. in their study [15]. However, no association between gender and β Thalassemia has been observed upon statistical analysis.

The substantial outcome of our study was the detection of HCV infection among 282 (86%) transfusion-dependent β -thalassemia patients in Karachi. High frequency of HCV has been published by Younas et al., i.e., HCV infection in 42% of β -thalassemia patients [18] 40.5% in Mansour et al. [16], and 40% in Abed [19] in their research studies. Hence, an increase in the current trend of HCV infection among β -thalassemia patients is observed in our study. HBV infection was relatively less common among the test population with a frequency rate of 14%. Research studies conducted in Pakistan show a varying pattern of hepatitis B among transfusion-dependent β -thalassemia patients. Rahman et al. reported 6.4% prevalence of Hepatitis B [20], Mansour et al., observed 6.5% HBV cases in their study [16], Kapoor et al reported a 17% prevalence of HBV cases [21], and Shah et al observed the HBV infection frequency of 8.4% in their study [22]. Various factors contribute to a higher prevalence of transfusion-transmitted infections in multi-transfused β -thalassemia in Pakistan including family replacement and paid donors, use of substandard screening devices for screening of TTIs, lack of awareness, and unsafe health care practices in unregistered medical centers. Another important factor in the increased prevalence of HCV infection is that infected HCV donors are serologically negative in the window period and most blood banks are detecting anti-HCV antibodies. Therefore, Nucleic acid amplification testing (NAT) should be promoted to detect TTIs among blood donors. Studies have suggested that voluntary non-remunerated donors are better as they have less risk of TTIs.

Limitations: In the present study, a small number of variables were chosen, and no further information on the clinical state of the patient's records was gathered to give the healthcare professionals with more information about this chronic disorder.

CONCLUSION AND RECOMMENDATIONS

The study concluded that hepatitis B and C are frequently observed in multi-transfused β -thalassemia major patients due to insufficient safety measures, insufficient resources in transfusion-dependent thalassemia patients, and a fragmented blood transfusion system in Pakistan. Therefore, to prevent the spread of HBV and HCV, the recruitment of prospective blood donors and the use of highly sensitive and specific screening techniques should be ensured. Effective health planning strategies should be implemented by healthcare organizations to enhance public awareness of HBV and HCV infection. Awareness can be generated through electronic and print media in both urban and rural areas. Wide-spread educational and counseling sessions

should be lodged by the NGOs and public centers regarding its treatment. Active hemovigilance should be monitored on timely bases for infectious cases among β thalassemia patients. The formulation of a safe blood transfusion policy and implementation of standard laboratory screening procedures at all levels is strongly recommended. Accurate identification and clinical management of infected patients are highly advised. Further extensive epidemiological and community-based studies are urgently needed to investigate viral infections in the whole country using confirmatory techniques (PCR, RIBA, and NAT Techniques) are essential. Simple, easily performed, reliable and cost-effective methods like ECLIA and CLIA should be introduced for screening and diagnosis of hepatitis C. This facility should be made available at least to every district of each province. Health education initiatives are required to raise knowledge of the value of the hepatitis B vaccine, morbidities linked to blood-borne infections, and efficient blood screening.

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