PREVALENCE OF ANTI HCV IN TRANSFUSION DEPENDENT THALASSEMIA MAJOR PATIENTS:- SINGLE CENTRE STUDY

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ABSTRACT

Objective: Beta thalassemia major is a significant health problem in Pakistan, such patients are usually supported by chronic blood transfusion which may later complicates into transfusion transmitted infections of which HCV is the major concern. Determination of HCV prevalence in these patients will help in monitoring safety of blood transfusion in thalassemia centers. Taking into account these observations we determined HCV seropositivity among multi-transfused beta thalassemia patients registered at Fatimid Foundation Hyderabad.

Materials & Methods: It was a cross-sectional study carried out at Fatimid Foundation Hyderabad from January 2014 till June 2015. Total 292 transfusion-dependent beta thalassemia major patients of both genders were included who had received at least 10 or more transfusions with minimum age limit of 2.5 years in the study. Venous blood samples of patients were collected and tested for Anti HCV using Microparticle Enzyme Immunoassay (MEIA) technique on AxSYM machine with HCV version 3 kit.

Results: Out of 292 patients, 53 (18.2 %) were positive for anti HCV antibodies. Hepatitis C was found to be more prevalent in older age group and HCV seropositivity increased with increasing number of transfusions.

Conclusion: Prevalence of Anti HCV among multi transfused patients was found to be high. Introduction of more specialized techniques such as NAT (Nucleic Acid Amplification testing) is therefore recommended to reduce the chances of transfusion transmitted infections.

Key Words: Thalassemia major, Multi-transfused, HCV, HCV antibodies.

INTRODUCTION

Thalassemia syndrome is an autosomal recessive inherited disorder which is grouped into alpha and beta thalassemia according to defective alpha or beta globin chain synthesis. It is further classified according to type of mutation affecting number and degree of globin chain synthesis. Beta Thalassemia results from anomalous production of beta globin chain that may results in reduced production to complete absence of it [1-2]. Consequently, it may leads to transfusion dependent chronic hemolytic anemia. Approximately 5000-9000 children are born homozygous for beta thalassemia gene annually in Pakistan. An estimated carrier rate for gene is 5-7 % with 9 million carriers nationwide [3].

Allogeneic Hemopoietic stem cell transplant is the only curative option for transfusion dependent thalassemia major [4]. However, due to financial constraints and lack of suitable donor it remains beyond approach of most of patients. In this case regularly spaced transfusions with iron chelation is the only accessible therapeutic option.

Chronic blood transfusion puts these patients at higher risk to contract various infectious diseases including HCV [5]. National blood transfusion project (NBTP) was launched in March 2009 to regulate the transfusion system nationwide both from qualitative and quantitative aspects [6]. Despite all the preventive measures taken, transfusion transmitted infections (TTI) continue to be a source of concern in our settings [7]. Of the various TTIs, hepatitis B (HBV) and hepatitis C virus (HCV) are of serious issue. However, hepatitis C is more concerned amongst two because of decline in Hepatitis B prevalence due to vaccination [8].

HCV infection is a major health burden worldwide with more than 170 million individuals being affected and over 350000 deaths occurring annually [8,9]. HCV prevalence rate in general adult Pakistani population is 6.7 % [10]. This is alarming as HCV has a high chronicity rate (55 to 85 %) leading to chronic liver disease, cirrhosis and progression to liver failure and hepatocellular carcinoma [11].

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After implementation of blood product screening for HCV in early 1990s in Pakistan, there has been a decline in transmission of transfusion-associated HCV infection but still rates are high [12]. WHO in 2010 formed a global hepatitis program to assist member countries in fighting HBV and HCV infections. WHO guidelines 2014 recommend implementation of Nucleic Acid Testing (NAT) in blood screening [13,14]. Beta thalassemia major poses a considerable socioeconomic burden especially in a country like Pakistan with limited health budget and resources. Since multiple transfusions are inevitable for beta thalassemia patients, control of TTI especially HCV infection is of prime importance. To achieve this, surveillance of blood transfusion safety by periodic assessment of HCV infection prevalence is important. Our study aims to determine the current status of HCV seropositivity among multitransfused beta thalassemia major patients.

MATERIAL AND METHODS

Study Design: It was a cross-sectional study carried out at the Fatimid foundation Hyderabad from January 2014 to June 2015. Patients having received 10 or more transfusions of packed red cells with minimum age of 2.5 years were included in the study. The status of HCV was not known before enrollment since these patients start getting transfusions since the age of 6-8 months. Patients with Thalassemia Intermedia and other hematological disorders and medical conditions were excluded. Out of 390 transfusion dependent beta Thalassemia major patients a total of 292 patients were enrolled in the study after having met inclusion criteria.

Determination of HCV Prevalence: A short proforma was designed to document patients's demographics, brief transfusion history and other relevant information. 5 mL venous blood samples were collected from each patient in gel top tubes using aseptic techniques. Samples were allowed to clot and serum was separated for determination of anti HCV antibody using MEIA technique on AxSYM machine with HCV version 3 kit. Percentage of the patients who tested positive for anti HCV was computed.

Statistical analysis: Data was analyzed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Frequency of patients positive for anti HCV was calculated and categorized in to different age groups. p value less than 0.05 was taken as significant.

RESULTS

A total of 292 transfusion dependent thalassemia major patients having met the inclusion criteria were tested for anti HCV antibodies. Out of them 165 (56.5 %) were males and 127 (43.5 %) were females with male to female ratio 1.3:1. The age of patients at the time of study ranged from 2.5 years to 27 years. The mean age of patients was 8.24 ± 3.5 and the median age was 14.5 ± 5 years. The demographic profile and some clinical features of patients are given in Table-1.

The interval between each successive transfusion ranged from 10 days to 4 weeks maximum. Out of 292 patients only 125 (42.8 %) were receiving transfusion regularly from one center. The rest 167 (57.2 %) received transfusions occasionally from other centers too.

Only 19.5 % of patients were receiving one transfusion per month while majority of patients (57.9 %) were receiving 2 transfusion per month and 22.6 % were receiving 3 or more transfusions (Table-1). Anti HCV antibody was detected in 53 (18.2 %) subjects. Out of total 292 patients 3 (1 %) of our patients were co-infected with Hepatitis B. The low rate of HBV infection was due to the high rate of vaccination in our study group (79 %) (Table-1).

Hepatitis C prevalence distribution in various age groups is shown in Table-2. HCV prevalence was significantly higher in patients aged more than 8 years compared to those aged below 8 years (31.4 % vs 10.8 %). Association of HCV seropositivity with number of transfusion is shown in figure-1. It is evident that HCV seropositivity increased more than 70% when there are more than 150 transfusion.

Figure-1: Association of hepatitis C seropositivity with number of transfusions.
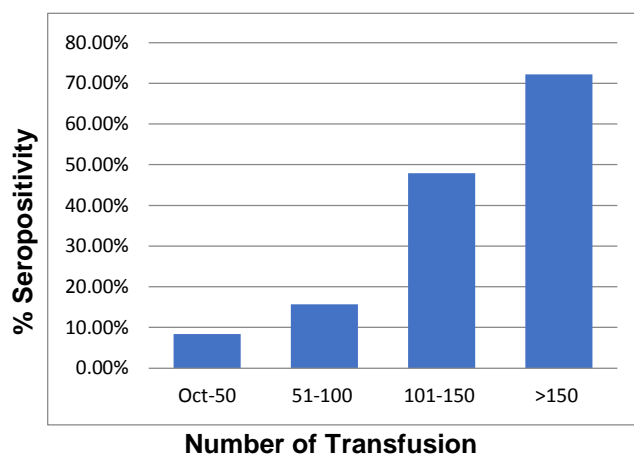
Table-1: The Demographic indicators and Clinical features of Multi-transfused Beta, Thalassemia major patients (n=292).

Variables	Numbers	Percentage
Sex		
Male	165	56.5 %
Female	127	43.5 %
Age at enrollment (in years)		
Range (2.5 to 27 years)		
Median	14.5 $\pm$ 5 years	
Mean	8.24 $\pm$3.54 years	
Transfusion per month		
One	57	19.5 %
Two	169	57.9 %
Three and more	66	22.6 %
Presence of Hepatomegaly	204	70 %
Presence of Splenomegaly	257	88 %
Patient co-infected with Hepatitis B	3	1 %
Patient vaccinated for Hepatitis B	233	79.8 %

Table-2: Hepatitis C prevalence distribution in various age groups.

Age group	No. of patients	Anti-HCV positive
2-8 years	175	19 (10.8 %)
> 8years	117	34 (31.4 %)

Table-3: HCV Prevalence in Multitransfused Beta-Thalassemia Patients in various Studies.

S.No	Country	Year of publication	No. of patients in study	HCV seropositivity	Ref
1	Pakistan (Islamabad/ Rawalpindi)	2017	Systematic review	47.2 %	Umar M. *et al.*
2	India	2017	207	24.64 %	Mukherjee K. *et al.*
3	Egypt	2016	97	37.11%	Mahmoud RA. *et al.*
4	Bangladesh	2014	200	2 %	Chakrabarty P. *et al.*
5	Pakistan (Rawalpindi)	2014	95	49 %	Din G. *et al.*
6	Pakistan (Karachi)	2012	160	13 %	Ansari SH. *et al.*
7	Pakistan (KPK)	2011	40	15%	Ali I. *et al.*
8	Iran	2009	206	28.1 %	Boroujerdnia MG. *et al.*
9	Pakistan (Quetta)	2007	150	30 %	Kapoor C. *et al.*
10	Turkey	2006	399	4.5%	Ocak S. *et al.*
11	Pakistan (KPK)	2005	250	56.8%	Shah SMA. *et al.*
12	Pakistan (Islamabad / Rawalpindi)	2004	75	42 %	Younus M. *et al.*
13	Thailand	2003	104	21	Wanachiwanawin W. *et al.*

DISCUSSION

Our study shows an alarming situation with high HCV prevalence rates. Out of 292 patients included in our study, 53 (18.2%) were anti HCV antibody positive. There is relatively high prevalence of HCV in our study of multitransfused thalassemia patients compared to prevalence in the general population (6.7%) reflects upon the inadequacies in blood transfusion safety [10].

This can be partly explained by the fact that 167 of 292 patients (57.2 %) were receiving transfusions at centers other than Fatimid foundation which may not be using standard blood screening techniques and precautions. The finding of HCV prevalence in our study is comparable to that found in several other studies done on multitransfused thalassemia patients in Pakistan and worldwide and is depicted in Table-3 [3,15,16]. While some studies show lower HCV prevalence in thalassemic [17,18], other studies depict higher rates especially in Egypt and Pakistan [10,12,19]. HCV prevalence rates are also remarkably high in older studies which included unscreened patients before screening of donated blood started [20,21]. It shows HCV prevalence varies geographically and locally in rural and upscale urban population and also varies with time.

In our study population 79 % were vaccinated for HBV and so we found only 3 (1 %) of patients to be HBV positive (Table-1). This figure also indicates the success of immunization goals.

Mukherjee *et al.* also found 99 % of their patients to be vaccinated for HBV and prevalence of HBV in their study was 3.4 % [22].

In our study of 292 patients, male to female ratio was 1.3:1 (Table-1). Male predominance was also noted in several other studies [12,19,22]. While Boroujerdnia *et al.* quoted female preponderance in their study [23].

The age of patients at the time of enrollment in our study ranged from 2.5 years to 27 years with mean age of 8.24+3.5 and the median age of 14.5 ±5 years (Table-1). Other studies showed similar findings [5,12,19]. The interval between each successive transfusion in our study ranged from 10 days to 4 weeks maximum which is similar to that found in the study by Mukherjee *et al.* which was 7 days to 1 month [22]. Only 19.5 % of patients were receiving one transfusion per month while majority of patients (57.9%) were receiving 2 transfusion per month and 22.6% were receiving 3 or more transfusions (Table-1). Chandi Kapoor *et al.* had similar findings in their study [5].

175 of our patients were aged between 2-8 years and 19 (10.8 %) of them were HCV positive while 117 patients were aged above 8 years and 34 (31.4 %) of them were HCV positive (Table-2). Thus 34/53 (64 %) of our HCV positive cases were older than 8 years. Other studies also found increased HCV prevalence in older age group which was statistically significant [5,12,19,23]. In our study, HCV seropositivity was directly proportional to the number of transfusions. Thus, it increased from 8.4 % to 15.7 %, 47.9 % and 72.2 % in those who had received 10-50, 51-100, 101-150 and more than 150 transfusions respectively (Figure-1). Other studies reported similar finding [5,12,23].

HCV prevalence is high in our study and other studies in Pakistan (Table-3). Blood transfusion screening for HCV infection in Pakistan is presently done by immunoassays as Nucleic acid–based tests are expensive. This increases the chances of transmission during the window period which is 6 weeks for immunoassays as compared to 2 weeks for NAT [13,24].

Transmission can occur even if the donor is negative for HCV by both serology and serum HCV RNA. It was established by Idrees *et al.* who determined the presence of HCV RNA in liver biopsies of patients with abnormal liver tests but without detectable serum HCV RNA and anti-HCV antibodies in sera. HCV RNA was detected in liver biopsy specimens in 23 of 31 patients (74.2 %) who were negative for both anti-HCV antibodies and serum HCV RNA [25]. This indicates that even the best method of screening blood cannot prevent transmission of HCV so besides improving blood screening techniques, we have to focus on a comprehensive plan for HCV infection control in the general population. Also detailed history and clinical evaluation along with liver function tests (LFTs) should be considered to exclude suspected blood donors.

CONCLUSION

Significantly high prevalence of anti-HCV among our patients implies TTIs to be the major health issue in chronically transfused patients. It questions the reliability of donor selection criteria and screening strategies adopted to screen blood products. It is suggested that endorsement of more specialized techniques such as NAT (Nucleic acid testing) will help reduce the TTI due to its ability to detect viral DNA/RNA during window period even before seroconversion for HCV. Routine assessment of transfusion dependent patients for TTIs especially HCV should be done at each center to monitor safety and efficacy of the screened blood. Moreover, it also helps in early detection and treatment of infection.

AUTHORS CONTRIBUTION

Musarrat Jehan: Paper writing literature Review

Maria Ali: Paper writing literature Review & statistical Analysis.

Veena Kumari: Data collection & entry of Data in SPSS.

Mahadev Harani: Principle Author Review of manuscript & proof reading.

Rab Nawaz Memon: Director & Incharge of Project.

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