Original Article

Hep B & C in Thalassemic Children

Frequency of Hepatitis B and Hepatitis C Seropositivity Among Repeatedly Transfused Thalassemic Children

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ABSTRACT

Objective: To determine the frequency of Hepatitis B and Hepatitis C seropositivity among repeatedly transfused thalassaemic children at a tertiary care hospital in Punjab.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Department of Paediatrics, Poonch Medical College Rawalakot from March 2016 to September 2016.

Materials and Methods: This study involved 300 children of both genders aged between 2-12 years presenting with beta-Thalassemia Major having ≥10 transfusions at the time of presentation. A written informed consent was taken from parents of each patient before they underwent laboratory testing for hepatitis B and C. Various social and demographic factors were also related with the seropositivity of both the visruses.

Results: Mean age of the patients were 6.95±3.19 years. There were 169 (56.3%) male and 131 (43.7%) female patients in the study group. The number of transfusions ranged from 10 to 149 with a mean of 70.55±39.31. 31 (10.3%) children were seropositive for hepatitis B. The frequency of Hepatitis B seropositivity increased significantly with increasing age of the patient and with increasing number of transfusions. 128 (42.7%) children were seropositive for hepatitis C. The frequency of Hepatitis C seropositivity increased significantly with increasing age of the patient and with increasing number of transfusions.

Conclusion: The frequency of Hepatitis B and C seropositivity was found to be 10.3% and 42.7% respectively among repeatedly transfused thalassaemic children presenting at a tertiary care hospital in Punjab. The frequency increased significantly with increasing age of the patient and number of transfusions received before presentation.

Key Words: β-Thalassemia Major, Blood Transfusions, Hepatitis B, Hepatitis C

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INTRODUCTION

Thalassemia's are inherited disorders characterized by abnormal production of haemoglobin and are associated with low haemoglobin production and excessive destruction of red blood cells. Pakistan has the highest number of children with transfusion dependent thalassemia in the world due to high frequency of the gene, consanguineous marriages, high birth rate, and large population size[1].

It has been estimated that over 4000 cases of transfusion dependent β-thalassemia major are born in Pakistan per year.

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The average life expectancy of β- thalassemic patients in Pakistan is 10 years. This life expectancy has improved due to availability of multiple transfusions along with chelation therapy[1,2]. However, these transfusions do have their side effects which vary from minor blood transfusion reaction to transmission of infections mainly Hepatitis B and Hepatitis C which is prevalent in the sub-continent[3].

Shaker et al. (2011) reported the frequency of Hepatitis C seropositivity to be 25% in repeatedly transfused thalassemia patients at a tertiary are hospital in Egypt. Boroujerdnia et al. (2009) in Iran and Vidja et al. (2011) in India reported this frequency to be 28.1% and only 2% respectively[4,5,6].

Yonus et al. (2004) reported Hepatitis-C seropositivity in 42% of repeatedly transfused thalassemic patients in Islamabad, Pakistan[7]. Similar frequency was reported by Nazir et al. (2014) who observed Hepatitis-C seropositivity in 41% of repeatedly transfused thalassemic patients in Lahore, Pakistan[8]. Hussain et al. (2008) in Peshawar, Sadiq et al. (2013) in Sargodha and Sheikh et al. (2015) in Multan reported this frequency to be 41.7%, 54.2% and 68.2% respectively in repeatedly transfused thalassemic patients[9-11]. However, comparatively lower frequency has been reported by

Ansari et al. (2012) in Karachi and Hayat et al. (2013) in Peshawar being 13.1% and 13% respectively[12,13].

Comparatively the reported frequency of Hepatitis B seropositivity is lower as compared to hepatitis C being 2% in India and 1.25% in Karachi, 2% in Peshawar, 3.5% in Multan and 9.2% in Sargodha [6,10-13]. However, much higher frequency (32.5%) has been reported in Egypt[4].

Thus both the hepatitis B and C are frequent among repeatedly transfused thalassemia patients. Compared to India (2%) which is much similar in geographical, population and socio-economic aspects, the frequency of Hepatitis C among thalassemic patients reported in Pakistan (41% - 68.2%) is alarmingly higher[6,7-11,14]. Also there is great degree of disparity among local studies where the frequency of Hepatitis B varies from as low as 1.25% in Karachi to 9.2% in Sargodha [10,12]. A similar disparity is also observed about the frequency of Hepatitis C, which varies from as low as 13% in Peshawar to 68.2% in Multan[11,13]. An important preventable cause behind this is the poor screening efficacy of Blood Banks dealing with such transfusions. This can partially explain the variability observed in previous studies about the frequency of Hepatitis C and B.

At the moment, only a single study is available reporting the frequency of Hepatitis C among repeatedly transfused thalassemia patients at a tertiary care hospital in Lahore while the frequency of Hepatitis B is still undetermined[8]. Furthermore, keeping in view the variation in the existing literature from different hospitals, there is need to determine the frequency of hepatitis B and C in repeatedly transfused thalassemia patients at another tertiary care hospital which will provide local baseline statistical data and will give an insight of disease burden among local thalassaemic population.

MATERIALS AND METHODS

This cross-sectional study was conducted at Department of Paediatrics, Poonch Medical College Rawalakot from March 2016 to September 2016. Sample size of 300 cases was calculated with 95% confidence level, 5% margin of error while taking expected frequency of Hepatitis B seropositivity to be 9.2% in repeatedly transfused thalassemic children in Pakistan[10]. Patients were selected by Non-Probability, Consecutive Sampling. Children of any gender aged between 2-12 years diagnosed of β-Thalassemia Major having received repeated blood transfusions were included in the study. Children of Hepatitis B or Hepatitis C positive mothers (antenatal record of the mother) were excluded from the study.

Diagnosis of thalassemia was made upon patients having repeated blood transfusions (≥10) and haemoglobin electrophoresis reporting 100% HbF (foetal haemoglobin). Children with history of ≥10 transfusions since birth (as per history and clinical record). 3ml of blood was acquired by venepuncture from cubital fossa. The sample was allowed to clot and a separate third generation ELISA kit for Hepatitis B and C was used to determine seropositivity from the isolated serum of sample. An immediate single line (≤5sec) was marker of accurate test and a double line with in 5 minutes was taken as marker of seropositivity.

300 pediatric patients presenting in the outdoor of Department of Pediatric Medicine, Children Hospital, Lahore who met the inclusion criteria were enrolled into this study. Detailed history and written informed consent were obtained from the patient's attendants. 3 ml of blood was taken by venipuncture from cubital fossa and seropositivity for hepatitis B and C was checked. Patient's demographic details along with number of transfusions and seropositivity for hepatitis B and C was noted and recorded into the attached proforma. All the samples and tests were performed by a single resident to eliminate bias. Confounding variables were controlled by exclusion.

All the collected data was entered and analyzed through SPSS version 21. Numerical variables; age and number of transfusions have been presented by mean ±SD. Categorical variables i-e gender and seropositivity for Hepatitis B and Hepatitis C have been presented by frequency and percentage. Data has been stratified for age, gender and number of transfusions to address effect modifiers. Post stratification chi-square test has been applied taking $p \leq 0.05$ as significant.

RESULTS

Mean of the study participants was 6.95±3.19 years. There were 169 (56.3%) male and 131 (43.7%) female patients in the study group. The number of transfusions ranged from 10 to 149 with a mean of 70.55±39.31. Majority (n=112, 37.4%) of the children had 51-100 transfusion as the time of presentation followed by 109 (36.3%) children who had received 10-50 transfusions. Only 79 (26.3%) children had >100 transfusions. All these findings have been summarized in Table 1.

Table No.1:Baseline Characteristics of Study Sample

Characteristics	**Participants n=300**
Age (years)	6.95±3.19
Age Groups	
• 2-5 years	111 (37.0%)
• 6-9 years	108 (36.0%)
• 10-12 years	81 (27.0%)
Gender	
• Male	169 (56.3%)
• Female	131 (43.7%)
Number of Transfusions	70.55±39.31
• 10-50	109 (36.3%)
• 51-100	112 (37.4%)
• 101-146	79 (26.3%)

31 (10.3%) children were seropositive for hepatitis B. The frequency of Hepatitis B seropositivity increased significantly with increasing age of the patient; 2-5 vs. 6-9 vs. 10-12 years (6.3% vs. 9.3% vs. 17.3%; p=0.043) and with increasing number of transfusions; 10-50 vs. 51-100 vs. 101-146 (6.4% vs. 8.9% vs. 17.7%; p=0.035). However, there was no significant difference among male (9.5% vs. 11.5%; p=0.576) and female gender. All these findings have been summarized in Table 2. 128 (42.7%) children were seropositive for hepatitis C.

Table No.2: Frequency of Hepatitis B Seropositivity

Characteristics	Hepatitis B Seropositivity n (%)	P value
Overall	31 (10.3%)	-
Age Groups		
• 2-5 years	7/111 (6.3%)	0.043*
• 6-9 years	10/108 (9.3%)	
• 10-12 years	14/81 (17.3%)	
Gender		
• Male	16/169 (9.5%)	0.576
• Female	15/131 (11.5%)	
Number of Transfusions		
• 10-50	7/109 (6.4%)	0.035*
• 51-100	10/112 (8.9%)	
• 101-146	14/79 (17.7%)	

Chi-square test,
* Observed difference was statistically significant

Table No.3: Frequency of Hepatitis C Seropositivity

Characteristics	Hepatitis C Seropositivity n (%)	P value
Overall	128 (42.7%)	-
Age Groups		
• 2-5 years	37/111 (33.3%)	0.029*
• 6-9 years	49/108 (45.4%)	
• 10-12 years	42/81 (51.9%)	
Gender		
• Male	74/169 (43.8%)	0.656
• Female	54/131 (41.2%)	
Number of Transfusions		
• 10-50	36/109 (33.0%)	0.019*
• 51-100	50/112 (44.6%)	
• 101-146	42/79 (53.2%)	

Chi-square test,
Observed difference was statistically significant

The frequency of Hepatitis C seropositivity increased significantly with increasing age of the patient; 2-5 vs. 6-9 vs. 10-12 years (33.3% vs. 45.4% vs. 51.9%; p=0.029) and with increasing number of transfusions; 10-50 vs. 51-100 vs. 101-146 (33.0% vs. 44.6% vs. 53.2%; p=0.019). However, there was no significant difference among male (43.8% vs. 41.2%; p=0.656) and female gender. All these findings have been summarized in Table 3.

DISCUSSION

Thalassemias are inherited disorders characterized by abnormal production of hemoglobin and are associated with low hemoglobin production and excessive destruction of red blood cells. Pakistan has the highest number of children with transfusion dependent thalassemia in the world due to high frequency of the gene, consanguineous marriages, high birth rate, and large population size[1]. The average life expectancy of β-thalassemic patients in Pakistan is 10 years. This life expectancy has improved due to availability of multiple transfusions along with chelation therapy[1,2]. These transfusions do have their side effects which vary from minor blood transfusion reaction to transmission of infections mainly Hepatitis B and Hepatitis C which is prevalent in the sub-continent[3].

However, there was great disparity in the existing evidence on the frequency of Hepatitis B and Hepatitis C seropositivity among thalassemic children receiving repeated transfusions which necessitated the present study. The objective of this study was to determine the frequency of Hepatitis B and Hepatitis C seropositivity among repeatedly transfused thalassemic children at a tertiary care hospital in Punjab. It was a cross sectional study conducted at Department of Pediatric Medicine, Children Hospital, Lahore over 6 months after the approval of synopsis from 04/03/2016 to 03/09/2016.

This study involved 300 children of both genders aged between 2-12 years presenting with beta-Thalassemia Major having ≥10 transfusions at the time of presentation. A written informed consent was taken from parents of each patient.

The age of the patients ranged from 2 years to 12 years with a mean of 6.95±3.19 years. A similar mean age among repeatedly transfused thalassemic children has been reported previously by Hussain et al. (6.8±3.6 years), Younus et al. (6.5±4.8 years), Sadiq et al. (6.3±3.30 years) and Sheikh et al. (6.21±3.07 years) in local population[7,9-11]. Nazir et al. (7.8±4.4 years) and Ansari at al. (8.45±6.42 years) reported relatively higher mean age among repeatedly transfused thalassemia children[8,12].

There were 169 (56.3%) male and 131 (43.7%) female patients in the study group giving a male to female ratio of 1.3:1. Khattak et al. (55.29% vs. 44.71%) reported a similar male predominance with a male to female ratio of 1.24:1. Yonus et al. reported a much higher male to female ratio of 1.8:1 at Pakistan Institute of Medical Sciences, Islamabad[7]. Hussain et al. rather reported a female predominance (48.0% vs. 52.0%) among repeatedly transfused thalassemic children at Pakistan Institute of Medical Sciences Islamabad[9].

The number of transfusions ranged from 10 to 149 with a mean of 70.55±39.31. Sheikh et al. reported a similar mean number of transfusions (73.92±50.22) among such patients at The Children's Hospital Multan[11].

31 (10.3%) children were seropositive for hepatitis B. Our results are in line with those of Sadiq et al. who reported the frequency of Hepatitis B seropositivity to be 9.2% in repeatedly transfused thalassemic children at Combined Military Hospital Sargodha[10]. Comparatively lower frequency of Hepatitis B seropositivity has been reported in a number of other studies at other thalassemia centres; 2% in India and 1.25% in Karachi, 2% in Peshawar and 3.5% in Multan[6,11-13] while much higher frequency (32.5%) has been reported in Egypt[4]. The frequency of Hepatitis B seropositivity increased significantly with increasing age of the patient; 2-5 vs. 6-9 vs. 10-12 years (6.3% vs. 9.3% vs. 17.3%; p=0.043). A similar association with increasing age has been described previously by Sheikh et al. (none vs. 0.7% vs. 2.8%)[11]. A possible explanation for this increase can be increased number of transfusions over time increasing the risk of exposure evident from the fact that the frequency of Hepatitis B seropositivity also increased significantly with increasing number of transfusions; 10-50 vs. 51-100 vs. 101-146 (6.4% vs. 8.9% vs. 17.7%; p=0.035).

128 (42.7%) children were seropositive for hepatitis C. Our results are similar to those of Yonus et al. (42%), Nazir et al. (41%) and Hussain et al. (41.7%) who also reported similar frequency of Hepatitis C seropositivity among repeatedly transfused thalassemia children in local population[7,8,9]. Sadiq et al. and Sheikh et al. reported relatively higher frequency of 54.2% and 68.2% respectively[10,11]. However, comparatively lower frequency has been reported by Ansari et al. (2012) in Karachi and Hayat et al. (2013) in Peshawar being 13.1% and 13% respectively[12,13].

The frequency of Hepatitis C seropositivity increased significantly with increasing age of the patient; 2-5 vs. 6-9 vs. 10-12 years (33.3% vs. 45.4% vs. 51.9%; p=0.029). A similar association with increasing age has been described previously by Sheikh et al. (14.1% vs. 37.4% vs. 48.5%)[11]. A possible explanation for this increase can be increased number of transfusions over time increasing the risk of exposure evident from the fact that the frequency of Hepatitis C seropositivity also increased significantly with increasing number of transfusions; 10-50 vs. 51-100 vs. 101-146 (33.0% vs. 44.6% vs. 53.2%; p=0.019).

Thus the frequency of Hepatitis B and C seropositivity was found to be 10.3% and 42.7% respectively among repeatedly transfused thalassemic children presenting at a tertiary care hospital in Punjab which was in accordance with the existing literature[14-16]. The frequency increased significantly with increasing age of the patient and number of transfusions received before presentation. This increase in frequency with increasing age suggests an association of seropositivity with increasing cumulative risk from increasing number of transfusions and in turn the increasing risk of exposure[17,18]. This frequency of Hepatitis C seropositivity is alarmingly higher and necessitates effective screening measures at Blood Banks to decrease this complication of transfusion with its associated morbidity and mortality.

CONCLUSION

The frequency of Hepatitis B and C seropositivity was found to be 10.3% and 42.7% respectively among repeatedly transfused thalassemic children presenting at a tertiary care hospital in Punjab. The frequency increased significantly with increasing age of the patient and number of transfusions received before presentation.

Author's Contribution:

Concept & Design of Study:	Amna Mateen
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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