Original Article

# Correlation of Hepatitis B with multiple blood transfusions in children of Thalassemia major

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## ABSTRACT

**Objective**: To assess the correlation of Hepatitis B (HBV) virus with multiple blood transfusions in patients of Thalassemia major (TM).

**Study Design**: Descriptive study.

**Place and Duration of study**: This was conducted in the Thalassemia center, Bolan Medical Complex Hospital Quetta for a period of six months.

**Patients and Methods**: One hundred and fifty (150) patients of Thalassemia major (already diagnosed) who received two or more blood transfusions were included in this study. Blood sample from these 150 thalassemic patients was scrutinized for HBsAg.

**Results**: All 150 thalassemia patients were in the age range of 6 months to 20 years Younger patients aged 0-4 years required transfusion every 4.6 weeks while patients above 15 required every 2 weeks. Every TM patients received a mean of 167.64 $\pm$ 121.01 units of blood. A substantive number 25 (17 %) were HBsAg positive .Direct correlation was found between HbsAg positivity and number of blood transfusions.

**Conclusion**: Conservative management with blood transfusion is probably the best and sometimes the only survival for patients of TM in our country but it carries a substantial amount of risk of acquiring hepatitis B due to repeated blood transfusions. It is extremely important to sensitize the public regarding prevention of the disease

**Key Words**: Beta thalassemia, HBV, Multiple blood Transfusion(s), HbsAg.

## INTRODUCTION

Beta thalassemia is the most common single gene disorder in Pakistan with a gene frequency of 5-8% and about 8-10 million carriers in the country[1]. There are currently 50,000 to 100,000 thalassemia patients and every year 5,000 babies are born with the deadly disease[2]. Over the past three decades, regular blood transfusions and iron chelation has dramatically improved the quality of life and transformed thalassemia from a rapidly fatal disease in early childhood to a chronic disease compatible with prolonged life[3]. Patients with thalassemia major who receive blood transfusions regularly to maintain optimal hemoglobin (Hb) level frequently suffer from the hepatitis infection. Screening of blood for HBsAg reduces the risk of transmission but cannot eliminate it entirely, because of window period and low titer HBV infections and HBV variants[4]. Nearly eighty percent of the carriers of hepatitis B virus (HBV) belong to Asian subcontinent where the prevalence ranges from 8-10 %. Higher prevalence of Hepatitis B has been reported from various parts of Pakistan[5]. As thalassemia major patients undergo blood transfusion every 20 to 30 days in order to maintain their hemoglobin level above 9 g/dl, they are at high risk of contracting hepatitis B infection[6].

## PATIENTS AND METHODS

A total of 150 patients were included in this study. The patients fulfilled the following criteria: They were diagnosed with thalassemia major, were above six months of age and had received blood transfusions more than once. Patients who were critically ill were excluded from the study. Every third patient was included in this study to decrease bias. A detailed clinical history and examination was done. Following this sample of blood was taken from patients after informed consent and Hepatitis B surface antigen (HbsAg) EIAgen (Elisa) HBsAg kit was used to detect seropositivity of HBV (Clone Systems Code 07-1000E). The data collected was analyzed using SPSS software version 10.Mean, and Standard deviation and percentages for Age, sex and number of blood transfusions and also sex ratios were reported .Correlation regression equation was applied to assess the correlation between hepatitis B and multiple blood transfusions.

## RESULTS

A total of 150 transfusion dependent patients with thalassemia major constituted the study population. Their age ranged from 9 months to 20 years with the mean age of 9.3 $\pm$ 4 years. Fifty patients were under the

age of 9 years and only 8 % above 15 years. There were 96 (64 %) males, 54 (36 %) females with a male to female sex ratio of 1.8 to 1.0. Statistically this difference was very significant (P<0.0001)

The interval with which these patients required blood transfusion ranged from 1-10 weeks .The mean interval between two transfusions was 3.1 weeks. Every patient was exposed to 17 different donors/year. The requirement of blood transfusion was increasing proportionately with the increase in age of the patients. The patient's age group 0-4 years required transfusion after every 4.6 weeks, while patients above 15 years of age required blood after every 2 weeks. On each visit they were transfused only one unit of packed red cells regardless of their demand. The total number of transfusion ranged from 6-636 units. All the patients received about 25147 transfusions. Every thalassemic patient received mean 167.64 + 121.01 units and in this way each patient was exposed to an average of 17 different donors per year.

Hepatitis B surface antigen (HBsAg) was positive in 1 (6 %) in the patient's age ranging from 9 months to 4 years, 12 patients (20 %) in age range 5-9 years, 9 patients in age ranging from 10-14 years and only 3 (25%) in group of patients above 15 years of age. The maximum seropositivity of viral marker was detected in patients of 5 years of age. None was positive below three years of age. On consideration of number of transfusions and HbsAg seropositivity none was positive in patient group who received less than 20 transfusions and only one patient was seropositive in the group of patients who received 21-50 transfusions and the rest of the seropositivity was seen in the patients who received more than 50 transfusions. Statistically this increase in prevalence was significant. Sex wise distribution showed HbsAg positivity in 5 (9 %) out of 54 female and 21 (22 %) out of 96 male patients.

# DISCUSSION

During the past twenty years, an effective form of treatment with red cell transfusion and iron chelation has led to steadily improved survival of these patients[7]. Even then the patient's die in the second decade from intractable congestive heart failure, cirrhosis or other complications[8]. In the present study the highest age of TM patient was 20 years. The age ranged from 9 month to 20 year and the mean age was 9.3±4.0 years. There was downward trend in the number of patients after the age of 14 years. Only a few patients (8 %) were above 15 years of age and about 80 % of the patients fell in the range of 5-14 years of age. Madan and Sharma from India conducted a study in the 11-18 years old age group of thalassemics[9]. The present study also shows that survival of patients fairly well up to the mid of second decade of life. The most common reported causes of death in patients of thalassemia major are endocrine failure, hepatic cirrhosis and cardiac failure which are due to iron overload resulting from blood transfusion[10]. This analysis of age distribution suggests that the survival of thalassemia major patients is markedly low in our country.

There were 96(64 %) males and 54 (36 %) female patients in the present study. Male to female ratio was 1.8:1.0. Kyriako A, Savva also described that thalassemia is more common and more severe in males then females[11]. The preponderance of males over females in the present study is difficult to explain. One possible reason is the fact that the people are more concerned with the health of male offspring and hence are more likely to seek medical care for them.

Different transfusion regimen has been employed with baseline hemoglobin level ranging from 8-12 g/dl for the management of TM. The interval between transfusions varies considerably between patients and the scheme of transfusion adopted. In the present study the interval between transfusions ranged from 1-10 weeks with a mean of 3.1 weeks. The difference was even more striking when calculated for different age groups .Transfusion requirement increased with age and interval between transfusions decreased. Similar results were observed in two studies, one by Tillman and Schroter[12] and other by Kontoghiorghes et al[13] Interval ranged from 1-13 weeks in these studies

The total number of blood transfusion varied with the age of the patients. It ranged from 6 to 636 units of packed red cells, with an average of 167 units. This supports to the earlier studies carried where it ranged from 5 to 662 units in TM patients studied by Gratwick et al[14], Kontoghiorghes[13], Flynn[15], Graziano et al[16], and Leon et al[17].

Hepatitis B surface antigen (HbsAg) was used to screen patients for hepatitis B virus (HBV). The frequency of HbsAg in multitransfused children of thalassemia major was 17 %. In the male patients, frequency was 21 % (20/96) while in female patients frequency was 9 % (5/54). The frequency of post transfusional HBV infection observed in the present study was in agreement with 20% in Indian thalassemic patients conducted by Irshad M and Peter S[18]. On the contrary the prevalence of 5 % has been reported by Ahmad and Shamsi[19] and by the AIDS-Haemophilia French Study Group[20]. However Yadev et al could find even lower prevalence of only 3%[21] and Naseerullah found none to be positive for HbsAg in his study[22]. In another study conducted by Rahman M and Lodhi Y in the Institute of Hematology & Blood Transfusion Service (IHBTS) Punjab, Lahore reported even lower frequency 1/60 (1.7%) to be positive for HBV[23] Similarly in Saudi Arabia a study conducted by EL-Hazmi and Ramia presented figures of 14.7 % positivity for HBV in

Riyadh 14.7 %, Jaizan 37 %, Khaiber 39.6 % and in AL-Hofouf 21.4 % indicating hyperendemicity of HBV in certain regions of Saudi Arabia[24]. These differences correlate well with the exposure rate to HBV in the general population of that region. The possible explanation for the high prevalence of HBV positivity in the present series of patients may be due to the infrequent facility of HbsAg testing for preventive measures. In the present study none was positive for HbsAg who had received up to 20 units of blood transfusions, 4 % in patient group who had received 21-50 transfusions, 19 % in patient group who received 51-100, 101-250 transfusions and it increased to 22 % in patients who received more than 250 units of blood transfusions. These results agree with the observation of Yadev et al who observed significant similar increasing trend in seropositivity of viral markers along with the increase in the number of transfusions[21].

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