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BETA THALASSEMIA;
IMPAIRED GLUCOSE TOLERANCE IN CHILDREN WITH BLOOD TRANSFUSION DEPENDENT BETA THALASSEMIA

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ABSTRACT… Background: Inadequate Blood Transfusion is responsible for various problems in children with Thalasseima. On the other hand, repeated transfusions are related with hazards. About 25-50% of the children with thalassemia major have impaired glucose tolerance (IGT) or diabetes. **Objectives:** To find out the frequency of IGT in children with blood transfusion dependent β thalassemia. **Study Design:** Descriptive analytical study. **Setting:** Department of Pediatrics, Shahida Islam Teaching Hospital, Lodhran. **Period:** 1st July 2017 to 31st December 2017. **Material and Methods:** Known 120 cases of beta Thalassemia major children between 3-17 years of age that were regularly transfused. Demographics, disease history and personal information regarding all the patients were collected. Glucose tolerance test was performed and Serum ferritin levels were measured. Results were analyzed by SPSS software version 20.0. **Results:** There were 78 (65.0%) children between 3-10 years and 42 (35.0%) between 11-17 years. There were 70(58.3) male and 50 (41.7%) female. Frequency of impaired glucose tolerance was noted in 15 (12.5%). **Conclusion:** Frequency of IGT is high amongst children with thalassemia major having regular blood transfusions.

Key words: Thalassemia Major, Blood Transfusion, Impaired Glucose Tolerance.

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INTRODUCTION

Thalassemia, was first illustrated by Cooley and Lee in 1925.[1] It is characterized by anemia, growth retardation, hepatosplenomegaly, juandice and bone changes. Genetic mutation cause reduction or halt in the synthesis of ß-globins chains. No national record is available in Pakistan but it is estimated that annually, approximately 5000-9000 children are born with ß-thalassemia with a carrier rate of about 5-7%.[2] The continuous iron overload in beta thalassemia major is the result of multiple blood transfusion, ineffective erythropoiesis, amplified GI absorption of iron and insufficient physiologic response for excreting excessive iron.

Iron overload may cause accumulation of iron in parenchyma tissue of liver and other tissues like heart and pancreas that leads to endocrine complications. Common manifestations are cirrhosis, cardiomyopathies and damage to pancreas. Early diagnosis at the early stages with proper iron chelating therapy and well-timed use of deferoxamine, diabetes can be delayed for many years.[3-7] Abnormal glucose tolerance is the commonest endocrine complication.

The exact mechanism of abnormal glucose homeostasis in β-thalassemia major is not known. It is credited mainly to insulin deficiency resulting from iron deposition leading to toxic effects and insulin resistance in the pancreas.[8-10] Iron deposition in liver and muscles result in insulin resistance and persistency of the insulin resistance aided by reduction of circulating insulin leads to IGT and diabetes.[11,12]

Late diagnosis of these cases may result in fatal complication that rise the need of glucose tolerance test and serum ferritin level for early diagnosis and prevention of those complications. Therefore, we decided to note the effect of various

factors on oral glucose tolerance test (OGTT).

MATERIAL AND METHODS

One hundred and twenty children with ß-thalassemia major (confirmed by Hb electrophoresis) were included in this study, aged between 3-17 years. All these children were being regularly transfused at Department of Pediatrics, Shahida Islam Teaching Hospital from 1st July 2017 to 31st December 2017.

The approval of institutional ethical committee was acquired before the study. Written consent was taken from the guardians/parents. Demograhic information, age at first blood transfusion, frequency/year of blood transfusion, age at the start of iron-chelation therapy, duration and its compliance, family history of diabetes and past history of splenectomy were noted. Anthropometry and related systemic examination were done.

Patient having any of the acute illness, liver disease, hemolytic anemia other than thalassemia and previously diagnosed diabetes cases were excluded. OGTT was estimated according to WHO's definition of IGT and diabetes. OGTT was done in the morning following a 3 days period on carbohydrate diet and 8-10 hours of overnight fast.

A fasting blood sample of 2ml was taken. Plasma glucose was noted 2 hours later after glucose was ingested in a dose of 1.75 g/kg up to a maximum of 75 g. Blood glucose was recorded and IGT was labeled if 2 hour plasma glucose was >140 mg/dL and less than 200 mg/dL (7.8- 10.3 mmol/L) and fasting plasma glucose (FPG) was <126 mg/dl (7.0 mmol/L). FPG of > 126 mg/dL (7.0 mmol/L) or 2 hour post plasma glucose (PPG) > 200 mg/dL (11.1 mmol/L) was labeled as diabetes. Serum ferritin levels were also noted. Data was analyzed by SPSS-20 statistical software.

RESULTS

There were 78 (65.0%) patients between 3-10 years and 42 (35.0%) between 11-20 years with a mean + SD of 8.05+4.2 years. There were 70 (58.3%) male and 50 (41.7%) females. Frequency of blood transfusions was, 73 (60.8%) had 1-5 transfusions while 47 (39.2%) >5 transfusions.

IGT was found in 15 (12.5%) cases. Patients with IGT, 10(66.7%) were between 3-10 years and 5 (33.3%) between 11-20 years. Patients with IGT, 8 (53.3%) were male and 7 (46.7%) females. Frequency of blood transfusion in patients with IGT were recorded as 4 (26.7%) had 1-5 transfusions while 11(73.3%) had >5 transfusions. In patients with IGT, Hepatitis B and C were noted 2 (13.3%) and 1 (6.7%) respectively.

Age (Years)	Number (%)
3-10	78 (65.0%)
11-20	42 (35.0%)
Total	120 (100%)
Mean + SD = 8.05 ± 4.2 Years	

Table-I. Age distribution amongst all the patients

Gender	n (%)
Male	70 (58.3%)
Female	50 (41.7%)
Total	20 (100%)

Table-II. Gender distribution amongst all the patients

No. of Transfusions	n (%)
1-5	73 (60.8%)
>5	47 (39.2%)
Total	120 (100%)

Table-III. Frequency of blood transfusions amongst all the patients

Hepatitis	n (%)
B	6 (5.0%)
C	5 (4.2%)
No	109 (90.8%)
Total	120 (100%)

Table-IV. Frequency of hepatitis B and C amongst all the patients

IGT	n (%)
Yes	15 (12.5%)
No	105 (87.5%)
Total	120 (100%)

Table-V. Frequency of IGT amongst all the patients

Age (Years)	n (%)
3-10	10 (66.7%)
11-20	5 (33.3%)
Total	15 (100%)

Table-VI. IGT amongst age groups

No. of Transfusions	n (%)
1-5	4 (26.7%)
>5	11 (73.3%)
Total	15 (100%)

Table-VII. IGT and blood transfusions

DISCUSSION

Diabetes mellitus has been found as one of the most common endocrine disorder in thalassemia major.[3-6] Prevalence of IGT in this study was high (12.5%). A study conducted by Platis et al[13] on 40 patients with β thalassemia major aged between 15-45 years, 16 patients (40%) had diabetes and 18 patients (45%) had IGT. In another study conducted on 28 beta thalasssemia major patients by Sougleri et al. approximately 7.5% had IGT.[14] The study of Gamberini et al. showed that the prevalence of IGT and diabetes was reduced in recent years because of early diagnosis and chelating therapy with desferral.[15] The cause of diabetes and IGT was insufficient admission of patients and parents for treatment with desferral and the result of that is iron overload.[15]

Incidence of Diabetes increases with age in patients with β thalassemia major.[5] Chern et al. noted the mean age of diabetes in 89 patients, was 4.17y, while the mean age of IGT was 4.9±14.6y. There is no significant difference between sexes in association with diabetes and IGT.[6] Several studies revealed that in patients that in younger age, chelating therapy had been started, the prevalence of complications such as secondary hemochromatosis and diabetes are lower.[6,13] In the study done in 1995 in Italy and in 2003 in Shiraz, irregular intake of deferoxamine identified as a risk factor for IGT.[16-18] We didn't have enough information about desferal administration in the past 10 years. However, numerous studies have shown that regular use of deferoxamine with appropriate dose is one of the ways to postpone developing diabetes or IGT.

In order to prevent iron overload the iron levels should be evaluated periodically and regularly.[16] Data suggested that serum ferritin level under 2500 μg/l, development of Diabetes mellitus is less common.[14]

CONCLUSION

Frequency of IGT is high amongst children with thalassemia major having regular blood transfusions. Studies with bigger sample size could help identifying factors influencing this high frequency.

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– Unknown –

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Iqbal Ahmed	Main concept and data collection for study.	
2	M. Ammar Sadiq	Data analysis	
3	Umair Arshad	Data analysis compilation of results.	
4	Hafiz M. Anwar ul Haq	Paper drafting and discussion.	
5	Sobia Tabassum	Methodology and drafting.	
6	Arshia Sabir	Introduction and background of topic.	
7	Hafiz M. Ejaz ul Haq	Editing and Drafting	