

Frequency of Abnormal GTT in Children with Beta Thalassemia Major

JAMAL ANWER, MASOOD IQBAL BABER, KIFAAT ULLAH NIAZI

ABSTRACT

Aim: To determine the frequency of abnormal oral GTT in children with BTM.

Study design: Cross sectional

Place and duration of study: Department of Pediatric including both indoor and outdoor, SZMC/H, RYK from 1st April 2014 to 25th July 2015.

Methods: In this study 89 patients were included. The given Performa filled and record was maintained by a third year FCPS resident.

Results: In our study, we included B Thalassemia Major patients between the age of 5 to 15 years and we found that out of 89 patients, 22 were having abnormal GTT.

Conclusion: Abnormal oral glucose tolerance test is found to be a common entity in patients with beta thalassemia major. This is more prevalent in older children especially who are having poor chelation.

Keywords: Frequency, Glucose Tolerance Test (GTT), Beta Thalassemia Major (BTM).

INTRODUCTION

Beta thalassemias (β thalassemias) are a group of inherited hematologic disorders which are caused by decrease or absent synthesis of the beta chains of hemoglobin. This may result in variable outcomes ranging from clinically asymptomatic individuals to severe anemia. Globally the annual incidence is estimated to be 1 in 100,000. Beta thalassemia is an autosomal recessive disorder caused by mutations in the HBB gene on chromosome 11. The severity of the disease depends upon the nature of the mutation¹. Depending upon the nature of mutation, Beta thalassemia syndrome may be described in three main forms which include thalassemia major, thalassemia intermediate and thalassemia minor.

Mutation in HBB gene leads to decreased beta-chain synthesis which leads to the underproduction of Adult Hemoglobin (HbA). This will express as microcytic hypochromic anemia which may lead to congestive cardiac failure so the patient must undergo a blood transfusion for survival. In beta thalassemia, the spleen causes increased red blood cell destruction due to ineffective erythropoiesis and this leads to release of excessive iron into the bloodstream¹. More over increased gastrointestinal iron absorption and repeated blood transfusions lead to iron overload, ultimately resulting in iron toxicity. This iron toxicity produces different complications (growth failure, cardiomyopathy, endocrinopathies, hepatitis leading to cirrhosis etc)^{1,2}.

Department of Pediatrics, Sh. Zayed Medical College / Hospital, Punjab, Rahim Yar Khan

Correspondence to Dr. Jamal Anwer, Associate Professor, . Email: drjamalanwer2000@yahoo.com, Cell: 03007829858

Epidemiology / Etiology: There are more than 200 mutations of β thalassemia. About 20 common alleles constitute 80 % of the known thalassemia worldwide; 3% of the world's population carries gene for β thalassemia¹. In β thalassemia Major, there are different etiological factors of abnormal GTT or DM. This may be due to the deposition of iron in pancreas and liver. The patients with β thalassemia Major have both insulin deficiency and insulin resistance. Suggested risk factors for development of glycemic abnormalities in patients with β thalassemia Major include repeated blood transfusion, high level of serum ferritin, family history of Diabetes mellitus, genetic factors of iron overload, older children and liver diseases^{3, 4,5,6,7}.

Glucose tolerance test: In *oral glucose tolerance test* (OGTT), a standard dose of glucose is taken by mouth and after two hours blood levels are checked. Since 1970s, the World Health Organization and other organizations related to diabetes, agreed on a standard dose and duration.

Preparation: Usually the OGTT is performed in the morning because glucose metabolism can exhibit a diurnal rhythm with a significant decrease in the afternoon. Prior to the tests, the patient is instructed to fast for 8–12 hours.

Procedure:

- A baseline (zero time) blood sample is taken.
- Afterward the patient is given a measured dose of glucose solution to drink within 5 minute.
- The samples of blood are drawn at intervals for measurement of glucose. For simple diabetes screening, the most important sample is the 2 hour sample. So the 0 and 2 hour samples may be the only required samples.

Dose of glucose: WHO recommended 75g of oral glucose.

Test Result Description

- Fasting plasma glucose should be below 110mg/dL. Fasting levels between 110 and 125mg/dL are borderline indicate "hyperglycemia". The fasting levels repeatedly at or above 126 mg/dL are diagnostic of diabetes.
- For a 2 hour GTT with 75g intake, a glucose level below 140 mg/dL is normal. Plasma glucose between 140mg/dL to 200 mg/dL indicate "Impaired GTT" and the level more than 200mg/dL at 2 hours confirm a diagnosis of diabetes.

Sample method: Venous sample wither by venous puncture or capillary sample.

METHODOLOGY

Inclusion criteria:

- Children with Beta thalassemia major
- Age of the patients between 5 to 15 years

Exclusion criteria:

- Children of hemolytic anemia other then Beta thalassemia major
- Age of the patients less than 5 years or more then 15 years

RESULTS

In this study, we included patients of beta thalassemia major between 5 to15 years of age. Out of 89 patients, 22 were having abnormal results of oral glucose tolerance test, remaining were having normal results. 7 patients were between 5 to10 years and 15 were between 11 to 15 years. Regarding the gender, 13 were boys and 9 were girls.

Fig. 1: Number of patients with normal and abnormal GTT

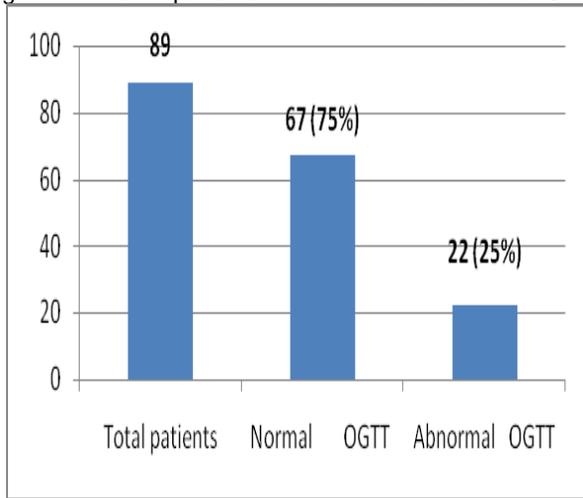


Fig.2: Age distribution (in years)

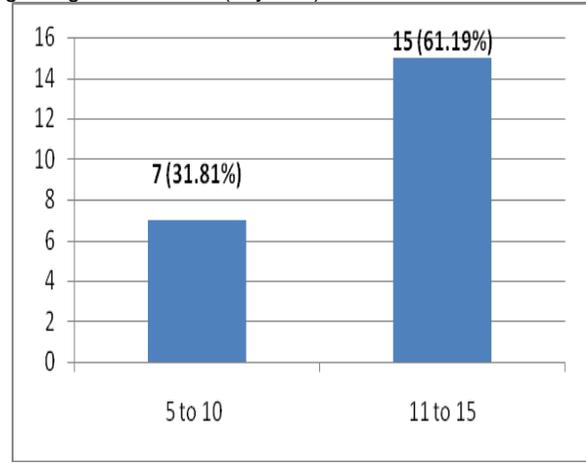
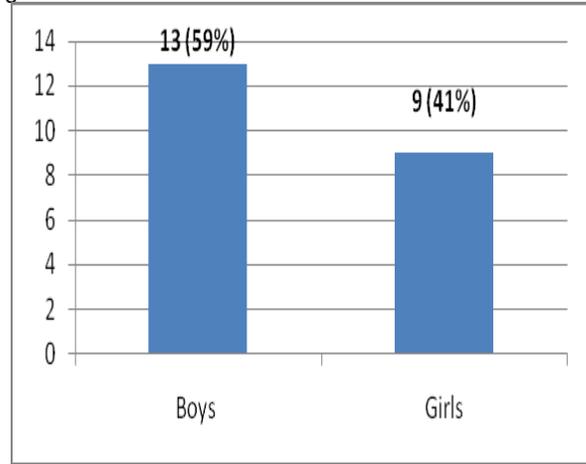


Fig. 3: Gender Distribution



These results show that 75% patients were having normal GTT while the frequency of abnormal results was 25%. The patients between 5 to 10 years of age were 7(31.81%) and between 10 to 15 years were 15(61.19%). Out of these patients with abnormal GTT, 59% were boys and 41% were girls.

DISCUSSION

Beta thalassemia major in one of the Hemoglobinopathies in which excessive hemolysis requires repeated blood transfusion. This and some other factors lead to iron overload. One of the complications of this iron overload is endocrinopathies due to the deposition of this overloaded iron in different endocrinal glands. DM and IGT are still prevalent complications in patients with BTM.

In this study, the frequency of IGTT is 25%, so a high prevalence of glycemic abnormalities in the patients with BTM is demonstrated.

In this study, we proved that poor chelation, and subsequently hemosiderosis of the pancreas and liver appear to be a major cause for impaired glucose metabolism in the patients with BTM. This is also supported by decreased insulin secretion in response to iron overload. A longitudinal study in thalassemic children showed progressive decrease in the beta cell function with age. Dmochowski K, Finegood DT et al found that persistent insulin resistance along with decreasing level of circulating insulin may lead to glucose intolerance and diabetes mellitus, which have a high prevalence in patients with thalassemia major⁸. Khalifa AS, Salem M et al found that the prevalence of diabetes was 10.4% (5 of 48) and IGT was 14.6% (7 of 48) among BTM, however patients of thalassemia intermedia had no abnormal glucose tolerance⁹. In the study conducted by Ashraf T. Soliman, Mohamed Yasin et al demonstrated high prevalence of glycemic abnormalities in adolescents with BTM¹⁰. Department of Pediatric Ibin Al-Balady Hospital found that 9.7% of patients suffering from BTM had impaired glucose tolerance test and 1.1% were diagnosed with diabetes¹¹. Bablu Kumar Gaur¹, Sunita Koreti et al found that the prevalence of impaired glucose tolerance was 20%¹². V. De Sanctis, G. D'Ascola et al demonstrated that long term chelation therapy does not prevent the development of abnormal oral glucose tolerance in chronically transfused patients. Intensive chelation therapy is needed to prevent tissue damage¹³. Arrigo T¹, Crisafulli G et al demonstrated that in respect to controls non-diabetic patients exhibited significantly elevated fasting plasma glucose levels and persistently higher glycemic responses to OGT, whereas their overall insulin output was significantly lower¹⁴. Sara Malik, Serajuddaula Syed et al says that endocrine complications include intolerance to glucose in adolescence and unconcealed diabetes in later life, mainly due to iron deposition in the pancreas¹⁵. Cario H, Holl RW et al found that insulin resistance is of central importance for the development of diabetes mellitus in patients with secondary haemochromatosis⁶. Ghergherehchi R, Habibzadeh A et al β -Thalassemia major patients had significantly more abnormal OGTT than the control group¹⁶. Matter RM, Allam KE et al found that thalassemic patients suffering from diabetes or having impaired glucose tolerance, displayed a higher degree of pancreatic and hepatic siderosis as compare to the patients with normal glucose tolerance or controls¹⁷. Hafez M, Youssry I et al found that abnormal glucose tolerance is common in multi-transfused beta-thalassemia major patients and could be attributed to early impaired beta-cell function with increasing insulin resistance¹⁸. Dehshal MH, Hooghooghi AH et al say that to a certain extend the

concentrations of fasting serum insulin were similar between the patients and the control groups, serum insulin levels were appreciably lower in the thalassemia patients one hour and two hours after oral glucose ingestion compared with the healthy controls¹⁹. In their study Krüger N, Stubbe P et al demonstrated abnormal glucose tolerance test in 14 patients (47%) before and in seven (23%) during deferoxamine infusion²⁰. Due to hemosiderosis pancreas is affected in beta thalassemia major but Theochari M, Ioannidou D et al found that among the patients with normal ultrasound, 25% had abnormal OGTT²¹.

Toumba M, Sergis A et al in their study "Endocrine complications in patients with Thalassaemia Major" reviewed that one of the endocrine complications of beta thalassemia patients is abnormal OGTT²². In their study "Abnormal oral GTT in beta thalassemia" Christopher D. Saudek, Robert M. Hemm et al found that Glucose Intolerance interrelated significantly with number of transfusions received and with the age of the patients²³.

CONCLUSION

Beta Thalassemia major is one of the crippling disorders. In our study we found that endocrinopathies as Diabetes Mellitus may be presented as abnormal OGTT in many patients. Iron overload with all the complications including endocrinopathies should be dealt with intensive use of iron chelators and appropriate monitoring. Moreover Intensive glucose monitoring during the late childhood and adolescence appears to be an efficient method in screening for hyperglycemia and could be a valuable guide to initiate insulin therapy.

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