



## Abnormal GTT (Glucose Tolerance Test) in Multitransfused $\beta$ Thalassemia Major Patients –In Vivo Biochemical Reactionary Effect

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### Abstract

**Background:** *Iron interferes with insulin action. Iron interferes inhibition of glucose production by insulin in liver. Hepatic extraction and metabolism of insulin is reduced with increasing iron stores, leading to peripheral hyperinsulinemia (51) and the initial and most common abnormality seen in iron overload condition is insulin resistance.(23)*

**Method:** *About 1 ml of fasting blood of patient was collected in a plain glass vial and then plasma separated. 1.75gm/kg body weight glucose dissolved in water was given to the patient & time was noted. 4 samples were collected at a time interval of half an hour for two hours, after giving glucose.*

*Determination of blood glucose was done by glucose oxidase peroxidase method*

**Conclusion:** *Significant variation was found ( $p$  value < 0.001) in children with impaired glucose tolerance compared to normal glucose tolerance with respect to age, weight, age of diagnosis.*

**Keywords:** *Abnormal GTT,  $\beta$  thalassemia.*

### Introduction

$\beta$ -thalassemia is associated with ineffective erythropoiesis, bone marrow expansion and rapid destruction of erythrocytes. The clinical course is characterized by severe anaemia, growth retardation, typical facies (maxillary hyperplasia, flat nasal bridge and frontal bossing), marked hepatosplenomegaly, cachexia and pathological bone fractures<sup>1</sup>. Anaemia demands frequent blood transfusion to maintain life. Present transfusion protocols have increased life expectancy of patients with  $\beta$ -thalassemia but siderosis is a major clinical complication of the treatment.

The only curative treatment for this disease is bone marrow transplantation which has variable success rate. Appropriate chelation therapy can prevent or limit these complications. In India, most thalassemic children are under transfused and do not get appropriate chelation therapy because the cost of treating a thalassemic child varies from few thousands to a lac per year. The result is diffuse organ damage caused by iron deposition in various organ.

Iron overload may cause deposition of iron in parenchymal tissue of liver and other tissues like heart and pancreas in one year of transfusions. As

the iron overloading progress, the capacity of transferrin to bind and detoxify iron may be exceeded and non transferrin bound fraction of plasma iron may promote the generation of free hydroxyl radicals, propagators of oxygen related damage. The free radical generated can damage cellular membrane, protein and DNA resulting in wide range of impairment in cellular function and integrity.<sup>(7)</sup> This manifest as cirrhosis, cardiomyopathies and damage to pancreas leading to diabetes which is most common mode of death.<sup>(2)</sup> Assessment of serum ferritin level can give idea regarding starting of chelation therapy, which will reduce the concentration of ferritin and effective in preventing iron induced tissue injury and prolonging life expectancy worldwide. Depression accounts for grave economic implications

### Methods

This prospective study was conducted in the department of pediatrics, M.G.M. Medical College, Indore at C.N.B.C and M.Y. hospital.

### Duration

- This study was conducted between Oct. 2010 and Sept. 2011.

### Sample Design

This study was conducted on 100 children with  $\beta$ -thalassemia major aged between 1-15 years being regularly transfused at Dept. of Pediatrics, M.G.M. Medical College, for period of 1 year, after taking the consent from the parents and explaining them the purpose and method of study.

### Inclusion Criteria

- Child suffering from  $\beta$ -thalassemia major only as confirmed by Hb electrophoresis.
- Age of thalassemic child should be between 1-15 years.
- Attending dept. of pediatrics, M.G.M. Medical College.

### Exclusion Criteria

- Patient suffering from any major disease like liver disease.

### Glucose Estimation by – GOD-POD Method

#### Principle

The aldehyde group of glucose is oxidized by glucose oxidase to give gluconic acid and hydrogen peroxide. The hydrogen peroxide is broken down to water and oxygen by peroxidase. This oxygen reacts with 4-amino antipyrine in the presence of phenol to form a pink coloured compound quinonemine dye. The intensity of the colour developed is proportional to glucose in the sample, which can be measure at 530 nm.

### Results

A total of 100 cases between age group of 1-15 years were studied.

#### Age Wise Distribution of Cases

Table – 1

Age Groups (Years)	No. Of Cases	% Of Cases
1 – 15 Years	35	35%
6 – 10 Years	43	43%
11 – 15 Years	22	22%
TOTAL	100	100%

Out of 100 cases, 35 cases were from age group 1-5 years, 43 cases were from age group 6-10 years and 22 cases were from age group 11-15 years.

#### Prevalence of Impaired Glucose Tolerance in Thalassemic Children

Table 2

Glucose Tolerance	No. of Cases	Male	Female
Normal GTT	85	48	37
Impaired GTT	15	7	8
Diabetic	0	0	0

Out of 100 cases, 15 had impaired glucose tolerance test, out of which 7 were males and 8 were females.

#### Characteristics of cases of Normal GTT and Impaired GTT in Thalassemic Children

Table 3

Patient Characteristics	Normal Gtt	Impaired Gtt	P Value
Age (Yrs) (Mean $\pm$ SD)	6.8 $\pm$ 2.5 Yrs	9.9 $\pm$ 2.7 Yrs	<0.001
Body Weight (Kg) (Mean $\pm$ SD)	18.7 $\pm$ 6.7 Kg	26 $\pm$ 8.0 Kg	<0.001
Age Of 1 <sup>st</sup> Blood Transfusion (Mean $\pm$ SD)	13.9 $\pm$ 3.5 Mnth	9 $\pm$ 1.8 Mnths	<0.001

It is evident from the table that significant variation was found in cases with impaired glucose tolerance test compared to normal glucose tolerance with respect to age, weight, age of 1<sup>st</sup> blood transfusion.(p value <0.001)

### Discussion

Of the 100  $\beta$  thalassemia major patients, 35 patients belong to age group 1-5 yrs, 43 patients belong to age group 6-10 yrs, and 22 patients belong to age group 11-15 yrs.

Of the 100  $\beta$  thalassemia major patients, 48 were females and 52 were males.

Oral glucose tolerance test was done to detect the prevalence of diabetes in  $\beta$  thalassemia children. Serum estimation included ferritin, SGOT, SGPT.

Serum ferritin was found to be elevated in all the patients of thalassemia studied. It was found to range from 2000 to 10216ng/ml with a mean value of 4363.4ng/ml.

It has been previously reported by Pootrakul (1981), George (1994), Faragion (1982), Caterina (1998), agrawal (1991) and Dubey (2004) that iron overload in the form of ferritin may be due to inappropriate chelation therapy or higher intestinal absorption and secondary to lower Hb levels.

Khalifa (2004) reported that impaired glucose tolerance is common in multiple transfused beta thalassemia major patients which was attributed to progressive and early loss of  $\beta$  cell mass along with persistent insulin resistance.

Of the 100 patients studied, 15 were found to have an impaired glucose tolerance while none were found to be diabetic. Of the 15 patients with impaired glucose tolerance, 7 were males and 8 were females. Varying prevalence of impaired glucose tolerance has been previously reported by other workers. Zuppinger (1979) reported it to be 86%, khalifa (2004) 14.6%, de sanctic (1986) reported it to be 37%, Saudek (1997) reported it to be 50%, El-Hazmi (1994) reported in 24% patients while Dubey (2004) reported it to be in 27.5% in their work. Significant variation (p<0.001) was found in patients with impaired glucose tolerance with respect to age, weight, age of diagnosis and

number of transfusions. Patients with impaired glucose tolerance had a mean transfusions of  $142.5 \pm 100.2$  times while those with normal glucose tolerance had  $50.5 \pm 22.5$  times of transfusions.

Patients with impaired glucose tolerance who had fasting glucose >110mg% and 2 hour glucose load concentration  $\geq 140$ mg% (WHO recommendation 1997) had SGOT, SGPT and ferritin level higher than those patients with normal glucose tolerance. Difference in these values was found to be highly significant (p<0.001).

Abnormal glucose homeostasis in patients with beta thalassemia major is attributed mainly to insulin deficiency resulting from toxic effect of iron deposited in pancreas and from insulin resistance. The insulin resistance may come from iron deposition in liver. The presence of impaired glucose tolerance along with elevated SGOT, SGPT and ferritin level may be attributed to the glucose intolerance associated with insulin resistance and may be direct or indirect consequence of hepatic damage. (Pappas,1996).

Serum values were analysed based on number of transfusions. Patients with transfusion more than 100 times had SGOT, SGPT and ferritin level greater than the patients who had transfusions less than 100 times and this difference was statistically significant (p value <0.001). Of the 22 patients with more than 100 transfusions, 12 were found to have impaired glucose tolerance while of the 78 patients with less than 100 transfusions, 3 were detected to have impaired glucose tolerance. Shalabh (2004) & Zanini (1985) have reported that chances of getting abnormal glucose tolerance increases with number of transfusions and serum ferritin and Saudek (1977) reported that glucose intolerance significantly correlated with number of transfusion received.

Impaired glucose tolerance detected in all the patients who had more than 100 transfusions may be due to insulin resistance and insulin secretion that develop with long term hypertransfusions therapy in thalassemic children. Dandona (1983) has reported patients had hepatic dysfunction of varying severity and suggested that the initial disturbance of

carbohydrate metabolism in transfusional siderosis is insulin resistance, similar to that found in chronic liver disease. Overt diabetes is probably a later event, occurring when significant damage to pancreatic cells has occurred.

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