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Incidence of impaired glucose tolerance and diabetes mellitus in transfusion dependent thalassemia patients of rural Bengal - An institutional study

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ABSTRACT

Introduction: Thalassemia is the world's commonest monogenic disorder. Molecular biology and genetics have revealed more than 200 mutations of thalassemia syndrome. These children become symptomatic from progressive haemolytic anaemia. They have to take lifelong treatments with regular packed red blood cell transfusion. Our body has no effective means of iron excretion and this leads to progressive iron accumulation in various organs after prolonged blood transfusion. This results in dysfunction of liver, heart and endocrine system and increased mortality. Iron toxicity to pancreatic beta cell leads to impairment in glucose metabolism.

Materials and Methods: Our study aims to find out the incidence of impaired glucose tolerance (IGT) and diabetes mellitus (DM) in transfusion dependent thalassemia major patients. This is an observational descriptive study carried out from January 2017 to June 2018. The study included 48 samples. There post-prandial blood sugar level and glycated haemoglobin (HbA1c) was analysed. Any proved case of juvenile diabetes mellitus was excluded from the study.

Result and Discussion: We found that the incidence of IGT and DM were 12.5% and 4.16% respectively in our study population. The blood sugar level was significantly high in study group (p=<0.0001) as compared to the control group. The present study showed strong correlation between units of blood transfusion and blood sugar level as well as HbA1C percentage (in both cases p= <0.00001.)

Conclusion: Thalassemia patients receiving regular blood transfusion are at increased risk of developing IGT and DM. Early initiation of chelation and judicious use of blood transfusion must be considered for these patients to prevent such complications.

1. Introduction

Thalassemia, also known as cooley's anemia is an inherited blood disorder transmitted in autosomal recessive manner and now prevalent all over the world.[1] The incidence of new homozygous state of thalassemia is around 50000 cases per year.[2] 1% to 17% population in India carries the beta thalassemia gene.

Patients with thalassemia major present a state of chronic anaemia with growth retardation, bone marrow expansion, splenomegaly, endocrinopathies, and hypercoagulability. If left untreated, the children usually die before their first birthday, due to severe cardiac decompensation.[3]

Once a child is diagnosed to have thalassemia homozygous disorder, he or she has to take lifelong

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treatments, such as regular three weakly filtered PRBC transfusion. Regular transfusion eventually leads to excess iron in the body which gets deposited in various organs.[4]

Without treatment, most of the children developed heavy iron overload and serious organ damage before adolescence.[5] Many patients developed severe iron deposition in pancreas leading to irreversible damage of the beta cells and ultimately resulting in glucose intolerance and overt diabetes mellitus. In India, 12% thalassaemic patients are reported to suffer from diabetes mellitus and 14% suffering from glucose intolerance.[6]

2. Aims and Objectives

Our study intends to measure the incidence of diabetes mellitus and impaired glucose intolerance in transfusion dependent thalassemia major patients and to search for correlation between impaired glucose tolerance and number of blood transfusions.

3. Materials and Methods

Ours was a prospective study conducted from January 2017 to June 2018. Cases were defined as people with thalassemia major confirmed by HPLC. Cases those had been transfused irrespective of their age and sex were selected in the study period. Number of blood transfusion in these cases were more than 20 times. Patients were thoroughly screened negative for HIV, HBsAg and HCV. All cases of proved juvenile diabetes mellitus were excluded from the study.

All HPLC done by HPLC Variant –II. To estimate the occurrence of diabetes mellitus and impaired glucose tolerance we have chosen two parameters, one is post-prandial blood sugar level and another is glycated haemoglobin (HbA1c) as per WHO guideline. The glucose was estimated by GOD-POD method. Hb A1C was estimated by Nyco Card. Data entered in Microsoft Excel and checked for accuracy. Data was analysed with the help of SPSS version 20.

Diabetes mellitus and glucose intolerance was diagnosed according to criteria made by WHO. Post prandial blood glucose if between 140-200 mg/dl, was categorized as impaired glucose tolerance, if more than >200 mg/dl was classified in diabetes mellitus.

4. Results

48 transfusion dependent homozygous thalassemia patients are included in the study. The mean ± SD age of the control participants were 8.5 ±1.62yrs with a male to female ration=1:1.82. There was no statistical significance of age variation between male and female group. Among transfusions dependent 48 thalassaemic patients, beta thalassemia major cases were 35(72.92%), E-β thalassemia were 9(18.75%), S-β thalassemia were 03 (6.25%) and one case of Sickle cell disease 01(2.08%).

Average transfusion received were 79.37±30.63 units (Maximum – 145 & Minimum 20 units).

In the present study impaired glucose level was seen in 8(16.67%) transfusion dependent thalassemia patients. Diabetes mellitus in two (4.16%) cases and impaired glucose tolerance in 6 (12.5%) cases. The mean ±SD blood sugar level of study group was 112.60±25.68 mg/dl. In control group it was 87.25±11.6 mg/dl. The blood sugar level was significantly high in study group (p=0.004).

The mean ±SD HbA1C level of the study group was 5.44±1.31% and of control group was 3.78±0.50%. The HbA1C is significantly correlated with blood sugar level in study group (p= 0.0001)

The HbA1C is not significantly correlated with blood sugar level in control group (p= 0.861).

The present study shows strong correlation between units of blood transfusion and blood sugar level as well as HbA1C percentage in both cases p= <0.00001

5. Discussion

In thalassaemic patients, who received regular transfusion, diabetes is an important complication.,[7] in present study, we assessed frequency of impaired glucose tolerance and DM in transfusion dependent thalassemic patients.

Although, life expectancy is improved by blood transfusion in thalassemia patient by increasing haemoglobin level and thus oxygen carrying capacity, still secondary haemosiderosis, endocrinopathies and other organ dysfunctions are among the most debating conundrums here.[8]

In our present study average age of participant 9.79 ± 2.75 years almost similar to the study of Kamalakshi G Bhat**,** Prakash K Periasamy.

Prevalence rates of glycaemic abnormalities in transfusion dependent thalassemia major patients in different studies are given in Table 1.

Table 1: Comparative studies on impaired glucose level in different studies.

Authors and references	Age (y) Range (Mean)	IGT Number (%)	DM Number (%)
Thuret I et al.[9]	0.6-61.2	-	13(6 %)
Belhoul KM et al.[10]	(15.4 ± 7.6)	-	40(10.5%)
Bejaoui M et al.[11]	3 month -31 years (10.7)	-	13(4.2%)
Present Study	9.79±2.75	6(12.5%)	2(4.16%)

It showed that the incidence of DM varies from 4.2% to 10.5%. In our study it was 4.16%. None of these studies looked for incidence of impaired glucose tolerance, but we found 6 cases (12.5%). In another study by Platis et al. on patients with beta thalassemia major patients, (40%) had diabetes and 18 patients (45%) had IGT.[12]

HbA1c which is a glycoprotein in nature was first isolated by Huisman et al[13] in 1958. The HbA1c is an effective tool for diagnosis of Diabetes.[14]

Vogiatzi et al, 2009[15] found that Diabetes mellitus (14%) was one of the major complications in patients with thalassemia major and receiving multiple (90) transfusion. In our study it is about 16.6% (considering both IGT & diabetes mellitus).

Although the pathophysiology of diabetes mellitus is not clear but Cooksey et al, 2004 suggested, the concomitant presence of transfusion related iron overload contributes in the development of DM in this population.[16] After 10-20 consecutive transfusions approximately 5 grams iron is accumulated in tissues leading to iron overload. The iron burden on the body can be estimated by measuring serum ferritin, serum iron and total iron binding capacity. Several studies in different part of the world by different research worker showed that serum ferritin is increased in transfusion dependent thalassaemic patients.

In patients with beta thalassemia major, due to multiple blood transfusion there is increased serum ferritin. In addition, iron absorption from gastrointestinal tract and poor iron excretion the serum iron increases and deposited in various organs including pancreas. This leads to impaired glucose tolerance. Several studies mentioned diabetes mellitus as a one of the most common endocrine disorders in thalassemia major patients.[17–19]

6. Conclusion

Homozygote thalassemia patients generally presents after 6 months with severe anemia, mild icterus, and enlarged liver and spleen. All ransfusion dependent thalassemia (TDT) patient starts blood transfusion between 7 months to 36 months of age to maintain optimal haemoglobin. The annual minimum transfusion requirement is roughly 200ml/kg/year. In our institution on an average the patients received PRBC 19.5 units/year (average 19 days interval). Our incidence of IGT and DM were 12.5% and 4.16% respectively. The deposition of iron in pancreas lead to impaired glucose tolerance and diabetes mellitus due to altered beta cell function. The blood sugar level is directly correlated with frequency and total amount of PRBC transfused. Prevention and management of IGT and DM is a major challenge for them. Diagnosis of impaired glucose tolerance by PPBS estimation and early intervention can prevent these patients from developing overt diabetes mellitus. Total number of blood transfusion and its frequency should be judiciously planned. Proper chelation could improve the quality of life in these patients.

7. Source of Funding

None.

8. Conflict of Interest

None.

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