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Prevalence of Diabetes and Impaired Glucose Tolerance Test in Patients with Thalassemia Major

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Abstract

***Background*:** Diabetes is one of the most common endocrine disorder worldwide that due to high prevalence and chronic nature of diabetes imposes a heavy cost on health care system. Therefore this study aimed to assess prevalence of diabetes among patients with beta thalassemia major.

***Materials and Methods*:** This descriptive study was conducted on 364 patients with beta thalassemia major that received at least 100 blood bags. For evaluation of diabetes among these patients, fasting blood sugar and glucose tolerance test were done. Finally relationship between age, gender, age at beginning of transfusion and chelating therapy with occurrence of diabetes were analysis by SPSS-17 software.

***Results*:** Among 364 patients with mean age of 17.7±4.9 years prevalence of diabetes was 15.1% (58 patients) that 37.9% (22 patients) were women and 62.1 (38 patients) were men.

***Conclusion*:** Due to high prevalence of diabetes in patients with beta thalassemia major, regular check up for endocrine disorders should be consider in these patients.

Introduction

Beta thalassemia is one of the most common single-gene disorders that require regular blood transfusion. Repeated blood transfusions in these patients lead to the accumulation of iron in the body that result in damage to critical organs such as liver, pancreas and heart. One of the most frequent endocrine complication in thalassemia major patients is diabetic so that 25-50 % these patient have impaired glucose tolerance test or diabetes [1-5].

In these patients several years before the onset of diabetes, impaired glucose tolerance occurs. If the disorder is diagnosed in the early stages with proper iron chelating therapy and timely use of deferoxamine diabetes mellitus can be delayed for many years [1, 5]. Otherwise the complication may first appear as diabetic ketoacidosis and endangers the patient's life. In this step iron chelating therapy cannot be effectively to improve the pancreatic function of patients.

Due to the high prevalence of the disease in the province, attention to repeated complications of transfusion therapy, iron chelating therapy and incomplete treatment is important. However, early diagnosis and proper treatment of the diabetic patient should always be considered. This study aimed to evaluate frequency of impaired glucose tolerance test In order to plan for early monitoring and early diagnosis of diabetes in patients with thalassemia.

Materials and Methods

This descriptive study conducted on 384 patients with thalassemia major. Written consent was obtained from each participant and the study was approved by the medical ethics committee of Zahedan University of Medical Science. All patients with thalassemia major that have received at least 100 blood bags were included in the study. Exclusion criteria were reception of less than 100 blood bags, acute disease at the time study and history of diabetsis. Two ml blood was taken from fasting patients and 1.75 g/kg glucose solution was given orally to them and 2 hours later blood sampling was repeated.

The glucose level was measured by glucose peroxidase method and by autoanalyzer and finally recorded in relevant forms. The two hours glucose level between 140 and 200 mg/dl, was regarded as a impaired glucose tolerance test. Fasting glucose above 126 mg/dl and 2-hour glucose level above 200 mg/dl were also considered as a diabetic. Finally obtained data was analyzed by SPSS-17 statistical software.

Results

This study was conducted on 384 patients with beta thalassemia major that referring to Ali Asghar hospital for blood transfusion and follow up. The age range of patients was between 10 to 30 and the mean age was 17.7±4.9 years.

The age range of all patients was as follow: 138 (10-15 years), 124 (15-20 years), 96 (20-25 years) and 26 (25- 30 years) individuals (p=0.02). In this study 24 patients (6.3%) and 58 patients (15.1%) had IGT and Diabetes mellitus, respectively. Among all patients, 158 (41.1%)

were female and 226 patients (58.9%) were male. In female patients, 12 individuals (7.6%) had impaired glucose tolerance and 22 of them (13.9%) had diabetes and in male patients impaired glucose tolerance and diabetes was observed in 12 (5.3%) and 36 (15.9%) individuals, respectively. There was no significant difference between sexes. From overall patients, 141 individuals had started deferral injection (chelating therapy) at aged 2-5 years old, that in these cases an impaired glucose tolerance and diabetes was observed in 10 (7.1%) and 26 (18.4%) patients, respectively. In the remaining 141 patients that had started chelating therapy age under 2 years old, impaired glucose tolerance was seen in 8 patients (5.6%) while diabetes was observed in 16 individuals (11.3%). There was no significant difference between groups (Table 1). From 356 patients, 264 individuals had serum ferritin above 2000 µg/l that 46 of them (17.4%) had diabetes and 16 patients (6.1%) had impaired glucose tolerance. In 92 patients, serum ferritin was below 2000 µg/l that in this group, 10 (10.9%) and 6 (6.5%) individuals had diabetes mellitus and IGT, respectively. There was significant difference between two groups (p<0.05) (Table 2).

In our study, 171 patients (45%) were between 30 and 45 Kg, that among these patients, 10 individuals (5.8%) had IGT and 30 individuals (17.5%) had diabetes. The weight of 105 patients was lower than 30 Kg of which 4 (3.8%) and 12 (11.4%) individuals had IGT and diabetes, respectively. In 104 patients with the weight over 45 Kg, 10 (9.6%) individuals had IGT while 14 patients (13.5%) had Diabetes. There was no significant difference between groups.

Discussion

This study performed on 384 patients with beta thalasemia major, referred to Ali Asghar Hospital for blood transfusion and follow up. The mean age of patients were 7.17-9.4 years with the age range of 10-30 years. On the other hand only 26 of the patients were older than 25 years which represents the fact that in our patient's population, most are young, and also because of adverse effect of treatment and lack of proper follow up or inappropriate use of iron chelation therapy die at younger age.

In patients with beta thalassemia major, because of high blood transfusion, high iron absorption from gastrointestinal tract and lack of adequate iron excretion, damage due to excessive iron accumulation and iron deposition in various organs such as kidney, pancreas and heart may occur. Several studies mentioned diabetes mellitus as a one of the most common endocrine disorder in thalassemia major patients [1-4].

In similar study was done by Platis et al. on 40 patients with Beta thalassemia major aged between 15-45 years, 16 patients (40%) had diabetes and 18 patients (45%) had IGT. In Diabetic patients, the mean serum ferritin was 3083 µg/l while in patients with IGT, it was 2255 µg/l. Because of small number of patients in this study, the prevalence of diabetes and IGT in contrast with previous studies is much higher [6]. In another study conducted on 28 beta thalasssemia major patients by Sougleri et al. approximately 7.5% had IGT.

In the study of 89 patients aged 3-29 years that was done by Chern et al. IGT and diabetes were observed in 7 (8.5%) and 16 (19.5%) patients, respectively [4,7].

The study of Gamberini et al. showed that the prevalence of impaired glucose tolerance and diabetes in recent years because of early diagnosis and chelating therapy with desferral is reduced. 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 [8]. In our study, among 384 patients, 24 patients (6.3%) had IGT and 58 (15.1%) had diabetes mellitus, which is consistent with previous studies. Incidence of Diabetes mellitus in patients with beta thalassemia major increases with age [3, 14]. Several studies revealed that diabetes mellitus is more common in patients in second decade of life [3].

In another study was done by Chern et al. the mean age of diabetes in 89 patients, was 4.17, while the mean age of IGT was 4.9±14.6. There is no significant difference between sexes in association with diabetes and IGT [4].

In our study the mean age of IGT and diabetes were 18.9±5.5 and 19.6±4.4, respectively and as previous studies there is no significant difference between sexes in association with diabetes and IGT.

In general, the body has little ability to excrete excess iron, thus patients with beta-thalassemia major that treated with transfusion, are at excess risk of clinical complications such as diabetes mellitus.

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 [4, 11, 6].

In this study, among 181 patients had started chelating therapy at age under 2 years old, diabetes mellitus was observed in 16 individuals (11.3%). Of 225 patients started chelating therapy at age over 2 years old, 42 individuals (8.6%) had diabetes mellitus. In this study there was no correlation between deferoxamine and diabetes due to inadequate information about the way of administration and the amount of it. In the study was done in 1995 in Italy and in 2003 in Shiraz, irregular intake of deferoxamine identified as a risk factor for IGT [12-14]. 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.

Thalassemic patients received 20 units of packed red blood cells and therefore about 4 grams of iron (equivalents to total iron stores in healthy male adult) is added to the body iron stores. Because There is no way to remove excess iron from the body, iron overload can cause side effects such as liver and spleen enlargement , cardiomyopathy, endocrine disorders including impaired growth and development, delayed puberty, hypo-thyroidism and hypo-parathyroidism, pancreatic insufficiency, diabetes mellitus and death [3].

Several studies showed that serum ferritin levels reflect body iron content and 1 µg/l of it is equivalent to 8 mg of iron. In order to prevent iron overload the iron levels should be evaluated periodically and regularly [12]. The amounts of serum ferritin level that prevent complications of iron overload in these patients are 1,000 µg/l or 1000-1500 µg/l [9].

The study was done by Chern showed that in the cases with serum ferritin level under 2500 µg/l , developing of Diabetes mellitus is less common [7].

In the study that was done by Kattamis et al. the prevalence of diabetes mellitus in patients with thalassemia major who had serum ferritin less than 2000 µg/l was 3.8% and In patients who had a serum ferritin level higher than 2000 µg/l, the prevalence of diabetes was estimated 14.6%. It also revealed that the serum ferritin higher than 2000 µg/l requires high dose chelating therapy.

Of 264 patients (74.2%) with serum ferritin levels greater than 2000 µg/l, 46 (17.4%) had diabetes mellitus and 16 patients (6.1%) had impaired glucose tolerance respectively that is showed a higher prevalence of impaired glucose tolerance and diabetes mellitus in patients with serum ferritin greater than 2000 µg/l. Considering the fact that without chelating agent such as desferal, body cannot excrete iron, it seems that the high prevalence of IGT in patients with thalassemia major is due to irregular or inadequate intake of desferral or poor quality of it. Overall, the results of this study suggests in patients with thalassemia major that treated with transfusion and deferoxamine, glucose tolerance test at least once every 6 months is recommended.

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Authors' Contributions

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Conflict of Interest

The authors declare no conflict of interest.

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