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Assessment of glucose metabolism in thalassemia patients with type two diabetes in Thi-Qar/ Southern of Iraq

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***Abstract*---**The natural history of glucose metabolism in transfusion-dependent beta-thalassemia patients is characterized by deterioration of glucose tolerance over time. The current study involved 80 participate (40 thalassemia with diabetic 22 boy and 18 girl and 40 as control group 21 boy and 19 girl). The study was conducted at the Specialized Center for Endocrinology and Diabetes in Thi-Qar Governorate and some outpatient clinics for the period from January to April 2022. The results of the current study recorded a significant increase of involved parameters in thalassemia patients than control group in both compartment when compared all patients with all control, and when compared according to gender, also the results a non-significant difference between patients according age with except ALP.

***Keywords*---**assessment glucose, metabolism, thalassemia patients, type two diabetes.

Introduction

Beta thalassemia is a group of hereditary blood disorders characterized by abnormalities in the structure of the beta hemoglobin chains resulting in variable phenotypes ranging from severe anemia to individuals without clinical symptoms (Russo *et al.*, 2019). Beta thalassemia includes three main forms: thalassemia major, which is variously referred to as 'Coley's anemia' and 'intermediate anemia thalassemia intermediate and thalassemia minor also called 'beta thalassemia carrier 'beta thalassemia trait' or 'beta thalassemia trait. Heterozygous "thalassemia (Okab and Saleh, 2019). Thalassemia patients receive blood in regular manner to prevent complications such as chronic anemia and bone

changes. In the past 2 or 3 decades, blood transfusions have significantly increased lifespan and life expectancy in patients with thalassemia major (Angastiniotis and Lobitz, 2019). At the same time, the increased use of this treatment has led to complications of iron overload. One of the toxic effects of iron overload occurs in the endocrine glands (Darabi *et al.*, 2021). Endocrine complications may be due to treatment with irregular iron chelation in thalassemia patients in developing countries. Diabetes is one of the most common and dangerous diseases that can be considered the most important human metabolic disease (De Sanctis *et al.*, 2021). The most common complications of diabetes are cardiovascular disease, polyneuropathy, retinopathy, nephropathy, infection and sexual dysfunction. Patients with thalassemia major without diabetes or are eu-glycemic may have high fasting plasma insulin concentration and a high insulin resistance index, that suggesting the presence of insulin resistance before the onset of diabetes (Faselis *et al.*, 2020). Abnormal homeostasis model assessment (HOMA) indices for beta cell function (HOMAB) and insulin resistance (HOMA-IR) were also recorded in thalassemia major patients who did not present diabetes or exhibited eu-glycemic statuses (Sung *et al.*, 2020). The pathogenesis of growth failure in thalassemia is multifactorial and is mainly attributed to transfusion iron overload and consequent endocrine disorders, growth hormone deficiency, hypothyroidism, nutritional deficiencies, and extensive use of chelating agents especially desferoxamine (Pinto *et al.*, 2019). Other aetiologies, especially in suboptimally treated children, are increased metabolism, chronic anemia and hypoxia. Abnormalities of glucose tolerance and diabetes mellitus are common complications of thalassemia patients. While glucose intolerance occurs early during adolescence in TI-patients, diabetes more often occurs in later stages and is usually secondary to iron overload and later chronic liver disease. he development of diabetes in thalassemia has been attributed to impaired insulin secretion function as a result of chronic iron overload in the pancreas (Azami *et al.*, 2017). Selective immune system activation against pancreatic beta cells resulting in cell damage, and/or death of pancreatic cells due to lipid transformation. Iron-mediated diabetes can be partially reversed if treated early (Roep *et al.*, 2021). High doses of insulin are needed to correct blood glucose levels in diabetic patients. Experts recommend early screening and detection of impaired glucose and insulin resistance in all thalassemia patients starting at age 8-10 as the disease can be stopped before it progresses to overt diabetes in adulthood (Elena *et al.*, 2018).

Material and Method

Sample Collection

The current study involved 80 participate (40 thalassemia with diabetic 22 boy and 18 girl and 40 as control group 21 boy and 19 girl). The study was conducted at the Specialized Center for Endocrinology and Diabetes in Thi-Qar Governorate and some outpatient clinics for the period from January to April 2022. A three ml of venous blood were collected from both patients and control group, and the blood were leaved at room temperature for about half hour for coagulate a then centrifuged at 4000 RPM, then serum collected and frizzing until used. The parameters were estimated as following the FBS, HbA_1c, ALP, AST and ALT were estimated by cobes instrument and insulin were estimated by ELISA.

Statistical Analysis

The data of present study were analysis by using SPSS version 26 based in using independent t. test at p. value < 0.05 and < 0.01.

Results

Estimation of Diabetic and Liver Function Parameters in Thalassemia and Control Groups

Table 3-1 showed that both diabetic metabolic and liver function tests parameters increased significantly at p. value < 0.01 in thalassemia-diabetic patients compared with control group as shown in table 3-1.

Table 3-1: Diabetic and liver function parameters in patients and control

Parameters	Patients No. 40	Control No. 40	p. value
Age	15.2 ± 5.49	18.0 ± 3.75	< 0.001**
HbA_1c	7.31 ± 1.84	4.95 ± 0.35	< 0.001**
Insulin	28.9 ± 7.80	4.06 ± 0.90	< 0.001**
FBS	213.3 ± 49.0	87.8 ± 11.3	< 0.001**
HOMA-IR	15.2 ± 5.58	0.88 ± 0.22	< 0.001**
ALP	226.6 ± 40.7	87.4 ± 8.66	< 0.001**
AST	58.5 ± 6.04	14.0 ± 2.08	< 0.001**
ALT	58.3 ± 6.69	14.5 ± 2.86	< 0.001**

Estimation of Diabetic and Liver Function Parameters in Thalassemia and Control Groups according to Gender

Table 3-2 showed that both diabetic metabolic and liver function tests parameters increased significantly at p. value < 0.01 in thalassemia-diabetic patients in male and female compared with corresponding control group, with except age in female group not-recorded significant difference as shown in table 3-2.

Table 3-2: Diabetic and liver function parameters in patients and control

	Categories	Patients	Control	p. value
Age	Male No.22 vs. 21	14.5 ± 5.18	18.0 ± 3.92	0.018*
	Female No.18 vs.19	16.0 ± 5.88	18.1 ± 3.65	0.198
HbA_1c	Male No.22 vs. 21	7.50 ± 2.02	4.90 ± 0.38	< 0.001**
	Female No.18 vs.19	7.08 ± 1.60	5.00 ± 0.31	< 0.001**
Insulin	Male No.22 vs. 21	27.5 ± 6.99	3.90 ± 0.72	< 0.001**
	Female No.18 vs.19	30.5 ± 8.59	4.24 ± 1.06	< 0.001**
FBS	Male No.22 vs. 21	214.6 ± 54.9	88.0 ± 11.5	< 0.001**
	Female No.18 vs.19	211.7 ± 42.2	87.6 ± 11.3	< 0.001**
HOMA-IR	Male No.22 vs. 21	14.5 ± 5.32	0.86 ± 0.21	< 0.001**
	Female No.18 vs.19	15.9 ± 5.94	0.91 ±0.24	< 0.001**
ALP	Male No.22 vs. 21	217.2 ± 40.8	87.2 ± 8.93	< 0.001**

	Female No.18 vs.19	238.1 ± 38.6	87.6 ± 8.59	< 0.001**
AST	Male No.22 vs. 21	58.2 ± 6.69	14.1 ± 2.15	< 0.001**
	Female No.18 vs.19	58.7 ± 5.32	13.9 ± 2.06	< 0.001**
ALT	Male No.22 vs. 21	58.7 ± 7.07	15.0 ± 2.66	< 0.001**
	Female No.18 vs.19	57.8 ± 6.36	14.0 ± 3.06	< 0.001**

Estimation of Diabetic and Liver Function Parameters in Thalassemia Patients according to Age Group

Table 3-3 showed that both diabetic metabolic and liver function tests parameters not-scored significantly at p. value < 0.01 and p. value < 0.05 in thalassemia-diabetic patients, with except ALP increase with increasing age as shown in table 3-3.

Table 3-3: Diabetic and liver function parameters in patients

Patients	Patients 6 – 15 year	Patients 16 – 25 year	p. value
HbA_1c	7.47 ± 1.80	7.47 ± 1.91	0.545
Insulin	29.4 ± 7.91	28.3 ± 7.84	0.659
FBS	210.6 ± 55.3	216.6 ± 41.4	0.704
HOMA-IR	15.2 ± 5.81	15.2 ± 5.44	0.991
ALP	211.9 ± 30.6	244.6 ± 44.9	0.010
AST	58.0 ± 5.84	59.0 ± 6.42	0.634
ALT	58.3 ± 6.92	58.4 ± 6.60	0.939

Discussion

Iron overload in thalassemia-major patients affects glucose regulation and is mediated through several mechanisms. The pathogenesis of glycemic abnormalities in thalassemia major is complex and multifactorial (Coates *et al.*, 2016). It is mostly attributed to a combination of reduced insulin secretion capacity and insulin resistance. The exact mechanisms responsible for the development from normal glycemia to overt diabetes in these patients are still poorly understood, but are mainly attributed to insulin deficiency caused by the toxic effects of iron deposited in the pancreas and insulin resistance (De la Monte, 2017). The current study recorded a significant increase of diabetic parameters and liver function parameters in thalassemia male and female patients compared with control group, while the results not recorded a significant difference between thalassemia patients according to age, with except ALP scored a significant difference with increasing age. A similar finding to our result recorded by recent study performed by Zhang *et al.* (2021), their study recorded a significant in mean age and diabetic parameters in thalassemia patients and the percent of diabetic among thalassemia patients in Chines population 14.41%, also noted the thalassemia patients with high BMI have lower age mean and high diabetic parameters mean compare with normal BMI patients. In my opinion, the reason for the high rates of diabetes and the decrease in life expectancy for patients with high BMI may be due to the synergistic effect between the amounts of blood transfused and the consequent deposition of iron and to the effect of body mass

on glucose metabolism. A study of Chahkandi *et al.* (2017), in Iran also reported the mean age of thalassemia patients was 14.38 year, and showed the percent of diabetic among thalassemia patients was 14.3%. the high percent of diabetic disease among thalassemia patients may be due to the endocrine gland disorder that results from deposition of iron. The study of Zehra et al. (2018), showed the thalassemia patients suffer from muscle fatigue, weight loss, and polydipsia were the most common endocrine complications. However, when compared according to diabetes status, polydipsia, urination, and weight loss were significant complications in multiple blood transfusion diabetic patients. Au *et al.* (2008), and Li *et al.* (2014), It was investigated that the glucose homeostasis is closely related to iron deposition in the heart but not to iron deposition in liver, which may be attributed to the fact that iron deposition in the liver was easily affected by iron chelation treatment. Therefore, iron deposition in the heart is an effective predictor of diabetes development in patients with beta thalassemia major. Multiple meta-analysis confirmed that the iron overload was common cause of glucose metabolic disorder, but the specific mechanisms were unclear [22, 23]. Serum ferritin and iron deposition are commonly used to assess iron deposition in thalassemia patients. "iron deposition used to assess iron deposition does not appear correct" (Gomber *et al.*, 2018). Forlani et al. (2016), recorded that the relation between ALT/AST and T2D risk might be explained by factors other than non-alcohol fatty liver disease, since circulating ALT/AST are not specific markers of non-alcohol fatty liver disease and can also increase in response to liver injury from other causes, such as drug toxicity and infection. A previous studies of Lazo et al. (2010), and Zou et al. (2018), confirmed that even a slight decrease in serum concentrations of AST and ALT has a significant relationship with decreased liver fat content and cirrhosis. and improvement in insulin resistance. Therefore, it is possible to explain the continuous rise in liver enzymes in thalassemia patients and is related to the increase in the level of liver fat, as well as the high proportion of insulin resistance in thalassemia patients.

Conclusion

The high level of iron deposition in thalassemia patients is one of the main causes of diabetes and endocrine disorders, and the persistently high rate of liver enzymes in patients increases the level of liver fat and increases the proportion of insulin resistance.

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