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Research Article

Frequency of Insulin Resistance in People with Thyroid Dysfunction

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Abstract

Background: Thyroid dysfunction is an endocrine disorder with a recognized association with type 2 diabetes mellitus. Thyroid hormones have a remarkable effect on glucose metabolism and can cause insulin resistance (IR). This study was aimed at assessing the relationship between IR and thyroid dysfunction.

Methods: This case–control study was conducted at the endocrinology outpatient clinics of Ibrahim Malik Hospital and Omdurman Military Hospital in Khartoum State, Sudan between May 2018 and January 2019. Fasting blood glucose (FBG), fasting insulin level, and thyroid function test (TFT) were measured for each candidate and IR was estimated using the HOMA-IR equation.

Results: Thirty-one patients with thyroid dysfunction and fifty-seven control participants were enrolled. The highest mean FBG was found among cases (105.3 ± 15.7 mg/dl) compared to the controls (97 ± 12.1 mg/dl), but the difference was not statistically significant (*P*-value = 0.598). The mean fasting insulin level was 9.22 ± 4 IU/ml in the cases and 9.4 ± 4.2 IU/ml in controls, without a significant difference (*P*-value = 0.681). The highest HOMA-IR score was found among cases (2.4 ± 1.2). It was 2.4 ± 1.3 in hyperthyroidism, 2.3 ± 1.1 in hypothyroidism, and 2.4 ± 1.2 in controls, and the difference was insignificant (*P*-value = 0.859). IR was higher in the cases (58.1%) compared to the controls (52.6%) but again not statistically significant (*P*-value = 0.396). Among cases, IR was encountered in 61.9% and 50% of hyperthyroid and hypothyroid patients, respectively.

Conclusion: Patients with thyroid dysfunction have some level of IR that was not statistically significant when compared with controls.

Keywords: thyroid dysfunction, insulin resistance, type 2 diabetes mellitus

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1. Introduction

Thyroid disorders are the second most common endocrine disorder after diabetes mellitus. The global epidemiology of thyroid disorders varies from one zone to another depending on iodine sufficiency and deficiency in the area. In Sudan, according to a national study conducted in 1997, the overall burden of all types of goiter was 22%, ranging from 5% in Khartoum to 42% in Upper Nile states [1]. On the other hand, the study by Perros *et al.* showed the overall prevalence of thyroid diseases in people with diabetes mellitus was 13.4%. The occurrence of insulin resistance (IR) in patients with thyroid disorders leads to increased morbidity through its role in the existence of the metabolic syndrome [2].

The thyroid hormones thyroxine (T4) and triiodothyronine (T3) have a large effect on glucose metabolism. Maintaining a normal blood glucose level requires a balance between the intake and production, which is organized by hormones that decrease the blood glucose level, such as insulin, and those that increase it, such as thyroid hormone, glucagon, and glucocorticoids [3].

Normally, thyroid hormones stimulate the nuclear transcription of several genes in almost all body cells, leading to higher total cellular metabolic enzymes. Concerning their role in carbohydrate metabolism, in addition to increasing insulin secretion [3], they elevate glucose uptake by cells, increasing gastrointestinal absorption by upregulating glucose transporter 4 (GLUT4), which elaborates glucose transport, and, through the same action, stimulate glycolysis by upregulating phosphoglycerate kinase. Thus, they act synergistically with insulin to improve glucose utilization in the peripheral tissues [4].

In hyperthyroidism (HR), there is high hepatic glucose generation via the aforementioned mechanisms, and elevated fasting postprandial insulin and pro-insulin levels. Moreover, it correlates with IR. In the tissues, it leads to impaired glucose uptake because of insulin insensitivity, which is caused by the secretion of adipokines such as interleukin 6 (IL6) and tumor necrosis factor alpha (TNF alpha) by adipose tissue [5].

In hypothyroidism, numerous in vitro studies were conducted compared to those in humans, and it was found that there is IR in the peripheral tissues caused by deregulated metabolism of leptin [4]. Other features comprise changed blood flow, impaired GLUT4 translocation, reduced glycogen synthesis, and diminished muscle oxidative capacity. In human studies, a decrease in glucose extraction and blood flow in the muscles and adipose tissue of hypothyroid patients was noticed, causing IR [5]. Other aspects of those with subclinical hypothyroidism are impaired lipid regulation and the occurrence of the metabolic syndrome [4].

IR is characterized by insufficient tissue response to the action of insulin, causing high insulin secretion which leads to metabolic abnormalities such as cardiovascular disease, type 2 diabetes mellitus, polycystic ovary syndrome, nonalcoholic fatty liver disease, and others [6].

This study investigates the relationship between IR and thyroid disorders compared to healthy individuals.

2. Materials and Methods

This case–control study was conducted at the endocrinology outpatient clinics of Omdurman Military Hospital and Ibrahim Malik Hospital (Khartoum, Sudan) between May 2018 and January 2019.

Thirty-one patients with thyroid dysfunction and fifty-seven control participants were randomly enrolled in the study. All patients with a history of thyroidectomy, diabetes mellitus, chronic kidney disease, multiple comorbidities, and pregnant women were excluded.

Moreover, 6 ml of venous blood was drawn from all candidates for testing insulin, glucose levels, and thyroid hormones. The blood samples were stored at –20°C until all samples were collected and were then tested at the same time.

The reference values were as follows: thyroid-stimulating hormone (TSH): 0.4–7.8 mU/l, T3: 0.8–3.0 nmol/l, T4: 50–150 nmol/l, fasting blood glucose (FBG) < 100 mg/dl, and insulin level: 1.1–32.0 IU/ml.

HOMA-IR stands for Homeostatic Model Assessment of IR. This is an equation that helps calculate the presence and extent of IR in an individual. It reveals the dynamics between the baseline FBG and the amount of insulin produced in response. Low HOMA-IR means good insulin sensitivity. A small amount of insulin is sufficient to maintain glucose homeostasis, while a higher HOMA-IR denotes more IR.

The healthy IR range is 0.5–1.4; <1.0 indicates optimal insulin sensitivity; >1.9 indicates early IR; and >2.9 indicates significant IR.

HOMA-IR equation = (Fasting glucose [mg/dL] × fasting insulin [µU/mL] / 405).

All subjects were given verbal and written information concerning the study and, after entering the study, signed a written consent form regarding all information received. The study protocol was approved by the Ethics Committee of the Sudan Medical Specialization Board (SMSB), the Director of the Omdurman Military Hospital and Ibrahim Malik Hospital.

2.1. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS v.21.0). The analyzed data are presented in tables designed by Microsoft Excel 2010. The ANOVA test was used for continuous variables and the Chi-Square test for categorical variables. Also, Pearson's correlation was used between HOMA-IR score and thyroid profile among the case group. The *P*-value was considered as significant at the level of 0.05.

3. Results

This study enrolled 31 thyroid disease patients (21 with HR and 10 hypothyroidism) as a case group and 57 normal individuals as a control group. Table 1 presents the demographic characteristics of the participants.

The thyroid function test (TFT) profile showed that TSH was significantly higher in controls than in hypothyroidism and HR patients (4.6 mU/l [1.7–7.2] vs 2.1 mU/l [0.6–14.4] vs 0.6 mU/l [0.005–15.4]; *P*-value = 0.001), T3 was higher among HR patients than in hypothyroidism and control group, it was 4.3 nmol/l (0.38–102.7) vs 1.5 nmol/l (0.46–16.9) vs 1 nmol/l (0.8–2.0), respectively; *P*-value = 0.001. Similarly, T4 was significantly higher among HR patients compared to hypothyroidism and controls 101 nmol/l (14–338) vs 79 nmol/l (3.9–116) vs 93 nmol/l (67–134), respectively; *P*-value = 0.001. The highest mean of FBG was found among HR patients (108.8 ± 16.5 mg/dl) followed by controls (97 ± 12.1 mg/dl) and hypothyroidism (91.9 ± 28.7 mg/dl), but the difference was not statistically significant (*P*-value = 0.598). The mean fasting insulin level was 10.1 ± 3.3 IU/ml in hypothyroidism, 9.4 ± 4.2 IU/ml in controls, and 8.8 ± 4.3 IU/ml in HR, without a statistically significant difference (*P*-value = 0.681). The highest HOMA-IR score was found in HR (2.4 ± 1.3) followed by hypothyroidism (2.3 ± 1.1) and controls (2.2 ± 1.1), and the difference was not significant (*P*-value = 0.859) (Table 2).

Table 3 illustrates that patients in the case group (58.1%) showed more IR than those in the control group (38.6%), however, the difference was not statistically significant (*P*-value = 0.396).

Table 4 reveals that IR occurred in 61.9% of HR patients and in 50% of hypothyroidism patients without a statistically significant difference (*P*-value = 0.403).

By using Pearson's correlation, the HOMA-IR score exhibited a weak, insignificant negative correlation with TSH levels (r = –0.175; *P*-value = 0.345) and T4 levels (r = –0.224; *P*-value = 0.216), and a weak positive correlation with T3 levels (r = 0.092; *P*-value = 0.623) (Table 5).

4. Discussion

The aim of this study was to assess the relation between IR and thyroid dysfunction, to find out if there is a link between hypo/HR and fasting insulin levels and IR, and to compare the presence of IR in people with thyroid dysfunction and healthy people without thyroid disorder.

The study did not show a significant difference in both insulin levels (*P*-value = 0.681) and HOMA-IR scores (*P*-value = 0.859), as well as IR (*P*-value = 0.396), and this could be due to the small sample size and the patients were using their anti-thyroid drugs or thyroxine, which may have affected the results.

Despite it being insignificant, FBG was higher in HR patients than in controls and hypothyroidism patients (108.8 ± 16.5 mg/dl vs 97 ± 12.1 mg/dl vs 91.9 ± 28.7 mg/dl; *P*-value = 0.598). This is supported by Ohguni *et al.*, who cited that there was no statistically significant difference in fasting plasma glucose among thyroid disease patients and controls [7]. However, on the other hand, Maratou *et al.* reported HR and subclinical hyperthyroidism (SHR) had higher glucose levels compared to the euthyroid group ($P < 0.05$) [8].

Insignificantly, fasting insulin is greater in hypothyroid patients (10.1 ± 3.3 IU/ml) followed by controls (9.4 ± 4.2 IU/ml) and HR (8.8 ± 4.3 IU/ml). The first part is supported by Purohit *et al.*, as they found insulin levels were greater in the hypothyroid group followed by the hyperthyroid and euthyroid groups [9]. This is also supported by other studies done on subclinical hypothyroidism [10, 11], and on hypothyroidism and subclinical hypothyroidism versus euthyroid [12]. In contrast, Kunal *et al.* (2012) reported insulin levels were raised in HR more than in hypothyroidism and euthyroid state. In our study, insulin levels in hyperthyroid patients were lower than in controls, which could be due to the effect of medications.

The study demonstrated that HOMA-IR scores were higher in HR (2.4 ± 1.3) than in hypothyroidism (2.3 ± 1.1) and in controls (2.2 ± 1.1). In addition, IR was encountered in 61.9% and 50% of hyperthyroid and hypothyroid patients, respectively. This relation is supported by previous statistically significant studies which found HOMA values were significantly higher in the hyperthyroid and hypothyroid groups as compared to the EU group [13], and other two studies done on subclinical hypothyroidism/subclinical and overt hypothyroidism [14, 15]. However, another study reported the opposite of the above mentioned, citing that HOMA-IR is greater in hypothyroid (17.29 ± 15.61) and lower in hyperthyroid (1.72 ± 2.46) compared to euthyroid (3.33 ± 0.78) [9].

The main limitation of this study is the small sample size, and the current use of medications affects thyroid functions as well as IR parameters.

5. Conclusion

IR affects both hypo and HR due to high insulin secretion and impaired tissue sensitivity to it.

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Ethical Considerations

Ethical clearance was obtained from the Council of Internal Medicine, Sudan Medical Specialization Board (SMSB). All enrolled patients signed a written consent form before they

joined the study groups.

Competing Interests

The authors declare that they have no competing interests to disclose.

Availability of Data and Material

All data is available upon request.

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Table 1: The characteristics of the study group.

	Case (N = 31)	Control (N = 57)	P-value
Age (yr)			
<30	14 (45.2%)	33 (57.9%)	0.503
30–50	15 (48.4%)	23 (40.4%)	
51–70	2 (6.5.%)	1 (1.8%)	
Gender			
Female	29 (93.5%)	55 (96.5%)	0.442
Male	2 (6.5%)	2 (3.5%)	
BMI (kg/m^2)			
Underweight	0 (0%)	10 (17.5%)	0.070
Normal	21 (67.7%)	27 (47.4%)	
Overweight	5 (16.1%)	11 (19.3%)	
Obese	5 (16.1%)	9 (15.8%)	
Thyroid disorder			
Hyperthyroidism	21 (67.7%)	—	
Hypothyroidism	10 (32.3%)	—	

BMI: Body mass index.

Table 2: The laboratory investigations of study group.

	Hyperthyroidism (N = 21)	Hypothyroidism (N = 10)	Control (N = 57)	P-value
TSH (mU/l); Median (max–min)	0.6 (0.005–15.4)	2.1 (0.6–14.4)	4.6 (1.7–7.2)	0.001
T3 (nmol/l; Median (max–min)	4.3 (0.38–102.7)	1.5 (0.46–16.9)	1 (0.8–2.0)	0.001
T4 (nmol/l); Median (max–min)	101 (14–338)	79 (3.9–116)	93 (67–134)	0.001
FBG (mg/dl); Mean ± SD	108.8 ± 16.5	91.9 ± 28.7	97 ± 12.1	0.598
Fasting insulin (IU/ml); Mean ± SD	8.8 ± 4.3	10.1 ± 3.3	9.4 ± 4.2	0.681
HOMA-IR score; Mean ± SD	2.4 ± 1.3	2.3 ± 1.1	2.2 ± 1.1	0.859

TSH: Thyroid stimulating hormone; T3: Triiodothyronine; T4: Thyroxine; FBG: Fasting blood glucose; IR: Insulin resistance.

Table 3: The distribution of insulin resistance among the study group.

	Case (N = 31)	Control (N = 57)	P-value
Insulin resistance			
Yes	18 (58.1%)	30 (52.6%)	0.396
No	13 (41.9%)	27 (47.7%)	

Table 4: The insulin resistance among hypothyroidism and hyperthyroidism patients.

	Hypothyroidism (N = 10)	Hyperthyroidism (N = 21)	P-value
Insulin resistance			
Yes	5 (50%)	13 (61.9%)	0.403
No	5 (50%)	8 (38.1%)	

Table 5: The Pearson's correlation between HOMA-IR score and thyroid profile among case group.

	Correlation coefficient (r)	P-value
HOM-IR *TSH	–0.175	0.345
HOM-IR *T4	–0.23	0.216
HOM-IR *T3	0.092	0.623

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