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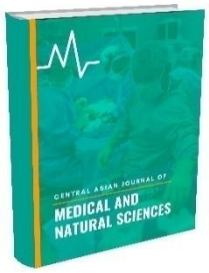

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The relationship between leptin, thyroid hormone and insulin resistance in obese diabetic patients

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Abstract: Background; Globally, obesity is a health crisis. Obesity raises the risk of CVD, T2DM, musculoskeletal problems, digestive system diseases, respiratory issues, and psychological issues that might interfere with daily life. It might kill you. Overweight and obesity are health risks, according to the World Health Organization. A BMI of 30 kg/m2 or higher defines obesity. Type 2 diabetes and obesity are intricately related. Type 2 diabetes patients are 90% overweight. Insulin resistance, a key pathogenesis of type 2 diabetes, is mediated by obesity-induced chronic inflammation. In obese diabetic patients, we examined the diagnostic and follow-up value of specific adipokines(Leptin) and thyroid indicators (FT3,FT4,TSH).
Methodology: The study comprised 50 overweight and 50 obese women, as well as a control group of 70 healthy, normal-weight women who came to Thi-qar to attend the Al-habobi and AL-naseriah Teaching Hospital between October 1, 2022, and February 2, 2023. Leptin was measured using an enzyme-linked immunosorbent assay (ELISA). Thyroid hormone (FT3, FT4, and TSH) was also measured using an electrochemiluminescence (ECLIA) immunoassay. FBS was measured using a colorimetric technique, while HBA1C was measured using a fluorescence immunoassay (FIA).
Results; Leptin levels were significantly lower in obese diabetic patients compared to age-matched healthy controls, and FT4 levels were significantly lower in obese diabetic patients compared to age-matched healthy controls, according to the current study. Instead, FT3 and

TSH are increased.
Conclusions: From our results, we can conclude the relashinship between thyroid hormone and leptin have a value in the diagnosis and follow-up of a patient's obese diabetic.
Key words: obesity, adipocytokines, biomarkers, type 2 diabetes Mellitus, hypothyroidism

Introduction

An increase in body mass index (BMI) indicates an increase in mortality risk, and severe obesity (i.e., a body mass index > 35 kg/m 2) is currently a rapidly expanding segment of the worldwide epidemic (Frühbeck et al., 2013).

Obesity is the main cause of many long-term diseases, like high blood pressure, diabetes type 2, coronary artery disease, and some types of cancer. type 2 diabetes is most strongly associated with obesity (Fried et al., 2013; Frühbeck et al., 2013; Dyson, 2010) There is a close link between obesity and type 2 diabetes. 90% of patients with type 2 diabetes are overweight (Ahmed et al., 2019).

(DM) affects glucose, protein, and fat metabolism. This syndrome is caused by beta-Langerhans islet cell dysfunction or peripheral tissue insulin uptake. T1DM and T2DM are its main types of DM (Ahmed et al., 2019).

Insulin resistance (IR) is defined by either a reduced metabolic response of target cells to insulin or an impaired blood glucose-lowering effect of circulating insulin. It is a precursor to type 2 diabetes and a hallmark of obesity and inactivity (Burrows et al., 2017).

Obesity-related chronic inflammation contributes significantly to the development of insulin resistance, a key pathogenesis of type 2 diabetes (Johnson et al., 2012).

Adipose tissue (AT) contains adipose cells, immune system cells, endothelium cells, and stem/stromal cells. These cell types enable the tissue function as an endocrine organ, energy storage, and energy metabolism (Vegiopoulos et al., 2017).

Leptin comes from white adipose tissue. Leptin acts on cell-surface leptin receptors. Neuronal, hepatic, pancreatic, cardiac, and intestinal tissue have leptin receptors (Peelman et al., 2014).

Thyroid dysfunction is the most frequent metabolic condition after diabetes. Many factors—biological and geographical—affect thyroid dysfunction. In recent decades, researchers have studied thyroid hormones' regulation of human adipose tissue metabolism to better understand obesity's pathophysiology, therapeutic implications, and prospective medication discoveries (Sajjadi-Jazi et al., 2018).

Methodology

This case-control study included 50 overweight women and 50 obese women. The median age of the participants in the study was 35. A control group of 70 healthy, normal-weight women was also included in the study. A group visited thi-qar to see the Al-Habibi and AL-nasiriyia Teaching Hospitals. Doctors at Al-Habibi Teaching Hospital and Al-Mariah Teaching Hospital examined patients for this study between October 1, 2022, and February 2, 2023. We excluded men and also excluded women under the age of 30 years without taking into account the incidence of a specific

disease special thyroid dysfunction. Blood samples for the measurement of serum leptin, FT3, FT4, TSH, HBA1C, FBS, and C.peptide A total of 5 ml of blood was drawn from each patient and control subject; 2 ml were placed in an EDTA tube for HBA1C testing within 30 minutes, and the remaining 3 ml were placed in sterile gel tubes and allowed to coagulate at room temperature for 30 minutes before being centrifuged for 15 minutes at a speed of 3000 rpm to separate the components. The serum should be separated and kept at a temperature of -20 degrees Celsius until use. leptin were assayed by an enzyme-linked immunosorbent assay (ELISA), according to the operational manual of Snlog, China. FT3, FT4, TSH, and C. peptide performed with immunoassay using electrochemiluminescence (ECLIA) kits are compatible with Analyzers for immunoassays such as the Elecsys and the Cobas E411, according to the operational manual of ROCH, Germany. HBA1C is performed by fluorescence immunoassay (FIA) using AFIAS-6, according to the operational manual of Bodytech, S. Korea. FBS is performed by the colorimetric method by using a spectrophotometer, according to the operational manual of BIOLABO, France.

Statistical Analysis

The statistically significant differences were determined using SPSS (version 26).

Results

Table (1) shows that results revealed a significant decrease of leptin in obese diabetic patients in comparison with a control group (117.91±21.21 vs 212.10±32.58 pg/ml, P <0.001).

Table (1): Differences in Adipocytokine(hormone), leptin levels between obese diabetic patients and control.

parameters	Control mean±SD	Obese diabetic mean±SD	P.value
Leptin pg/ml	212.10±32.58	117.91±21.21	<0.001

Compared with healthy control: *** P<0.001, ** P<0.01

Table (2) shows that results revealed a significant increase of FT3 in obese diabetic patients in comparison with the control group (5.81±0.36 vs 3.94±0.26 pmol/L, P <0.001) respectively. The results of this study showed that there is a decrease significantly in FT4 among obese diabetic patients in comparison with the control group (14.12±0.46 vs 16.12±0.42 pmol/L, P <0.001) respectively. Moreover, there is an increase significant between the levels of TSH in the obese diabetic patient compared with a control group (2.83±0.07 vs 1.47±0.51 µIU/mL, P <0.001) respectively.

Table (2): The serum levels of thyroid hormone (FT3, FT4, and TSH) in obese diabetic patients compare to the control group.

parameters	Control mean±SD	Obese diabetic mean±SD	P.value
FT3 pmol/L	3.94±0.26	5.81±0.36	<0.001
FT4 pmol/L	16.12±0.42	14.12±0.46	<0.001
TSH µIU/mL	1.47±0.51	2.83±0.07	<0.001

Compared with healthy control: *** P<0.001, ** P<0.01

Discussion

the results showed a significant decrease in leptin concentration between the diabetic obese group compared to the control group P value (<0.001). This research corresponds to (Flier & Maratos-Flier, 2017a; Paz-Filho et al., 2015; Peelman et al., 2014; Wasim et al., 2016) (P >0.001,0.009,0.012). his decrease because of mutations in LEP or the LR gene and are known as congenital leptin deficiencies (CLD) (Farooqi & O'Rahilly, 2014). Genetic mutations in the leptin pathway can be a cause of human obesity and leptin deficiency. It is still unknown whether leptin can be effective in the treatment of fully established morbid obesity and its endocrine and metabolic consequences in adults (Licinio et al., 2004a). Leptin exerts immediate effects by acting on the brain to regulate appetite. Via ObRb-receptor binding in the hypothalamus, leptin activates a complex neural circuit comprising of anorexigenic (i.e. appetite-diminishing) and orexigenic (i.e. appetite-stimulating) neuropeptides to control food intake. Outside of the hypothalamus, leptin interacts with the mesolimbic dopamine system, which is involved in motivation for and reward of feeding, and the nucleus of the solitary tract of the brainstem to contribute to satiety. leptin in regulating energy and food consumption. When leptin decreases, the body gives a clear nervous signal of hunger and insufficient energy, which leads to increased appetite and food intake, in addition to lack of exercise, lack of adherence to a healthy diet, and consumption of carbohydrates in large quantities with sugars. This leads to obesity. This search is not compatible with (Flier & Maratos-Flier, 2017b). the result show increases significantly in leptin concentration in obese diabetics compared to the control group(P>0.001) As leptin reduces appetite and body weight, the paradoxical coexistence of obesity and hyperleptinemia suggests the pathology of "leptin resistance. Leptin resistance can be due to a defect in the intracellular mechanism or due to impairment in transport through the blood-brain barrier (Farr et al., 2015).

The results in this research showed, after calculating the concentration of thyroid hormones, that there is a significant increase in the hormone FT3 in obese diabetic patients included in the research compared to the control group (P<0.001). The results also showed a significant decrease in the hormone FT4 in obese diabetic patients included in the research, compared to the control group (P<0.001). Also, there was a significant increase in hormone TSH in obese diabetic patients included in the research, compared to the control group (P<0.001). The results of this search are consistent (Reinehr et al., 2006). the result showed TSH levels are at the upper limit of the normal range or slightly increased in obese children, adolescents, and adults and are positively correlated with BMI and Low fT4 with a moderate increase in T3 or free T3 (fT3) levels has been reported in obese subjects (Tagliaferri et al., 2001). One theory suggests an increased deiodinase activity leading to a high conversion rate of T4 to T3.

Further explanation is that inflammatory cytokines secreted from adipose tissue such as tumor necrosis factor-alpha, interleukin (IL)-1, and IL-6, inhibit sodium/iodide symporter mRNA expression and iodide uptake activity. A fall in leptin acts through the hypothalamus to increase appetite, decrease energy expenditure, and modify the neuroendocrine function in a direction that favors survival. As with the mouse gene, mutation of the human leptin receptor gene can also cause obesity with central hypogonadism and hypothyroidism. Leptin stimulates TRH secretion in the hypothalamus. Leptin produced in the pituitary is capable of inhibiting TSH secretion. Leptin secretion from adipose tissues

is regulated by stimulatory factors such as TSH, glucocorticoids, T4 and T3, and insulin as well as inhibitory factors such as cold and free fatty acids (Ahima et al., 1996b; Clement et al., 1998). One of these adipokines is Leptin which seems to be a promising link between obesity and alterations of thyroid hormones. The interrelation between leptin and TSH is bidirectional since TSH stimulates leptin secretion in addition leptin regulates TSH secretion as it promotes thyrotropin-releasing hormone gene expression directly in the paraventricular nucleus, ultimately stimulating TSH release (Sanyal & Raychaudhuri, 2016). This search is not compatible with (Chomard et al., 1985). In concordance with the hypothesis of increased thyroid hormone levels in obesity, and as the opposite, low TSH levels and low fT3 concentrations, increase in weight regain (Reinehr et al., 2008). Low T3 concentrations in patients may be due to impaired peripheral conversion of T4 to T3 associated with the altered nutritional state.

Obesity escalates the pathogenesis of T2DM through stimulation of insulin resistance. T2DM treatment has been restricted by little understanding of insulin resistance. However, several studies described the association between mitochondrial dysfunction, inflammation, hyperinsulinemia, and lipotoxicity with insulin resistance. Endoplasmic reticulum stress, oxidative stress, genetic background, aging, hypoxia, and lipodystrophy are also stated in the pathogenesis of T2DM through induction of insulin resistance (Pittas et al., 2004).

Conclusion

We can conclude from the results obtained for adipokines (leptin) and thyroid hormones (FT3, FT4, TSH) that there is a strong link between thyroid hormones and leptin and can be used for treatment and follow-up of people with obesity and diabetes around the world.

Declaration

Ethical approval is Not applicable.
Consent to participate is Not applicable.
Consent for publication is Not applicable.
Competing interests, the authors declare no competing interests

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