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Hashimoto Thyroiditis and Increased Blood Glucose Level

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Abstract:

Hashimoto Thyroiditis (HT), also known as chronic lymphocytic thyroiditis is an autoimmune disease in which the thyroid gland is gradually destroyed, that result in hypothyroidism. It should be noted that the thyroid hormones directly control insulin secretion, that's why in hypothyroidism the low levels of thyroid hormones will result in a reduction in glucose-induced insulin secretion by beta cells. This may result in many metabolic abnormalities as well as multiple clinical symptoms. Some studies suggest that blood sugar may be affected in hypothyroidism and levels may increase, which explains why there is an underlying connection between diabetes mellitus and thyroid dysfunction. Thyroid hormone analogs are used as management of thyroid dysfunction and diabetes mellitus type 2 (T2DM), but their effect on bone, muscles, and heart are major hurdles. This study aims to determine if there is a connection between hyperglycemia and HT and whether HT gets worse with hyperglycemia. It could be affirmed that a poor lifestyle or being diabetic could increase the risk for HT especially if you have genetic susceptibility to develop it. Results: there is a direct correlation between hyperglycemia and HT, this relationship is due to insulin resistance that occurs in HT which can lead to hyperglycemia and can result in diabetes. Conclusion: there are many factors involved in the homeostasis of blood glucose levels such as intact insulin secretory response. And not every HT patient is diabetic and not every diabetic patient has HT.

Introduction:

Hashimoto thyroiditis is a destructive autoimmune disease that targets the thyroid gland and causes hypothyroidism. It is characterized by gradual thyroid failure secondary to the autoimmune destruction of the thyroid gland. It is most prevalent between 45 and 65 years of age and is more common in women. It is caused by an immune response to thyroid autoantigens [1]. It should be noted that thyroid hormones have a profound influence on various physiological processes ranging from the metabolism of lipid, protein, and carbohydrate [4]. Type 2 diabetes mellitus (T2DM) has a close underlying pathology with thyroid dysfunction this association in part due to the shared risk factors between HT and T2DM such as high levels of estrogen, polycystic ovarian syndrome (PCOS), increasing age, and being overweight. Insulin resistance is also associated with thyroid dysfunction. The connection between T2DM and HT could be proven in a reported case in 2018, a 7-year-old female who had a 25-year history of T2DM diabetes and a 1-year history of chronic thyroiditis [8]. Another important fact to point out is that there are many complications to HT such as differentiated thyroid cancer (DTC) [7]. And mention must be made that DTC incidence is increasing by 6.5% making it fastest-growing cancer among Americans accompanied by an increased incidence of HT [7].A further complication of HT includes goiter and hypothyroidism count as the most common cause of it, an increased risk of heart disease, primarily because of high levels of low-density lipoprotein (LDL), problems of mental health such as depression. Myxedema as a result of untreated HT, this unusual, life-threatening condition can develop due to long-term extreme hypothyroidism, birth defects: children born to women with untreated- hypothyroidism due to Hashimoto's disease may have a higher risk of birth defects than Do babies born to healthy mothers [9].

A connection between inflammation and cancer has been recognized for over a century [7]. Another important connection to be recognized is the connection between hyperglycemia and HT.

Aim of the study:

To find the correlation between increased blood glucose levels and Hashimoto thyroiditis. To conclude if hyperglycemia worsens the condition of Hashimoto thyroiditis. Whether the hyperglycemia in Hashimoto thyroiditis results from poor diet management or common complications of HT such as diabetes mellitus.

Materials and Methods:

A study has been done by (Gierach M, Gierach J, Skowrońska A, Rutkowska E, Spychalska M, Pujanek M, Junik R.).In which 54 patients diagnosed with Hashimoto thyroiditis have been examined by researchers based on clinical picture and examination: autoantibodies (Anti-thyroid peroxidase anti-TPO) and Anti-Thyroglobulin (anti-Tg)[5]. Another study was done. The study was a prospective study was conducted in the Department of Endocrinology and Metabolism at a tertiary care center in India [9].

The period of the_study: The study period was from March 2012 to August 2013. The criteria for patients participating in the study: Patients ages were from 20 years and older, with a biochemical diagnosis of overt hypothyroidism have been recruited for the study. Patients satisfying glucose-based criteria for diabetes mellitus as recommended by the American Diabetes Association (ADA) have been from the study. Suspected or known cases of chronic kidney disease, abnormal hemoglobinopathy, hemolytic disorder, reticulocytosis, bone marrow disorders like aplastic anemia, myelodysplastic syndrome or recent (< 3 months) blood transfusion have also been excluded from the study [9].

Results:

Insulin resistance has been shown to be caused in hypothyroidism in various in vitro and where It was found that peripheral muscles became less responsive in hypothyroid condition. A direct relation between hypothyroidism and insulin resistance has been demonstrated by various authors. Other studies reported that thyroid hormones are necessary for the mobilization of the tissue lipids especially brown adipose tissues (BATs) which are the fuel for the production of heat. Hypothyroidism and decreased thyroid hormone level are responsible for decreased thermogenesis in BAT. Lipogenesis is an important factor for thermogenesis mediated by thyroid hormone [4]. In table 1 patients were re-evaluated 3 months after restoration to the euthyroid state. Following the correction of T4 and to 105.7 ± 36.9 ng/mL and TSH to 2.5 ± 3.5 μIU/mL, there was a reduction in the mean body weight by 3.5 kg. Likewise, there was an improvement in the hemoglobin from 11.7 ± 1.9 gm/dL to 12.1 ± 1.6 gm/dL. This was accompanied by a rise in the reticulocyte percentage from 0.9 ± 0.6% to 1.2 ± 0.7%. There was a fall in the HbA1c from 5.8 ± 0.7% to 5.6 ± 0.5% following correction of hypothyroidism, but there were no corresponding changes in Oral glucose tolerance test OGTT. Fasting glucose result was 86.8 ± 11.0 mg/dl (pre-therapy) and 87.5 ± 9.1 mg/dl (post-therapy), while the post glucose tolerance test 2 hours plasma glucose was 123.4 ± 35.6 mg/dl (pre-therapy) and 127.0 ± 28.8 mg/dl (post-therapy).[9]

Table 1. Comparison of anthropometry, hematological parameters, thyroid profile, glycemic indices and proportion of patients with abnormal glycemic parameters before and 3 months after the correction of hypothyroidism in 38 patients.

Parameter	**Pre therapy** **N = 38**	**Post therapy** **N = 38**	**P value**
Weight (kg)	61.0 ± 13.2	57.5 ± 14.3	0.004
BMI (kg/m2)	25.0 ± 4.2	24.1 ± 4.3	0.039
T4 (ng/mL)	12.6 ± 13.4	105.7 ± 36.9	< 0.001
TSH (μIU/mL)	98.1 ± 63.7	2.5 ± 3.5	< 0.001
Hb (gm/dL)	11.7 ± 1.9	12.1 ± 1.6	0.044
Reticulocyte (as % of total RBCs)	0.9 ± 0.6	1.2 ± 0.7	0.046
FPG (mg/dL)	86.8 ± 11.0	87.5 ±9.1	NS
PGPG (mg/dL)	123.4 ± 35.6	127.0 ± 28.8	NS
HbA1c (%)	5.8 ± 0.7	5.6 ± 0.5	0.009
No. (%) of patients with IFG (FPG ≥ 100 mg/dL)	4 (10.5%)	5 (13.1%)	NS
No. (%) of patients with IGT (PGPG ≥ 140mg/dL)	11 (29%)	11 (29%)	NS
No. (%) of patients with IFG and /or IGT	12 (31.6%)	15 (39.4%)	NS
No. (%) of patients with HbA1c ≥ 5.7	25 (65.7%)	17 (44.7%)	0.008
No. (%) of patients with HbA1c ≥ 5.7 with normal FPG and PGPG	16 (42.1%)	7 (18.4%)	0.035
No. (%) of patients with HbA1c ≥ 6.5%	7 (18.4%)	4 (10.5%)	< 0.001

BMI: body mass index; T4: thyroxin; TSH: thyroid-stimulating hormone; Hb: hemoglobin; FPG: fasting plasma glucose; PGPG: post glucose tolerance test 2 hours plasma glucose; HbA1c: glycated hemoglobin; IFG: impaired fasting glucose; IGT: Impaired glucose tolerance; NS: not significant ($p > 0.05$).Normal values T4: 55-135 ng/mL, TSH 0.5-5.0 μIU/mL, Hb: 12-14 gm/dL in females and 14-16 gm/dL in males, Reticulocyte (%)-0.5-1.5%. FPG < 100 mg/dL, PGPG < 140 mg/dL, HbA1c < 5.7%.[9]

Discussion:

The inciting events leading to the autoimmune response have not been fully elucidated, but multiple immunologic mechanisms that may contribute to thyroid cell damage have been identified including the following: CD8+ cytotoxic T-cell–mediated killing of thyroid epithelial cells. Cytokine-mediated cell death. T-cell activation leads to the production of an inflammatory cytokine such as interferon-γ in the thyroid gland, with resultant recruitment and activation of macrophages and damage to follicles. Binding of anti-thyroid antibodies (anti-thyroglobulin, and anti-thyroid peroxidase antibodies), followed by antibody-dependent cell-mediated cytotoxicity[1]. Blood sugar imbalances have been described as adding "fuel to the fire" in autoimmune thyroid disease by many practitioners who focus on reversing Hashimoto's[3]. This correlation is due to when there is a decrease in levels of thyroid hormone lead to decrease in metabolic rate, that result in low blood glucose levels that stimulates glucagon release from alpha cells of pancreas of which will result in hyperglycemia, in other words, low levels of thyroid hormone will cause a defective insulin secretion that leads to various metabolic anomalies in T2DM, spanning from hyperglycemia due to defective insulin-stimulated glucose uptake and upregulated hepatic glucose production, along with dyslipidemia, which includes impaired

homeostasis of fatty acids, triglycerides, and lipoproteins[4]. Another hypothesis is increased stress to the body will cause damage to the thyroid. When blood sugar levels are constantly fluctuating, the body experiences it as chronic stress. When the adrenals become stressed, they release an excess of the hormone cortisol, which can also lead to increased production of inflammatory proteins that are associated with a heightened immune response. This pattern eventually leads to an altered release of cortisol, which can, in turn, lead to numerous symptoms, including chronic fatigue, mood swings, and increased thyroid antibodies[3]. Hypothyroidism may falsely increase the levels of the HBA1C test, This may lead to errors in diagnosing pre-diabetes and diabetes in patients with hypothyroidism[2]. Preclinical investigations have demonstrated that carbohydrate response element-binding protein (ChREBP) is the pivotal transcription factor modulating the stimulation of hepatic lipogenesis mediated by glucose. It is the primary target of thyroid hormones in liver and white adipose tissues. ChREBP has been reported to be regulated by thyroid receptor-beta TRβ only and not by thyroid receptor-alpha TRα in liver and white adipose tissue[4]. It is worth considering that insulin resistance has been a proven condition in hyperthyroidism as well as hypothyroidism. Insulin resistance also leads to impaired lipid metabolism according to recent findings. Hence, it appears that insulin resistance is a possible link between T2DM and thyroid dysfunction. Insulin resistance and β cell function are inversely correlated with thyroid-stimulating hormone TSH which may be explained by insulin-antagonistic effects of thyroid hormones along with an increase in TSH. The higher serum TSH usually corresponds to lower thyroid hormones via a negative feedback mechanism. As TSH increased, thyroid hormones decreased and insulin-antagonistic effects are weakened. These observations demonstrate that insulin imbalance is closely associated with thyroid dysfunction and the phenomenon id mediated via β cell dysfunction.[4]

Conclusion:

There is a direct link between thyroid dysfunction and diabetes mellitus both type 1and type 2. Hashimoto's thyroiditis can lead to diabetes mellitus, and diabetes mellitus can result in autoimmune diseases such as Hashimoto's thyroiditis. Recent findings have evidenced the intricate bond between subclinical hypothyroidism and diabetes mellitus that deceptively contribute to major complications such as retinopathy, neuropathy, and cardiovascular events. It also can cause other autoimmune diseases such as Systemic lupus erythematosus (SLE). Not every diabetic patient has thyroid dysfunction and not every individual with thyroid dysfunction is necessarily diabetic. Hashimoto thyroiditis can be managed with a correct diet that is low in carbohydrates and low levels of refined sugar and a healthy lifestyle.

Future work:

More inclusive research on wither a poor lifestyle alone can be a risk factor to develop Hashimoto's thyroiditis, or if genetic susceptibility is necessary to develop this disease. To research if there is another solution other than thyroid hormone analogs as therapy for Hashimoto's thyroiditis due to its major side effects. Whether genetic screening of expecting mother can predict if the child will develop a thyroid dysfunction, or screening of diabetic patients to see if they can develop it.

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