

AN ELUCIDATORY REVIEW OF THE ASSOCIATION BETWEEN THYROID DISORDERS AND DIABETES

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ABSTRACT

Thyroid disease and Diabetes (type 1 and type 2) are known to be pathophysiologically associated. The implications of the associations have clinically relevant implications for insulin sensitivity and adequate management requirements. Interconnectedness of common signalling pathways forms the pathophysiological basis of this association. In the case of type 1 diabetes and autoimmune thyroid disease, linked genetic susceptibilities may be involved. Interactions between thyroid hormone and the basal mechanisms controlling appetite, energy expenditure and insulin sensitivity regulation / secretion governance are also significant to understand. A clearer understanding of the interactions between diabetes mellitus and thyroid hormones has the potential to assist in optimization of treatment in a select group of diabetic patients.

Key-Words: Diabetes Mellitus; Thyroiditis; Adipokines; Leptin

Introduction

Thyroid disorders and diabetes mellitus are two commonly encountered endocrine disorders managed by physicians in daily clinical practice. An observable and documented association between their pathological processes is documented and of benefit to treating physicians in further understanding the cause and thus management of these conditions.^[1] Thyroid hormones contribute to regulatory mechanisms in carbohydrate metabolism and pancreatic function, and the diabetic state affects thyroid function tests to variable extents. Varieties of thyroid abnormalities may coexist and interact with diabetes mellitus. The hypo and hyperfunction of the thyroid gland influences carbohydrate metabolism at the level of the functional unit of the pancreas: the islet cell, and GLUT governed glucose metabolizing biological cellular targets, posing important therapeutic and diagnostic intricacies. Moreover, thyroidal and islet cells are affected by diseases that are clinically and genetically associated, and where parallel autoimmune pathogenesis may be suspect.^[2]

Prevalence Of Thyroid Disorders

An observable statistic is that individuals with

diabetes have increased prevalence of thyroid disease. Approximately 6% of a randomized sample population have some form of thyroid disorder as a statement of general prevalence. However, the prevalence of diagnosed thyroid pathology increases to over 10% in the diabetic subset of the population sample. Patients of Type 1 diabetes have an even higher risk of autoimmune thyroid disorders. Studies indicate that up to 30% of women with Type 1 diabetes have some form of autoimmune thyroid disease. The prevalence of postpartum thyroiditis in diabetic patients reaches a three-fold increase relative to a healthy sample. Various data also indicates a higher than normal prevalence of thyroid disorders in type 2 diabetic patients, especially hypothyroidism being the most common entity thereof.

Thyroid disorders are the second most common disorders after diabetes in the United States, affecting up to 27 million Americans, wherein up to half this number may remain undiagnosed. Thus, the cross between the two populations is large and there is an augmented risk for individuals to be affected by both thyroid and diabetic disease simultaneously. Studies report that approximately 4 million people in the USA are

hypothyroid and receive thyroxine replacement therapy annually. However, hyperthyroidism is much less common, with a female-to-male ratio of 9:1. Young adults are primarily affected by Grave's disease whereas Toxic multinodular goitres tend to affect advancing age groups.^[3]

Frequency of Thyroid Disorders in the General Population and in Patients with Diabetes

Thyroid disorders are widely prevalent across different populations. The Whickham survey conducted in the late 1970s in the north of England revealed a prevalence of 6.6% of thyroid dysfunction in the general adult population.^[4] Whereas, the Colorado Thyroid Disease Prevalence study involving a population of 25,862 participants, reported hyperthyroidism in 9.5% of the individuals while 2.2% had a low TSH.^[5] The NHANES III study, a survey of 17,353 subjects from the United States demonstrated hypothyroidism in 4.6% and hyperthyroidism in 1.3% of their subjects.^[6] Further observations indicated an increased frequency of thyroid dysfunction with advancing age and a higher prevalence of thyroid disease in women compared to men and in diabetic subjects compared to non-diabetics.

Several research projects documented a higher than normal prevalence of thyroid dysfunction in the diabetic population. Perros et al. demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics with the highest prevalence in type 1 female diabetics (31.4%) and lowest prevalence in type 2 male diabetics (6.9%).^[7] A recent report indicated a prevalence of thyroid disorder among 12.3% of the Greek diabetic patients^[8] and among 16% of Saudi patients with type 2 diabetes^[9]. In Jordan, thyroid dysfunction was also present in 12.5% of type 2 diabetic patients.^[10] Thyroid disorders are almost always found to be more common in subjects with type 1 diabetes compared to those with type 2 diabetes.

Effects of Thyroid Disorders on Diabetes and Other Conditions

Euthyroid status is required for regulatory

homeostatic mechanisms and biological energy metabolism. Aberrance from this into hyperthyroidism or hypothyroidism may catalyze effects on blood glucose regulation in diabetic patients. Hyperthyroidism is generally associated with derangement of blood glucose control and increased insulin requirements. Excessive thyroid hormone causes increased hepatic production of glucose, increased absorption of glucose through the intestines, and increased insulin resistance. It augments glucose degradation product cycling between skeletal muscle and hepatic tissue and reduces glycogen stores in both locations. It also increases renal insulin clearance. Thyroid hormone affects adipokines and body adipose tissues. The combined effect of these various mechanisms is that hyperthyroidism and thyrotoxicosis can actually push predisposed patients into diabetic ketoacidosis.^[11] It is appropriate to consider an underlying thyroid disorder in individuals with unexplained weight loss patterns over a period of time in conjunction with deterioration of blood glucose control, and increased insulin requirements. At times, hyperthyroidism may unmask latent diabetes and incite ketoacidosis.^[12]

The link between diabetes and heart disease is well established and understood. Many diabetics suffer from coronary heart disease and / or heart failure. Hyperthyroidism and thyrotoxicosis exercise chronotropic influence over conductive myocardial tissue and thus are arrhythmogenic, and thyroid hormone has a high index of arrhythmogenicity. Such effect may trigger angina, aggravate existing heart failure and adversely interfere with the treatment of heart failure, as well as further predispose patients to the risk of other heart problems.^[3]

Untreated hyperthyroidism over a prolonged periods predisposes to bone demineralization and contributes to osteoporosis. Osteoporosis in general raises the risk of orthopedic fractures, making falling much more dangerous. Diabetics with peripheral neuropathy are constantly at increased risk of falls due to poor sensation and proprioceptive dysfunction. The coexistence of hyperthyroidism and diabetes, in addition to neurological complications, increases the risk of fractures, which are a major cause of disability

and morbidity, particularly in the elderly.

Hypothyroidism on the other side of the spectrum rarely causes significant changes in blood glucose control. It reduces renal clearance of insulin, and can cause previously stable insulin-managed patients to develop hypoglycemia. However more importantly, hypothyroidism may be accompanied by lipid profile abnormalities including derangement of total cholesterol, LDL and triglycerides. The lipid pattern typical of Type 2 diabetics which is in general abnormal resembles a low HDL, high triglycerides and high ratios of small, dense LDL particles. This deteriorates further when accompanied by hypothyroid burden, which may further contribute to cardiovascular disease and hence stroke in this subset of the population.^[13]

Mechanism of Action

Alteration of thyroid status has been described in association with diabetics unable to attain stable glycemic control. In diabetic patients, the nocturnal thyroid stimulating hormone (TSH) peak is blunted, as is the response to Thyrotropin Releasing Hormone (TRH).^[13] Reduced T3 levels have been observed in uncontrolled diabetic patients which occurs due to an impairment in peripheral conversion of T4 to T3, a phenomenon seen to normalize once glycemic control is attained. A study was done by Coiro et al. conducted among type 1 diabetics without any residual pancreatic beta cell function. The study reported that the establishment of glycemic control did not have the capacity to restore the normal nocturnal TSH peak suggesting a diabetic pathology dependent alteration in the central control of TSH.^[14]

The relationship between thyroid disorders and diabetes mellitus is characterized by complex interdependent interactions. Exaggerated levels of circulating insulin associated with insulin resistance diabetes has shown a tendency to have a proliferative effect on thyroid tissue resulting in hyperplasia of the thyroid, which allows increased formation of nodules^[15,16] and thus increasing the risk of ophthalmological complications in patients with Graves' disease. Additionally, thyroid hormone may further affect carbohydrate

metabolism through interactions with leptin, adiponectin, and gastrointestinal hormone ghrelin. We are still early in our understanding and exploration of this relationship. Management of subclinical hypo/hyperthyroidism and sufficiently aggressive management in overt hypo/hyperthyroid disorders with coexisting diabetes may prove beneficial both directly, and indirectly.

Conclusion

The thyroid gland plays a central role in the regulation of metabolism and has a major impact on the control and clinical course of diabetes. Untreated thyroid disorders can increase the risk of certain diabetic complications and may aggravate the mechanisms responsible for diabetic symptoms. Abnormal thyroid function can relatively easily be diagnosed through haematological laboratory testing, and effective treatment is available. Thus, periodic screening for thyroid disorders can be justified in diabetic patients. No official guidelines yet exist but prudent vigil from healthcare providers for the coexistence of these diseases has the potential to improve the quality of health care that can be provided.

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