Mini review

Changes in biochemical, immunological and inflammatory parameters in hyper and hypothyroidism: A systematic review

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ABSTRACT

This review presents an assessment of alterations in various biomarkers in hyper and hypothyroidism. In hyperthyroidism, the level of thyroid hormone increases while it decreases in the case of hypothyroidism. The thyroid gland has been implicated in a broad spectrum of carbohydrate metabolism, imbalance of lipid profile, and mineral metabolism. Autoimmunity and inflammatory reactions in the thyroid gland might lead to the conditions like hyper and hypothyroidism. Lipid profile dysfunction is common in hypothyroidism patients while a higher level of liver enzymes is associated with hyperthyroidism. Glucose level has been observed to increase in both conditions. Hypothyroid patients are more prone to autoimmune conditions in comparison to hyperthyroid patients. According to the type of thyroid disorder, the concentrations of various biochemical, immunological and inflammatory markers alter. The literature reviewed in this article establishes considerable changes in the above parameters among thyroid patients which might help further in the early diagnosis and management of thyroid dysfunctions.

Keywords: Hyperthyroidism; hypothyroidism; inflammation; autoimmune; biochemical markers.

INTRODUCTION

The thyroid gland is an endocrinal gland that secretes thyroid hormones named thyroxine (T4) and triiodothyronine (T3). First T4 hormone is secreted by the thyroid gland then it is converted into T3 by the removal of one iodine molecule. Both triiodothyronine and thyroxine help the body in the storage and use of energy (metabolism). Secretion of these hormones from the thyroid gland is directly under the control of thyrotrrophic hormone i.e., thyroid stimulating hormone (TSH). The thyroid hormones affect all the tissues of the human body and any disturbance in the formation of these hormones might affect the function of multiple organs (1). There are mainly two types of thyroid dysfunction one is hyperthyroidism and the second one is hypothyroidism. In hyperthyroidism, the level of thyroid hormones increases while, in hypothyroidism it decreases in the blood (2).

Thyroid disorders are one of the most common metabolic and endocrinal disorders worldwide as well as in India. Few research studies estimated the fact that forty-two million people are suffering from thyroid dysfunctions in India. Thyroid disorders are more common in the growing Indian population, especially in obese females (3,4). There are defects in hormone synthesis due to various causative factors like genetic and environmental factors which stimulate the pituitary gland leading to compensatory hyperplasia of the thyroid gland (5). Thyroid disorders being one of the most common metabolic disorders of today, it is necessary to analyze all the factors associated with this dysfunction. In this review article, the changes in biochemical, immunological & inflammatory parameters of several physiological functions and their correlation with thyroid disorders have been summarized. For this article, the relevant literature from the last thirteen years has been reviewed from different sources/databases like Google Scholar, MEDLINE, PubMed, etc. The collected information has been critically evaluated for its appropriateness for this topic.

Biochemical parameters

A significant increase has been observed in the level of glycosylated hemoglobin in hypothyroid patients in comparison to the control group. Also, a positive correlation has been shown between thyroid-stimulating hormone levels and glycosylated hemoglobin levels in diabetic and non-diabetic hypothyroid patients (3). The level of blood glucose was found to be significantly higher in hyperthyroid and hypothyroid patients when compared with the control group (60%, 90%, and 30%, respectively). The individuals suffering from hypo and hyperthyroidism had a higher frequency of
hypertension than the controls (6). The levels of glycosylated hemoglobin and glycated albumin were found to be directly related to thyroid disorders even in nondiabetic subjects. The concentrations of glycosylated hemoglobin and glycated albumin increase with any change in the level of thyroid hormones (7). Hypothyroid patients are at higher risk of having anemia due to the high level of glycosylated hemoglobin in contrast with hyperthyroid patients. The RBC life span can be used as a tool to prove the exact etiology of the elevation in the levels of glycosylated hemoglobin and blood sugar (8).

The levels of total cholesterol and low-density lipoprotein increase while high-density lipoprotein decreases in subclinical hypothyroid patients. The level of serum electrolytes i.e., calcium, magnesium, sodium, and phosphorous was found to be significantly lower in subclinical hypothyroid patients than in the controls (9,10). Lipid profile dysfunction is directly associated with thyroid dysfunction (especially hypothyroid) and monitoring lipid profile in thyroid patients can prevent cardiovascular diseases (11). Serum ferritin and iron levels have a direct correlation with hyperthyroidism and an increase in thyroid hormones level cause an increase in the concentrations of serum iron and ferritin (12). Hypothyroidism is linked with bone disorders as calcium level was found to be significantly lower and phosphorous level was found to be significantly higher in hypothyroid subjects in comparison with controls (13). A study conducted on forty-eight hypothyroid women has shown a positive correlation between serum-free T4 and calcium levels which can be used as a marker for calcium therapy (14). Elevated calcium and phosphorus level were also shown to be associated with hyperthyroidism, especially in the elder age group (15).

A study conducted by making three groups of subjects: hypothyroid, hyperthyroid, and control, has shown that thyroid dysfunction also affects the level of liver enzymes. The levels of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) were found to be significantly higher in hyperthyroidism than in hypothyroidism when compared with the control group (6,16). A study carried out on three subject groups of overt hypothyroid, subclinical hypothyroid, and euthyroid, established an association between hypothyroid with the level of serum creatinine and urea (17). The levels of serum urea and creatinine were found to be elevated in subclinical and overt hypothyroid subjects when compared with the control group. The study established the fact that renal function will be affected in case of hypothyroidism and serum creatinine phosphokinase can be used as a diagnostic marker in subclinical and overt hypothyroid patients (16,18).

**Immunological parameters**

Thyroid disorders affect immunological parameters and these effects were found to be more prominent in the case of hyperthyroidism in comparison with hypothyroidism (19). Serum autoantibodies against thyroid hormones can be a great marker to diagnose autoimmune thyroid diseases and can be used to measure the status of the diseases, the severity of the diseases, and response to treatment with antithyroid drugs (20). The level of various autoantibodies like thyroglobulin antibody (TG Ab), anti-thyroglobulin antibody (anti-TG Ab), thyroid peroxidase antibody (TPO Ab), and anti-thyroid peroxidase antibody (anti-TPO Ab) was found to be significantly higher in hyperthyroid patients than in the control group (4). A large number of hypothyroidism patients also had detectable concentrations of anti-TG and anti-TPO antibodies. These antibodies which are produced from the competent immune cells at the site of thyroid tissue destruction are merely markers of thyroiditis (autoimmune thyroidism) (21). The seropositivity of thyroid autoantibodies was found to be high. Especially anti-TPO was much higher than anti-TG which could be due to the antigenic variation between these two thyroid antigens (22). Both serum TSH and anti-TPO autoantibody can be used for the diagnosis of thyroiditis and SCH (subclinical hypothyroidism). SCH can be extended to overt hypothyroidism due to persistently high levels of anti-TPO antibodies in the blood (23).

Anti-TPO antibodies can be used for the diagnosis, management, and treatment of thyroid dysfunction because it is a considerable factor in the etiology of thyroid diseases. Moreover, thyroid hormone levels and autoimmunity can be affected by many environmental and genetic factors (5). Autoimmunity can be considered the most common cause of hypothyroidism due to the higher concentration of autoantibodies in the blood (like anti-TPO and anti-TG) (24). The fact that anti-TPO and anti-TG antibodies are more associated with thyroiditis than non-autoimmune thyroid disorders has to be explored more in Arab, Sudanese, and African populations (25). Anti-thyroid globulin has a positive association with IL-17f while anti-thyroid peroxidase has an association with IL-17a in a hypothyroid patient. Hence, a higher level of IL-17 leads to an increase in thyroid autoantibodies which might damage the thyroid gland (26). In India, vitiligo disease is linked
with thyroid disorders which makes it necessary to screen vitiligo patients for autoimmune thyroid diseases (AITD) on regular basis (1).

Inflammatory parameters

Subclinical hypothyroid patients have a high risk of an increased level of platelet activation and mean platelet volume (MPV) level which can lead to cardiovascular complications like atherothrombosis even after levothyroxine therapy (27,28). Subclinical and overt hyperthyroidism might lead to endothelial dysfunctions due to decreased fibrinolytic activity, hypercoagulability, & increased level of various interleukins. These changes are not only dependent on the etiology but also the severity of hyperthyroidism (29). A retrospective study on thyroid patients concludes that the serum C–reactive protein (CRP) level is associated with hyper & Hypothyroidism. The study has shown an inverse relationship between thyroid hormone and C–reactive protein (30,31). The level of salivary CRP was found to be higher in subacute thyroiditis patients as compared with Hashimoto’s thyroiditis patients and the euthyroid group. Salivary CRP level can be considered an inflammatory marker to diagnose abnormal thyroid conditions (32). The serum concentrations of inflammatory parameters like erythrocyte sedimentation rate (ESR), and procalcitonin (PCT) are increased in thyroid disorders (33). A positive correlation between some apoptotic markers and thyroid disorders has been observed. In Hyperthyroid patients, the serum levels of apoptotic markers like TNF-α, IL-8, and p53 increases which might damage thyroid gland (34,35).

CONCLUSION

Thyroid hormones affect the growth, development, and physiological functioning of almost all the tissues & organs like, kidneys, liver, etc. Changes in thyroid hormone levels also affect the blood concentrations of glucose, minerals, and lipids in various direct and indirect ways. Thyroid dysfunction affects carbohydrate metabolism whether the patient is diabetic or not. The mineral metabolism is affected more in female and elder thyroid patients. Various studies have shown that thyroid disorders are becoming more prevalent day by day resulting in undiagnosed cardiovascular, liver, and kidney diseases in the primary stage. The chances of cardiovascular manifestation will increase with prolonged thyroid dysfunction. The levels of the markers of liver diseases (SGOT and SGPT) and renal diseases (creatinine and urea) are associated with subclinical hypothyroidism. Thyroid disorders affect immunological parameters such as TG Ab, anti-TG Ab, TPO Ab, and anti-TPO Ab which can be used as markers for thyroid dysfunction. It has also been observed that thyroid diseases are associated with increased platelet activation which might increase the risk of atherothrombotic complications. A positive association of many inflammatory markers like CRP, PCT, ESR, and MPV levels has been established with thyroid dysfunction. Based on the literature reviewed in this article, it can be concluded that thyroid disorders play a significant role in the progression of diseases associated with multiple organs yet there is a need for more studies to establish the correlation between the type and severity of thyroidism and the organ affected.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES


