



Could Thyroid Disorders Be Better Understood and Dealt as a Thyroid Syndrome

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Abstract

Thyroid disorders are common worldwide. Thyroid dysfunction, both hypo- and hyperthyroidism may increase the risk of cardiovascular disorders. Current thyroid function tests may have limitations since they only measure the total or free T4 and/or T3 and TSH serum concentrations in peripheral blood and not the effect of T4 or T3 serum on different specific target tissues. Several comorbid conditions can interfere with the absorption or increase the clearance of levothyroxine. Among patients treated with thyroid replacement, under or overmedicated may-be at risk for adverse health consequences. A wide range of drugs may interfere with levothyroxine absorption, metabolism, and action. Patients report a lack of well-being, despite reaching euthyroid reference range of TSH, with psychological distress. If we will consider Thyroid related conditions as a syndrome then research perspective at the pathophysiology, interrelation between symptoms and comorbidities will be much broader that can lead researchers to get insights of different pathways in which thyroid gland functioning can be perceived and dealt therapeutically. The deliberation of thyroid disorder as a syndrome can affluence our knowledge of correlating cofounders, action of thyroid hormones on target tissues, underlying cause and thyroid health.

Keywords: Syndrome, hypothyroidism, hyperthyroidism, thyroid

General Understanding of Disease, Disorder and Syndrome

A disease can be defined as a medical condition of the body which disrupts the normal functioning and physiological processes. Each disease has its own signs and symptoms attributed to it. It can also be defined as an impairment of the normal state of the living animal or plant body or one of its parts that interrupts or modifies the performance of the vital functions, is typically manifested by distinguishing signs and symptoms, and is a response to environmental factors (as malnutrition, industrial hazards, or climate), to specific infective agents (as worms, bacteria, or viruses), to inherent defects of the organism (as genetic anomalies), or to combinations of these factors : sickness, illness [1].

Disorder is defined as a state of confusion or an upset in the systematic functioning of organ or system [2].

A syndrome is a term used to describe a collection of symptoms which are on-going. The word syndrome comes from the Greek “sundrome” which means concurrence of symptoms. Causes of syndromes can be genetic or from unknown causes and generally do not often have a clear cause and effect type connection [3].

Thyroid Disorders

Thyroid disorders are common worldwide. These diseases produces significant burden on economics. Previous studies on

thyroid disorders estimated that more than 80 million people in world are suffered from thyroid disorder. Thyroid dysfunction, both hypo- and hyperthyroidism may increase the risk of hypertension, renal complications, adverse blood lipid alterations, endothelial dysfunction and accelerated atherosclerosis, resulting in increased cardiovascular risk.

Hypothyroidism should be considered as a graded phenomenon with a wide variety of clinical conditions from subclinical hypothyroidism to myxedema. Subclinical hypothyroidism is a combination of serum thyrotropin (TSH) above the upper reference limit and normal free thyroxine (fT4) and free triiodothyronine (fT3) levels. This definition is only applicable in the absence of other acute or chronic recent or ongoing severe illness, assuming a stable thyroid function weeks or more before the evaluation and a normally functioning hypothalamic-pituitary-thyroid axis. Overt hypothyroidism is characterized by an elevated TSH, usually above 10 mIU/L, in combination with reduced circulating fT4 and fT3 levels.

Hyperthyroidism is the condition that occurs due to excessive production of thyroid hormones by the thyroid gland. Thyrotoxicosis is the condition that occurs due to excessive thyroid hormone of any cause and therefore includes hyperthyroidism. Some, however, use the terms interchangeably. Signs and symptoms vary between people and may include irritability, muscle weakness, sleeping problems, a fast heartbeat, heat intolerance, diarrhoea, enlargement of the thyroid, hand tremor, and weight loss [4-11].

Confounders in Hypothyroidism

Hypothyroidism and Hypertension

Hypertension affects 26.4% of the global adult population remaining the leading preventable risk factor for premature death and disability worldwide. Besides the majority of patients with primary (essential) hypertension, a subgroup of ~10% of patients is affected by secondary hypertension. Among the underlying diseases several are of endocrine origin and thyroidal impairments represent an even smaller percentage of the secondary hypertension cases; their incidence and form of presentation varies with age and studied population. Hypertension may be the initial clinical presentation for at least 15 endocrine disorders, including overt and subclinical hyperthyroidism and hypothyroidism. The correction of thyroid dysfunction may normalize blood pressure (BP) in most cases; therefore checking thyroid function is essential during the workup for hypertension [12-15].

Hypothyroidism and Atherosclerosis

Geo et al., 2013 [11], in his meta-analysis reported that subclinical hypothyroidism is associated with an increased carotid intima-media thickness, which may due to elevated thyrotropin (TSH), dyslipidemia and hypertension. Increased intima-media thickness can also be present in patients with serum TSH values less than 10 mIU/L, although there is significant heterogeneity.

Hypothyroidism and Renal Functions

Reduced T3 concentrations were associated with reduced kidney function cross-sectionally. The lack of association with the development of incident CKD suggests that altered thyroid function in the general population is not causally related to CKD development, but screening for thyroidal status may be especially relevant in persons with reduced kidney function [8].

Can We Correlate TSH To Predict T3 And T4 Functionalities At Tissue Level?

Current thyroid function tests may have limitations since they only measure the total or free T4 and/or T3 and TSH serum concentrations in peripheral blood and not the effect of T4 or T3 serum on different specific target tissues. Nonetheless, TSH concentration is a good functional marker of the effect of thyroid hormones in the pituitary tissue. We know that tissues take up iodothyronines by surface transporters and deiodinate T4 into the active form T3. The availability of T3 at the tissue level is regulated by three deiodinase isoforms (D1, D2, D3), but due to tissue heterogeneity, pituitary secreted TSH may not reflect what happens in other tissues. Therefore, TSH serum is not an appropriate indicator of peripheral tissue thyroidism [16-18].

Challenges in Treatment with Thyroid Disorder

Several comorbid conditions can interfere with the absorption or increase the clearance of levothyroxine. Among patients treated with thyroid replacement, those who are under- or overmedicated may be at risk for adverse health consequences associated with endogenous hypothyroidism or hyperthyroidism. A wide range of drugs may interfere with levothyroxine absorption, metabolism, and action. Patients report a lack of well-being, despite reaching euthyroid reference range of TSH. These patients often exhibit significant psychological impairment compared with age- and sex-matched controls. In some patients, symptoms of hypothyroidism persist despite adherence to treatment and normalisation of TSH [19]. The persistent symptoms may be unrelated to thyroid dysfunction. For example, a patient may present with fatigue and be found to have mild subclinical hypothyroidism, but without a

causal relationship between the two. In such cases, comorbidities including malabsorption and depression should be sought to account for the symptoms, but often, none can be identified [20].

Antithyroid therapy is the simplest way to treat hyperthyroidism. Antithyroid medicines cause the thyroid to make less thyroid hormone. These medicines usually don't provide a permanent cure. Once treatment with antithyroid medicine begins, the thyroid hormone levels may not move into the normal range for several weeks or months. The total average treatment time is about 1 to 2 years, but treatment can continue for many years [21].

Case Study of Metabolic Syndrome

The first description of patients with clustering of various metabolic abnormalities was as early as 1923 but it was more than five decades later, in 1988, that Reaven coined the term 'syndrome X' for this entity. The last two decades have brought forth a number of definitions and criteria to identify this condition.

In spite of the large number of controversies regarding the existence of Metabolic Syndrome as an entity and the nomenclature to be used, this conglomeration of various metabolic abnormalities has been widely accepted as a screening tool for identifying subjects at high risk of cardiovascular disease. While the various definitions proposed by different organizations have provided us with remarkable scientific insights into this syndrome, it has led down to a comprehensive understanding of symptom complex. After the definition of metabolic syndrome, the enduring research endeavours have looked at the metabolic complications in a wholesome way and has emerged with many screening and interventional tools for the same.

Reassessing Thyroid Disorder as a Syndrome

If we will consider Thyroid related conditions as a syndrome then research perspective at the pathophysiology, interrelation between symptoms and comorbidities will be much broader that can lead researchers to get insights of different pathways in which thyroid gland functioning can be perceived and dealt therapeutically.

The case study of metabolic syndrome could prove as a guiding light to reconsider the thyroid disorder as a syndrome. This consideration will encompass wider cause to effect scenario for better understanding and better management of thyroid health. The deliberation of thyroid disorder as a syndrome can affluence our knowledge of correlating cofounders, action of thyroid hormones on target tissues, underlying cause and thyroid health [22].

Conclusion

Since the present thyroid tests has certain limits as they only measure the serum TSH, T3 and T4 concentrations in peripheral blood but these levels varying in specific target tissues. Also the present line of treatment uses levothyroxine which tend to interfere with the absorption or increase the clearance and associated with numerous adverse health consequences. Thus, this review paper enlightens that the consideration of thyroid disorder as a syndrome can affluence our acquaintance of correlating cofounders, action of thyroid hormones on target tissues, underlying cause and thyroid health. Hence, thyroid should be considered as a syndrome so that the research perception towards pathophysiology, interrelation between symptoms and comorbidities will be considerably comprehensive, which would lead researchers to get conceptions of diverse pathways in which thyroid gland functioning can be alleged and dole out therapeutically.

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