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EC MICROBIOLOGY
Review Article

Serum Uric Acid Level in Thyroid Disorders

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Received: July 27, 2020; **Published:** September 24, 2020

Abstract

Background: The relationship between uric acid level and thyroid dysfunction has been investigated in several studies, which provided conflicting results. There are few data available regarding the association between the metabolism of thyroid dysfunction and uric acid and the evidence is conflicting. The association between the levels of TSH and serum uric acid has been weak. However, previous studies reported a high prevalence of hyperuricemia in both hypothyroidism and hyperthyroidism patients.

Aim: In this review, we will look into the relation between serum uric acid in thyroid patients.

Conclusion: Uric acid metabolism and production mainly go through the metabolic action of xanthine oxidase and xanthine dehydrogenase. Low oxygen, inflammation, etc. can speed up the metabolism of the enzyme and cause changes in uric acid levels, increasing the release of related cytokines. Thyroid hormones can therefore also change the level of cytokines produced by oxidative stress and inflammation, and the change in thyroid hormones can also cause the production of related cytokines and change the level of the enzyme, and ultimately affect the level of uric acid. The effects of FT3 and FT4 on uric acid may be through the transformation of purine nucleotides and uric acid excretion; further prospective studies are therefore needed to confirm these findings.

Keywords: *Thyroid Dysfunction; Uric Acid; Uric Acid Level in Thyroid Patients; Hypothyroidism; Hyperthyroidism*

Introduction

Normal thyroid function plays an important role in regulation of cellular activity and influences basal metabolic rate and general body metabolism [1]. For several reasons, patients with thyroid gland function or structure abnormalities are getting medical attention. They have symptoms due to physiological effects of increased or reduced thyroid hormone serum concentrations (hyperthyroidism, or hypothyroidism, respectively) [2]. The thyroid produces 100 percent circulating thyroxine but only about 5 percent ± 10 percent circulating triiodothyronine, the rest of which are derived by type I deiodinase peripheral monodeiodination of thyroxine in tissues such as heart, liver, kidney and gut mucosa. Type II deiodinase provides triiodothyronine in intracellular locations such as the central nervous system and pituitary [3].

Uric acid is the main catabolite in humans and higher primates for the purine metabolism. It is a weak organic acid, which exists mainly as a monosodium salt under physiological conditions. The predominant form is non-ionized uric acid, at a pH less than 5.75, which can occur in the urine [4]. In a normal population the upper limit of plasma uric acid can be described by a statistical range. Epidemiological

studies have generally accepted 7.0 mg/dl as the upper limit for adult men and 6.0 mg/dl for women [5]. The levels of uric acid are affected by both age and sex. The normal uric acid in the serum before puberty is 3.6 mg/dl for males and females. Following puberty, values increase to adult levels usually less than 1 mg/dl for women than for men. Many additional factors can result in transient fluctuations in uric acid levels, including exercise, diet, medications, and state of hydration [6]. Uric acid has been shown to directly inhibit the damage caused by free radicals and also to protect cell membranes and DNA [7].

Urate production is accelerated by purine rich diets, endogenous purine production, and high cell breakdown, and it is responsible for a minority of cases of hyperuricemia. The increase in uric acid is believed to be an intermediate factor in adipose tissue that regulates inflammatory endocrine disorders and may be an important factor leading to dyslipidemia and atherosclerosis. There are currently many studies on uric acid, and uric acid is also found to be related to cardiovascular disease, kidney disease, etc. but there are some studies on the correlation between uric acid and thyroid function, and there are also some controversies [8]. It is estimated at as much as 21% of the general population and asymptomatic hyperuricemia is present in 25% of hospitalized patients. Hyperuricemia's most common complication is gout, seen in 3.9 per cent of the U.S. population [9].

The relationship between uric acid level and thyroid dysfunction has been investigated in several studies, which provided conflicting results. There are few data available regarding the association between the metabolism of thyroid dysfunction and uric acid and the evidence is conflicting. The association between the levels of TSH and serum uric acid has been weak. However, previous studies reported a high prevalence of hyperuricemia in both hypothyroidism and hyperthyroidism patients [10].

Thyroid hormones are essential for the optimal functioning of nearly all body tissues and play a critical role in growth, cell differentiation and cellular metabolism. Thus, abnormal thyroid hormone production results in various biochemical abnormalities leading to increased risk of metabolic syndrome, cardiovascular and musculoskeletal disorders. A possible explanation for these potential associations is the ability of thyroid hormone to influence serum urate levels through regulation of glomerular filtration rate [11]. A recent study indicates that thyroid hormones and thyroid stimulating hormone (TSH) are correlated with the activity of each organ system but also influence the growth and development of the body, and it has been found that thyroid hormone concentration is due to different age and sex [12]. At present it is suspected that changes in the thyroid hormone have certain heritability, but most of the genetic possibilities cannot be explained; an investigation has also found genome-wide variations associated with FT3 and new loci associated with TSH [13].

In this review, we will look into the relation between serum uric acid in thyroid patients.

Hyperuricemia and hyperthyroidism

Hyperuricemia was found to be associated with age and gender, indicating that young people are more likely to develop hyperuricemia among obese and overweight people compared to older people, whereas women are more likely to develop hyperuricemia as they gain weight [14].

Researchers suggested hypothyroidism to be associated with hyperuricemia as early as 1955, but subsequent studies found a contradictory relationship between thyroid dysfunction and uric acid [15]. Some researchers have suggested that hyperuricemia and gout may increase hyperthyroid prevalence [16]. A study suggested that there was a linear correlation between FT4 and uric acid levels in the population without thyroid dysfunction and an increase in the incidence of hyperuricemia with FT4 [17]. In contrast, a large study of 2,359 consecutive patients with different degrees of thyroid dysfunction found no association between concentrations of UA and T4/TSH [18].

Another study found that; serum uric acid was significantly elevated in patients with hyperthyroidism, and the elevation correlated well with serum T4 before treatment as a group and during treatment in each patient. A significant elevation of serum uric acid was not present in patients with a transient mild thyrotoxicosis due to subacute thyroiditis [19]. A case-control analysis found that serum UA

levels in patients with severe hyperthyroidism were significantly elevated and were well associated with serum T4 concentrations before and during treatment, in line with our own findings [19]. Another study found that patients with hyperthyroidism due to the disease of Graves had significantly higher levels of uric serum acid than controls matched between age and sex [19].

Hyperuricemia and hypothyroidism

Thyroid dysfunction may affect renal physiology and growth, while thyroid function can overlap with kidney disorders. In turn, hypothyroidism slows all metabolic processes down. One such metabolic pathway is the pathway to purine metabolism. Hypothyroidism induces changes in uric acid levels by manipulating the pathway. In hypothyroidism, due to decreased cardiac output, increased peripheral vascular resistance, vasoconstriction of the renal vasculature, reduced renal response to vasodilators and decreased expression of renal vasodilators, such as vascular endothelial growth factor and insulin such as growth factor 1, renal blood flood flow. Due to reduced sensitivity to beta-adrenergic stimuli and decreased renin secretion, the glomerular filtration rate (GFR) is also reduced.

In a case-control study involving 98 patients in the subclinical hypothyroidism group, 89 in the overt hypothyroidism community, and 187 in the control group, Tayal., *et al*. [20] reported that the serum creatinine level in subjects with subclinical and overt hypothyroidism was significantly higher than that in the control group ($P < 0.01$). In a study of 356 subclinical hypothyroid patients in the case group and 331 in the control group, Liang., *et al*. [21] concluded that serum uric acid has risen significantly in subclinical hypothyroid patients. Arora., *et al*. [22], showed that serum uric acid levels were significantly higher in patients with overt hypothyroidism than in the control group. In this study the patient's TSH level was 36.44 ± 15.48. It appears, then, that serum uric acid is rising at high TSH levels.

Giordano., *et al*. reported a significant increase in hyperuricemia rates in patients with both hypothyroid and hyperthyroid compared to the general population [23]. A cross-sectional study of Ashizawa., *et al*. found an association between UA levels and subclinical hypothyroidism among women; however, no relation between hyperuricemia and hypothyroidism was observed [24]. Sidhu., *et al*. [25], stated that the serum level of both urea and creatinine in hypothyroidism was significantly higher than in hyperthyroidism. Saini., *et al*. [26] also reported the same results, but this association was not found in contrast to Qahtan., *et al*. Similarly, in other study on hypothyroidism patients, TSH was found to be positively correlated with uric acid, while FT4 was not correlated with uric acid [27].

Conclusion

Uric acid metabolism and production mainly go through the metabolic action of xanthine oxidase and xanthine dehydrogenase. Low oxygen, inflammation, etc., can speed up the metabolism of the enzyme and cause changes in uric acid levels, increasing the release of related cytokines. Thyroid hormones can therefore also change the level of cytokines produced by oxidative stress and inflammation, and the change in thyroid hormones can also cause the production of related cytokines and change the level of the enzyme, and ultimately affect the level of uric acid. The effects of FT3 and FT4 on uric acid may be through the transformation of purine nucleotides and uric acid excretion; further prospective studies are therefore needed to confirm these findings.

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Volume 16 Issue 10 October 2020