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Clinical evaluation of hypothyroid patients by estimation of uric acid

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Abstract
Many studies were done to assess serum creatinine and uric acid levels of hypothyroid patients. But, as far we know, no such study was done in our population. So, we designed this study in our population for evaluation of uric acid levels in hypothyroid patients and that might be helpful for clinical management of hypothyroid patients with hyperuricemia.
The present study was planned in the Department Of Biochemistry, Jawaharlal Nehru Medical College, Bhagalpur, Bihar. Total 50 patients diagnosed clinically and biochemically as hypothyroid were enrolled in the present study. The 25 patients were divided in Group A as Hypothyroid cases and remaining 25 patients were evaluated as a control cases. The blood collected in a plain vacutainer. Serum obtained after centrifugation was divided into two aliquots – one for thyroid profile and the other for uric acid, and were stored at -20 °C until analysis.
The data generated from the present study suggests that the Uric acid levels within physiological limits are observed as elevated in hypothyroid subjects. Hypothyroidism affects renal blood flow, GFR, tubular function and also water and electrolyte balance. Therefore, patients presenting with these biochemical abnormalities are recommended to be investigated for hypothyroidism and vice a versa.

Keywords: uric acid, hypothyroidism, hypothyroid, hyperuricemia

Introduction
A clavicle fracture, also known as a broken collarbone, is a bone fracture of the clavicle. Symptoms typically include pain at the site of the break and a decreased ability to move the affected arm. Complicatio Hypothyroidism, also called underactive thyroid or low thyroid, is a disorder of the endocrine system in which the thyroid gland does not produce enough thyroid hormone. It can cause a number of symptoms, such as poor ability to tolerate cold, a feeling of tiredness, constipation, depression, and weight gain. Occasionally there may be swelling of the front part of the neck due to goiter. Untreated hypothyroidism during pregnancy can lead to delays in growth and intellectual development in the baby or congenital iodine deficiency syndrome [1].
Worldwide, too little iodine in the diet is the most common cause of hypothyroidism. In countries with enough iodine in the diet, the most common cause of hypothyroidism is the autoimmune condition Hashimoto's thyroiditis. Less common causes include: previous treatment with radioactive iodine, injury to the hypothalamus or the anterior pituitary gland, certain medications, a lack of a functioning thyroid at birth, or previous thyroid surgery. The diagnosis of hypothyroidism, when suspected, can be confirmed with blood tests measuring thyroid-stimulating hormone (TSH) and thyroxine levels. Salt iodization has prevented hypothyroidism in many populations. Hypothyroidism can be treated with levothyroxine. The dose is adjusted according to symptoms and normalization of the thyroxine and TSH levels. Thyroid medication is safe in pregnancy. While a certain amount of dietary iodine is important, excessive amounts can worsen certain types of hypothyroidism [2].
Worldwide about one billion people are estimated to be iodine deficient; however, it is unknown how often this results in hypothyroidism. In the United States, hypothyroidism occurs in 0.3–0.4% of people. Subclinical hypothyroidism, a milder form of hypothyroidism characterized by normal thyroxine levels and an elevated TSH level, is thought to occur in 4.3–8.5% of people in the United States. Hypothyroidism is more common in women than men. People over the age of 60 are more commonly affected. Dogs are also known to develop hypothyroidism and in rare cases cats and horses [3].
Hypothyroidism is caused by inadequate function of the gland itself (primary hypothyroidism), inadequate stimulation by thyroid-stimulating hormone from the pituitary gland (secondary hypothyroidism), or inadequate release of thyrotropin-releasing hormone from the brain's hypothalamus (tertiary hypothyroidism). Primary hypothyroidism is about a thousandfold more common than central hypothyroidism [4].
Iodine deficiency is the most common cause of primary hypothyroidism and endemic goiter worldwide. In areas of the world with sufficient dietary iodine, hypothyroidism is most commonly caused by the autoimmune disease Hashimoto's thyroiditis (chronic autoimmune thyroiditis). Hashimoto's may be associated with a goiter. It is characterized by infiltration of the thyroid gland with T lymphocytes and autoantibodies against specific thyroid antigens such as thyroid peroxidase, thyroglobulin and the TSH receptor [5].
After women give birth, about 5% develop postpartum thyroiditis which can occur up to nine months afterwards. This is characterized by a short period of hyperthyroidism followed by a period of hypothyroidism; 20–40% remain

permanently hypothyroid [6]. Autoimmune thyroiditis is associated with other immune-mediated diseases such as diabetes mellitus type 1, pernicious anemia, myasthenia gravis, celiac disease, rheumatoid arthritis and systemic lupus erythematosus. It may occur as part of autoimmune polyendocrine syndrome (type 1 and type 2) [5].

Laboratory testing of thyroid stimulating hormone levels in the blood is considered the best initial test for hypothyroidism; a second TSH level is often obtained several weeks later for confirmation. Levels may be abnormal in the context of other illnesses, and TSH testing in hospitalized people is discouraged unless thyroid dysfunction is strongly suspected. An elevated TSH level indicates that the thyroid gland is not producing enough thyroid hormone, and free T4 levels are then often obtained. Measuring T3 is discouraged by the AACE in the assessment for hypothyroidism. There are a number of symptom rating scales for hypothyroidism; they provide a degree of objectivity but have limited use for diagnosis [5].

Table 1

TSH	T4	Interpretation
Normal	Normal	Normal thyroid function
Elevated	Low	Overt hypothyroidism
Normal/low	Low	Central hypothyroidism
Elevated	Normal	Subclinical hypothyroidism

Many cases of hypothyroidism are associated with mild elevations in creatine kinase and liver enzymes in the blood. They typically return to normal when hypothyroidism has been fully treated. Levels of cholesterol, low-density lipoprotein and lipoprotein (a) can be elevated; the impact of subclinical hypothyroidism on lipid parameters is less well-defined [7].

Very severe hypothyroidism and myxedema coma are characteristically associated with low sodium levels in the blood together with elevations in antidiuretic hormone, as well as acute worsening of kidney function due to a number of causes. In most causes, however, it is unclear if the relationship is causal. A diagnosis of hypothyroidism without any lumps or masses felt within the thyroid gland does not require thyroid imaging; however, if the thyroid feels abnormal, diagnostic imaging is then recommended. The presence of antibodies against thyroid peroxidase (TPO) makes it more likely that thyroid nodules are caused by autoimmune thyroiditis, but if there is any doubt, a needle biopsy may be required [5].

Many studies were done to assess serum creatinine and uric acid levels of hypothyroid patients. But, as far we know, no such study was done in our population. So, we designed this study in our population for evaluation of uric acid levels in hypothyroid patients and that might be helpful for clinical management of hypothyroid patients with hyperuricemia.

Methodology

The present study was planned in the Department Of Biochemistry, Jawaharlal Nehru Medical College, Bhagalpur, and Bihar. Total 50 patients diagnosed clinically and biochemically as hypothyroid were enrolled in the present study. The 25 patients were divided in Group A as Hypothyroid cases and remaining 25 patients were evaluated as a control cases. The blood collected in a plain vacutainer. Serum obtained after centrifugation was divided into two aliquots – one for thyroid profile and the other for uric acid, and were stored at -20 °C until analysis.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: patients diagnosed clinically and biochemically as hypothyroid

Exclusion Criteria: Patients with diabetes mellitus, hypertension, renal disease and those on drugs that affect uric acid excretion like thiazide diuretics

Results & Discussion

Thyroid hormones are important for functioning of almost every body organ or tissue so thyroid deficiency can cause a wide range of metabolic disturbances. Severe symptomatic cases of hypothyroidism can cause marked elevation of serum Uric acid either due to increased production or decreased excretion of uric acid or from a combination of two processes.

Hypothyroidism is associated with many biochemical abnormalities including increased serum creatinine and uric acid levels. The serum creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism [8]. Serum creatinine level may also be increased due to hypothyroid myopathy. Hypothyroidism, although rare, has been reported as a definite and authentic cause of rhabdomyolysis. As a result, hypothyroidism must be considered in patients presenting with acute renal failure and elevated muscle enzymes [9]. There is high prevalence of hyperuricemia and gout in hypothyroidism. In hypothyroidism the hyperuricemia is secondary to a decreased renal plasma flow and impaired glomerular filtration [10].

Table 2: Comparison of Demographic Details

Groups	Group A	Group B
Cases of	**Hypothyroid**	**Controls**
Age		
20 – 30 years	0	0
31 – 40 years	1	2
41 – 50 years	7	6
51 – 60 years	5	10
61 and above years	13	7
Sex		
Males	15	12
Females	10	13
Region		
Rural	9	11
Urban	16	14

Table 3: Comparison of Clinical parameters

Groups	Group A	Group B
Cases of	**Hypothyroid**	**Controls**
Parameter		
Serum FT_3 (pg/ml)	2.15 ± 0.12	2.95 ± 0.09
Serum FT_4 (ng/dl)	0.65 ± 0.1	1.35 ± 0.11
Serum TSH (mIU/ml)	7.5 ± 1.2	3.5 ± 0.2
Serum uric acid (mg/dl)	7.2 ± 0.6	3.9 ± 0.3

Mooraki & Basani10 reported a case of a young male hypothyroid patient with an elevated serum creatinine level (2.3 mg/dL), markedly elevated TSH level, severe hypercholesterolemia, hyperuricemia, and a creatinine clearance of 58 mL/minute. The patient started on levothyroxine supplementation and six weeks after thyroid replacement therapy his serum creatinine had declined to 1.4 mg/dL with an estimated creatinine clearance rate of 65 mL/minute. This was accompanied by reduction in serum uric acid and cholesterol levels. Eighteen months later his creatinine had further declined to 1.0 mg/dL

In hypothyroidism, because of low metabolic profile ADP levels will be more as against ATP. Hence adenine is oxidized through xanthine oxidase system and liberates more uric acid. The purpose of the present study was therefore to determine the relationship between renal function and thyroid status. Thurman JM *et al* shows Long-standing hypothyroidism can cause significant reversible changes in renal function such as a decrease in sodium resorption in the proximal tubules, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in urinary urate excretion, and a decrease in renal blood flow and glomerular filtration rate (GFR) [11]. del Greco FR, *et al*. [12]. shows in hypothyroid state, hypovolemia occurs due to decreased cardiac output shows fall in renal blood flow. Thyroxine was to an high in systemic and renal vasoconstriction and also finally leading to decreased renal blood flow [13].

The cause of the low renal plasma flow and GFR observed is believed to be normally due to the commonly hypodynamic state of the Cardio vascular system in hypothyroidism. K Reisman SH *et al*. [14] And Kaptein EM [15]. Hypothyroidism was related with low plasma renin, which might cause an high levels of creatinine and uric acid ranges.

The association between overt hypothyroidism and UA was first described by Kuzell *et al*. [16] and several subsequent studies have investigated the link between overt thyroid disorder and hyperuricemia with conflicting findings [17–20]. For example, Giordano *et al* reported a significant increase of hyperuricemia rates in both hypothyroid and hyperthyroid patients relative to the general population [21]. Similarly, a case-control study demonstrated that serum UA levels were significantly elevated in patients with overt hyperthyroidism and correlated well with serum T4 concentrations before and during treatment, consistent with our own findings. Moreover, serum UA levels were significantly decreased in patients with overt hypothyroidism [22]. In contrast, a large study of 2,359 consecutive patients with various degrees of thyroid dysfunction found no association between UA and T4/TSH concentrations [23]. An association between UA levels and subclinical hypothyroidism was observed among women in a cross-sectional study from Ashizawa *et al*; however, no relationship between hyperuricemia and hypothyroidism was observed [24]. Several factors could account for these discrepancies, including differences in the study populations (e.g. patients versus general population), sample sizes, and laboratory methods used to define TSH and T3/T4 values. To the best of our knowledge, this is the first cross-sectional study demonstrating the association between FT4 and UA concentrations in a general population without overt thyroid dysfunction, and it provides an accurate account of how thyroid function may affect the serum levels of UA.

The pathophysiology of renal function in hypothyroidism is multifactorial and many theories had been proposed. In hypothyroid state, cardiac output is decreased and circulating volume is diminished, resulting in a decreased renal blood flow or pre-renal insufficiency. In addition, the increase in systemic and renal vasoconstriction, probably from direct effect of thyroxine, may further lead to decrease renal blood flow. It may result in less exretion of uric acid.

Conclusion

The data generated from the present study suggests that the Uric acid levels within physiological limits are observed as elevated in hypothyroid subjects. Hypothyroidism affects renal blood flow, GFR, tubular function and also water and electrolyte balance. Therefore, patients presenting with these biochemical abnormalities are recommended to be investigated for hypothyroidism and vice a versa.

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