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HYPERURICEMIA IN HYPOTHYROIDISM: A CASE CONTROL STUDY.

Biochemistry

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ABSTRACT

Introduction: Hypothyroidism is one of the most common metabolic disorders. Prevalence of hypothyroidism in India is 11%. It is more common in women. Long standing hypothyroidism can cause significant reversible changes in renal functions. Thyroid dysfunction influences the purine metabolism, which may increase serum uric acid (UA) level due to decreased renal plasma flow and impaired glomerular filtration. Aim of this study was to evaluate serum uric acid levels in hypothyroid patients. To compare the serum uric acid levels among the euthyroids and hypothyroids. **Materials and Methods:** This is a case control study, conducted on 40 euthyroid subjects and 40 newly diagnosed cases of hypothyroidism, attending OPD under the Department of Medicine, KIMS, Hubli in the age group of 18-60 years over a period of 3 months. Patients with chronic renal failure, Diabetes mellitus, hypertension, liver diseases, cardio vascular diseases, pre-existing gout, pregnant women were excluded. Sample was collected. Serum T3, T4, TSH was analysed by Chemiluminescent Immuno assay method. Serum uric acid level was analysed by Uricase Trinder enzymatic and colorimetric method. Descriptive statistics such as mean and standard deviation (SD) for continuous variables were determined. Unpaired t Test was used to compare the mean of quantitative variables between Cases and Controls. p value of <0.05 was considered significant. **Results:** Mean serum uric acid levels were found significantly higher in hypothyroids compared to euthyroids (p value=0.008). **Conclusion:** These results imply that hypothyroidism can often cause hyperuricemia.

KEYWORDS

Hypothyroidism; Thyroid hormones; Uric acid; Gout.

INTRODUCTION

The thyroid gland is a major endocrine gland in the body that secretes triiodothyronine (T3) and thyroxine (T4). The pituitary and hypothalamus control the thyroid gland's ability to produce T4 and T3. As a result of a gradual decrease of T4 and, eventually, T3, an increase in serum thyroid-stimulating hormone (TSH) levels is an extremely early biochemical indicator of imminent thyroid failure. A thyroid hormone deficiency causes the condition known as hypothyroidism, which often slows down metabolism.[1]

Hypothyroidism is of two types – primary and secondary. It can occur due to various environmental and geographic factors which include dietary deficiency of iodine and genetic variations. The prevalence of primary hypothyroidism is 1:100, but 5:100 in subclinical hypothyroidism (2). It is more frequent in females than males (3). The gold standard test for screening hypothyroidism is the estimation of serum TSH. Further, blood testing of T3 and T4 will diagnose the type of hypothyroidism.

During tissue destruction, when nucleic acids are broken down, purines are released. As a result, the final product, uric acid, is formed mostly in the liver by the breakdown of purines derived from both endogenous and exogenous sources. 300 mg of uric acid are produced per day. Males have a total body pool of 1200 mg of uric acid, but females only have 600 mg. For females, normal serum uric acid levels range from 3-6.0 mg/dl and for males, from 3.5-7.0 mg/dl. The kidneys eliminate 70% of the uric acid from the body, and the gut bacteria that lives there break down the remaining 30% in the intestine, this process is called intestinal uricolysis. Thus serum uric acid levels depend on rate of purine synthesis, purine content of diet, degradation and salvage pathway, uric acid excretion [4].

By raising the basal metabolic rate, consuming more oxygen, and promoting heat generation, thyroid hormones (T4 and T3) regulate the rate of metabolism, impact growth, and regulate energy utilization [5]. The majority of the body's metabolic pathways are influenced by these hormones; one metabolic pathway that is impacted by thyroid hormone fluctuations is the purine metabolism. This results in an increase in the amounts of uric acid, which in turn causes hyperuricemia and gout [6].

Thyroid hormone has important effect on growth and development of kidney. Prolonged hypothyroidism can cause decreased renal blood flow which can be reversed with proper treatment [7]. Hemodynamic changes occur in hypothyroidism that leads to reduction in renal plasma flow and glomerular filtration rate, which also causes increase in the levels of serum uric acid [8,9].

Objectives

Aim of this study was to evaluate serum uric acid levels in hypothyroid patients. To compare the serum uric acid levels among the euthyroids and hypothyroids.

MATERIALS AND METHODS

This is a case control study, conducted on 40 euthyroid subjects and 40 newly diagnosed cases of hypothyroidism, attending OPD under the department of medicine, KIMS, Hubli in the age group of 18-60 years over a period of 3 months. Patients with chronic renal failure, Diabetes mellitus, hypertension, liver diseases, cardio vascular diseases, pre-existing gout, pregnant women were excluded. Hypothyroid patients diagnosed on the basis of clinical manifestation of hypothyroidism & TSH >5 microIU /ml. After explaining the procedures in detail to the subjects, written informed consent was obtained.

The blood investigations include

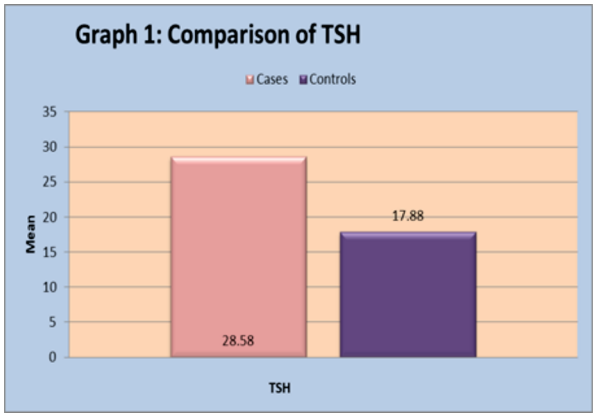
- Serum Uric acid – Uricase Trinder enzymatic and colorimetric method using fully automated biochemistry analyser (XL-1000)
- Thyroid profile test(T3,T4,TSH) – Chemiluminescent Immuno assay using hormone analyser (cobas e411)

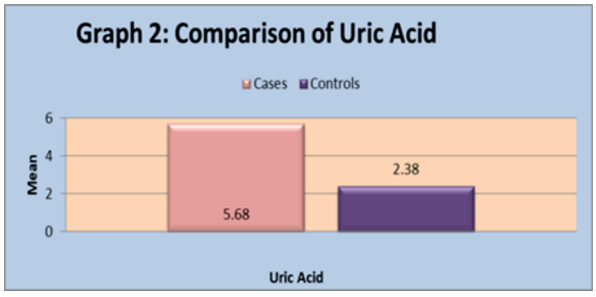
RESULTS

In this study, out of 40 hypothyroids,15 were found to have increased serum uric acid levels and 25 with normal values. Out of these 15 subjects 9 were females and 6 males. Out of 40 euthyroids, only 4 subjects had increased serum uric acid levels and 36 subjects had normal values. Out of these 4 subjects, 3 were females and 1 male. Table I shows the comparison of TSH and serum uric acid levels between the cases(hypothyroid) and the controls(euthyroid). Mean serum uric acid levels in cases were 5.68 mg/dL compared to 2.38 mg/dL in controls. Mean uric acid levels were significantly increased in cases compared to controls (p value = 0.008).

Table 1: Comparison of TSH and Uric Acid between Cases and Controls (N=80)

	Group		p Value
	Cases (n=40) Mean (SD)	Controls (n=40) Mean (SD)	
TSH (µIU/ml)	28.58 (31.47)	17.88 (2.01)	<0.001*
T3 (ng/ml)	0.854 (0.377)	1.5 (0.35)	<0.00001*
T4 (µg/dL)	6.42 (3.1)	9.57 (1.84)	<0.00001*
Uric Acid (mg/dl)	5.68 (1.83)	2.38 (1.12)	0.008*
Unpaired t Test, p Value *Significant			





DISCUSSION

Hypothyroidism is a clinical syndrome resulting from a deficiency of thyroid hormones, which in turn results in slowing down of metabolic processes. On the other hand, hyperthyroidism is a hypermetabolic state. The association between hypothyroidism and hyperthyroidism with hyperuricemia was demonstrated by numerous studies. In our present study, we found that hypothyroidism is associated with hyperuricemia.

In the study group, the mean serum uric acid value was 5.68 mg/dl, while the control group's was 2.38 mg/dl. This can be due to impacted renal physiology by hypothyroidism, which results in decreased renal plasma flow, impaired glomerular filtration, and impaired excretion of uric acid, all of which increase blood uric acid levels.

According to study conducted by Nagarajappa et al. (2014), there was a statistically significant rise in uric acid levels in patients compared to controls; the hyperuricemia was attributable to decreased renal plasma flow and urate excretion(9).

Studies by Gulab Kanwar et al. (2015), Gagandeep Sidhu et al. (2016), and Vijayapriya I Indrajith (2016) also revealed that hypothyroid patients had considerably higher blood uric acid levels than controls, and that hyperuricemia is a side effect of reduced renal plasma flow and poor glomerular filtration(10,11,12).

A Khan et al. (2010) case-control study revealed that hypothyroid patients had considerably higher serum uric acid levels than controls (7).

A similar study by Sarika Arora et al. (2009) revealed that hypothyroid patients' uric acid levels are significantly higher than those of euthyroid participants (13).

Ajaykumar et al.'s 2013 study also revealed that newly diagnosed hypothyroid individuals had higher uric acid levels, which decreased after six months of thyroxine replacement medications. According to this research, a thyroxine supplementation can reverse the increase in uric acid levels, which is caused by the hypothyroid action on the kidneys, which impairs excretion of uric acid (14).

In this study, the prevalence of hyperuricemia is high among hypothyroid group than euthyroid control group. Similarly, Giordano et al. (2001) observed a statistically significant rise in the incidence of gout and hyperuricaemia in patients with hypothyroidism(15). Although hyperuricemia was shown to be quite prevalent in the current investigation, no cases of gout were reported. This is comparable to a 2009 study by Tayal D et al. that demonstrated that in cases of overt hypothyroidism, hyperuricemia was present but no gout cases were reported(16).

According to study conducted by Marwah et al. (2015), their investigation assessed any potential connections between primary hypothyroidism and purine nucleotide metabolism. Uric acid and creatinine levels were significantly elevated in case group as compared to control group. This finding implies that a decrease in glomerular filtration and renal plasma flow is the secondary cause of hypothyroid hyperuricemia(17). Since the kidneys eliminate 75% of uric acid, poor renal function is one of the causes of hyperuricemia in hypothyroidism.

CONCLUSION

These findings suggest that hyperuricemia is commonly seen in hypothyroidism, which may lead to a small increased risk of gout in patients with untreated hypothyroidism. Therefore, we would emphasize the importance of the routine evaluation of serum uric acid levels in patients with hypothyroidism.

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