Original Article

STUDY OF SERUM URIC ACID LEVELS IN THYROID DYSFUNCTIONS

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ABSTRACT

Background
Hyperuricemia in thyroid dysfunctions has been linked to either impaired renal handling of uric acid or overproduction of uric acid. This study aimed to determine the serum uric acid levels in patients with thyroid dysfunction and to determine the link between thyroid dysfunction and hyperuricemia.

Methods
This prospective and quantitative study which was conducted at Department of Biochemistry, Manipal Teaching Hospital determined the serum uric acid concentrations of 30 years or older; male or female participants diagnosed with either hypothyroidism or hyperthyroidism. T3 and T4 was determined by chemiluminescence immunoassay (CLIA) and OEC VITROS dry chemistry analyzer was used to determine serum uric acid level. Data entry and analysis was done using SPSS version 23. Descriptive statistics using frequency with percentage and inferential statistics using non-parametric tests were used.

Results
In a total of 100 participants, prevalence of hyperuricemia was 42% (31% in hypothyroidism and 11% in hyperthyroidism). The mean serum uric acid in overall participants was 6.25±2.04 (6.55±1.84 in hypothyroidism and 6.05±1.71 in hyperthyroidism). Significant association was seen between thyroid status and hyperuricemia (p = 0.001). Also, significant difference (p = 0.02) was seen in serum uric acid between hyperthyroid and hypothyroid patients.

Conclusion
Higher prevalence rate of hyperuricemia was found among hypothyroid patients than in hyperthyroid subjects, and a significant association was found between thyroid dysfunction and hyperuricemia. This indicates need for more research to further uncover the mechanisms underlying it.

Keywords: Hyperthyroidism, Hyperuricemia, Hypothyroidism

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Citation
INTRODUCTION
Normal tissue metabolism depends immensely on the thyroid hormones (Triiodothyronine and Thyroxine) produced from the thyroid gland. So, abnormal functioning of thyroid gland resulting in either increased secretion (hyperthyroidism) or decreased secretion (hypothyroidism) of thyroid hormones may produce features of abnormally increased or decreased metabolism.1,3

Regarding uric acid, it is a product of the metabolic breakdown of purine nucleotides (adenine and guanine). It is synthesized primarily in the liver, intestines and the vascular endothelium as the end product of an exogenous pool of purines, and endogenously from damaged, dying and dead cells.4

A balance between purine synthesis plus ingestion and uric acid elimination through kidneys and intestine determine the uric acid concentration in body fluids.5 Elimination of uric acid is primarily dependent on the kidneys, whereas some of it is also eliminated through other regions like the gastrointestinal tract. Hyperuricemia may result due to over-production or under-elimination of uric acid or both. It has been observed that a large majority of individuals with hyperuricemia have defects in the renal handling of uric acid, in the form of decreased glomerular filtration, decreased tubular secretion and enhanced tubular reabsorption.6 A number of adverse consequences are associated with hyperuricemia like gout, nephrolithiasis and chronic nephropathy.7

A large number of studies have pointed out that hyperuricemia is observed among patients suffering from hypothyroidism as well as hyperthyroidism.8,9 Regarding hypothyroidism, the possible cause of hyperuricemia has been reported to be a decrease in renal filtration, whereas in case of hyperthyroidism, it has been found to be related to increased production of uric acid.8 Also, a significant correlation between thyroid function and purine nucleotide metabolism has been established.4

Considering the adverse consequences of hyperuricemia as well as the need to further understand the role of thyroid hormones in maintaining normal levels of uric acid in blood, this study aims to determine the serum uric acid levels and the prevalence rates of hyperuricemia in patients with hyper- and hypothyroidism, and to compare these parameters across the gender and age-groups in these patients.

The main aims and objectives of this study were to determine the prevalence rates of hyperuricemia in patients with hyper- and hypothyroidism that have visited Manipal Teaching Hospital as well as to compare the parameters between males and females, as well as different age groups.

METHODS
This was prospective and quantitative study con-ducted in Department of Biochemistry, Manipal Teaching Hospital for a duration of 1 year (Jan 2021-Jan 2022) after obtaining ethical clearance from the Institutional Review Committee of Manipal College of Medical Sciences (MEMG/IRC/418/GA). Patients who attended Manipal Teaching Hospital who underwent thyroid function test (TFT) and had thyroid hormones disarrangement along with the estimation of serum uric acid were taken. The reference ranges for the thyroid hormones and uric acid were taken from the lab of Department of Biochemistry, Manipal Teaching Hospital, Pokhara. The values for the different parameters were TSH: 0.4 – 6.2 T3: 1.4-4.2pg/mL, T4: 0.8-2 ng/mL, serum uric acid: 3.5 – 8.5 mg/dL (for males) and 2.5 – 6.2 mg/dL (for females).10 Samples were collected by convenient sampling method and sample size was 100.

Adult patients above the age of 18 who were classified as hypothyroid using following definitions: serum fT4 < 0.8 ng/dL and adult patients above the age of 18 who were classified as hyperthyroid using following definitions: serum fT4>2ng/dL were included in the study. Informed consent was taken from them prior to the study. Patients with subclinical hypothyroidism and subclinical hyperthyroidism were excluded in the study.

Correlation of the mean serum uric acid concentration between different categories of gender, age-groups and thyroid status was carried out. Thyroid function tests (TFTs) to determine T3, T4 and TSH was done by chemiluminescence immunoassay (CLIA method). OCD VITROS dry chemistry analyzer was used to determine serum uric acid level.

Data entry and analysis were done using SPSS version 23. Non-parametric chi-squared test was used to test the association between various categorical variables. Mann Whitney U and Kruskal wallis test (as the data was not normally distributed) were used to test the differences of serum uric acid levels between the various comparison groups. A p value < 0.05 was considered significant.

RESULTS
In the present study, 100 patients with thyroid dysfunction were considered for the evaluation of their serum uric acid levels. Among them, 55% were patients with hypothyroidism and 45% were with hyperthyroidism. Females comprised of 53% of the population whereas males comprised of 47%. Also, 35% were of age group 30 – 40, another 35% were of age group 40 – 60 and 30% were above 60 years.

Table 1: shows the prevalence rates of hyperuricemia in the overall participants and in patients of different thyroid status, gender and age groups. The prevalence of hyperuricemia in overall thyroid dysfunction
patients was found to be 42%, among which hyperuricemia in the hypothyroid population was much higher at 31% than the hyperthyroid group which showed a prevalence of 11%. A significant association was seen between thyroid status and hyperuricemia (p = 0.001) with hypothyroidism showing a much stronger predisposition. Gender and age group showed no significant association.

Table 2: Shows the comparison of mean serum uric acid concentration (mg/dl) between various categories of thyroid status, gender and age groups. The mean serum uric acid levels in the overall sample with thyroid dysfunction was found to be 6.25 ± 2.04. As illustrated, statistically significant difference (p<0.05) was seen in serum uric acid levels among patients of hyperthyroidism and hypothyroidism. Other categories of gender and age groups showed no significant differences between the groups.

Table 3: Shows prevalence rates of hyperuricemia across the different categories of thyroid status for subgroups of gender and age. As illustrated, no significant correlation was found across the various subgroups.

**Table 1: Status of uric acid in total study participants and according to subgroups of gender, age and thyroid status**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Normal Uric Acid Level (%)</th>
<th>Hyperuricemia (%)</th>
<th>Chi Square Test (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total participants</td>
<td>100</td>
<td>58</td>
<td>42 (%)</td>
</tr>
<tr>
<td>1 Thyroid status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>n = 45</td>
<td>34(75.5%)</td>
<td>11(24.4%)</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>n = 55</td>
<td>24(43.6%)</td>
<td>31(66.3%)</td>
</tr>
<tr>
<td>2 Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>n = 53</td>
<td>29(54.7%)</td>
<td>24(45.2%)</td>
</tr>
<tr>
<td>Male</td>
<td>n = 47</td>
<td>29(61.7%)</td>
<td>18(38.2%)</td>
</tr>
<tr>
<td>3 Age groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 – 40</td>
<td>n = 35</td>
<td>19(54.2%)</td>
<td>16(45.7%)</td>
</tr>
<tr>
<td>40 – 60</td>
<td>n = 35</td>
<td>20(57.1%)</td>
<td>15(42.8%)</td>
</tr>
<tr>
<td>&gt;60</td>
<td>n = 30</td>
<td>19(63.3%)</td>
<td>11(36.6%)</td>
</tr>
</tbody>
</table>

**Table 2: Comparison of the mean serum uric acid concentration (mg/dl) between different subgroups of gender, age and thyroid status**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Uric acid (mg/dl) Mean ± SD</th>
<th>Statistical tests (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total participants</td>
<td>100</td>
<td>6.25 ± 2.04</td>
</tr>
<tr>
<td>1. Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>n = 53</td>
<td>6.08 ± 2.11</td>
</tr>
<tr>
<td>Male</td>
<td>n = 47</td>
<td>6.22 ± 1.99</td>
</tr>
<tr>
<td>2. Age groups (Years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 – 40</td>
<td>n = 35</td>
<td>6.37 ± 1.91</td>
</tr>
<tr>
<td>40 – 60</td>
<td>n = 35</td>
<td>6.55 ± 1.88</td>
</tr>
<tr>
<td>&gt;60</td>
<td>n = 30</td>
<td>6.59 ± 1.89</td>
</tr>
<tr>
<td>3. Thyroid status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>n = 45</td>
<td>6.05 ± 1.71</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>n = 55</td>
<td>6.55 ± 1.84</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The present study shows a statistically significant association between thyroid status and hyperuricemia wherein prevalence of hyperuricemia among patients of hypothyroidism was found to be much more than in patients with hyperthyroidism.

The significant correlation between hypothyroidism and hyperuricemia may be attributed to impaired renal handling of uric acid. The relationship between the thyroid hormones and renal function has been known for several years. Both direct and indirect effects of thyroid hormone on renal function have been observed. The indirect effects are via the influence of thyroid hormones over the cardiovascular system and consequently the renal blood flow. Likewise, the direct effects have been attributed to the effects of thyroid hormones on Glomerular Filtration Rate. These dysfunctions are primarily the effect of reduced levels of thyroid hormone resulting in reduction of cardiac output leading to generalized hypodynamic state of the circulatory system. Long standing hypothyroidism has also been linked to renal defects such as decrease in sodium reabsorption in proximal convoluted tubule, impairment in the concentration and dilution ability of the distal tubules, decrease in urinary urate excretion, along with reduced renal blood flow and glomerular filtration rate. A similar finding of statistically significant higher levels of serum creatinine and serum uric acid was found in hypothyroid patients compared with those in control group in a study done in China. Similarly, other studies have also shown significant association between hypothyroidism and serum uric acid levels. Furthermore, evidence of impaired renal function in hypothyroidism has also been shown by a study done in Bangladesh, which found that mean serum creatinine was significantly higher in hypothyroid subjects than in healthy subjects. Also, the glomerular filtration rate was found to be lower in hypothyroid subjects as compared to healthy ones. On the contrary, no significant association between thyroid hormone levels and serum uric acid was seen in some studies like the study done in Bhopal, India.
which concluded that the correlation between thyroid dysfunction and hyperuricemia remains debatable and that more extensive research needs to be done to come to a reliable conclusion. Likewise, the study done in West Bengal, India, found no significant correlation between hypothyroidism and elevated uric acid levels. 

Also, the correlation between hyperthyroidism and increased serum uric acid levels has been described by some authors. They have attributed this to a possible increase in production of uric acid in the body due to abnormally increased metabolic activities consequent to elevation in thyroid hormone levels.

However, prevalence of hyperuricemia in hyperthyroid patients was found to be weak in this study when compared to hypothyroidism, which is also consistent with the findings of several other studies. Also, the study done in Siena, Italy, on hyperuricemia and gout in thyroid endocrine disorder showed that the correlation between hyperthyroidism and hyperuricemia was much weaker than the relationship between hyperthyroidism and hyperuricemia. Hence, though a number of studies have shown a positive correlation between thyroid dysfunction and serum uric acid levels, many others have shown insignificant and weak correlation between them thus highlighting the need for even more research in this area.

There are some limitations to this study. One of them is that the population sample under study was relatively small and only included patients of a single hospital. More accurate result would have been possible had we included a large and a more variable sample. Another limitation of the study is that it doesn’t take into consideration the patients with subclinical hypothyroid or hyper-thyroidism.

CONCLUSION

This study showed increased prevalence of hyperuricemia in patients suffering from hypothyroidism than those suffering from hyperthyroidism as well as a statistically significant association between thyroid status and hyperuricemia. These findings offer valuable information that points towards the possible underlying mechanisms for development of hyperuricemia.

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