ISSN 2822-2032 (Print) 2822-2040 (Online)

Medical Journal of Eastern Nepal

Volume 02, Number 01, Issue 03, January-June 2023, 16-20

Original Article

STUDY OF SERUM URIC ACID LEVELS IN THYROID DYSFUNCTIONS

*Anshu Bhattarai[1], Goma Kathayat[2], Poonam Karmacharya[1], Indu Tiwari[1], Surjit Singh[1]

[1]Department of Physiology, [2]Department of Biochemistry, Manipal College of Medical Sciences, Pokhara, Nepal

Submitted: 01st- February-2023, Revised: 20th-March-2023, Accepted: 21st-April-2023

DOI: https://doi.org/10.3126/mjen.v2i01.56195

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 chemiluminiscence immunoassay (CLIA) and OCD 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

***Corresponding Author:**
Anshu Bhattarai,
Email: anshu.bhattarai@manipalpokhara.edu.np
ORCID: https://orcid.org/0009-0008-7860-3465

Citation
Bhattarai A, Kathayat G, Karmacharya P, Tiwari I, Singh S, Study of Serum Uric Acid Levels in Thyroid Dysfunctions, MJEN. 2023 June; 2(1):16-20.

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.[6] Also, a significant correlation between thyroid function and purine nucleotide metabolism has been established.[8]

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 conducted 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 chemiluminiscence 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 different subgroups of gender, age and thyroid status

S. N.			Normal Uric Acid Level n(%)	Hyperuricemia n(%)	Chi Square Test (p value)
	Total participants	n=100	58	42	-
1	**Thyroid status**				
	Hyperthyroidism	n = 45	34(75.5%)	11(24.4%)	p < 0.05 (significant)
	Hypothyroidism	n = 55	24(43.6%)	31(56.3%)	
2	**Gender**				
	Female	n = 53	29(54.7%)	24(45.2%)	p > 0.05
	Male	n = 47	29(61.7%)	18(38.2%)	
3	**Age groups**				
	30 – 40	n = 35	19(54.2%)	16(45.7%)	
	40 – 60	n = 35	20(57.1%)	15(42.8%)	p > 0.05
	>60	n = 30	19(63.3%)	11(36.6%)	

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

S. N.			Uric acid (mg / dl) Mean ± SD	Statistical tests (p value)
	Total participants	n=100	6.25 ± 2.04	-
1.	**Gender**			
	Female	n = 53	6.08 ± 2.11	p > 0.05
	Male	n = 47	6.22 ± 1.99	
2.	**Age groups (Years)**			
	30 – 40	n = 35	6.37 ± 1.91	
	40 – 60	n = 35	6.55 ± 1.88	p > 0.05
	>60	n = 30	6.59 ± 1.89	
3.	**Thyroid status**			
	Hyperthyroidism	n= 45	6.05 ± 1.71	p < 0.05 (significant)
	Hypothyroidism	n = 55	6.55 ± 1.84	

Table 3: Prevalence of hyperuricemia for hyper- and hypothyroidism according to different subgroups of gender and age

S. No	Variables	Total participants	Hyperthyroidism: Normal Uric Acid Level n(%)	Hyperthyroidism: Hyperuricemia n(%)	Hyperthyroidism: p value (Chi Square test)	Hypothyroidism: Normal Uric Acid Level n(%)	Hypothyroidism: Hyperuricemia n(%)	Hypothyroidism: p value (Chi Square test)
1	**Gender**							
	Male	n = 47	16(34%)	4(8.5%)	p > 0.05	14(29.7%)	13(27.6%)	p > 0.05
	Female	n = 53	18(33.9%)	7(13.2%)		10(18.8%)	18(33.9%)	
2	**Age-groups (Years)**							
	30-40	n = 35	11(31.4%)	4(8.5%)	p > 0.05	10(28.5%)	10(28.5%)	p > 0.05
	40-60	n = 35	10(28.5%)	5(14.2%)		8(22.8%)	12(34.2%)	
	≥ 60	n = 30	13(43.3%)	2(6.6%)		6(20%)	9(30%)	

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.[11,12] 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.[13,14]

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.[15]

Similarly, other studies have also shown significant association between hypothyroidism and serum uric acid levels.[8,16,17,18]

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.[19]

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.[20] Likewise, the study done in West Bengal, India, found no significant correlation between hypothyroidism and elevated uric acid levels.[21]

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.[22,23]

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.[24] 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 relation between hypothyroidism and hyperuricemia.[8]

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 hypo- 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.

Acknowledgements

We would like to acknowledge all the patients for participating actively in this research work without whom the study would not be possible.

Funding: None

Conflict of interest: None

Ethical approval: Yes

REFERENCES

1. Jameson JL, Mandel SJ, Weetman AP. Disorders of the Thyroid Gland. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, editor. Harrison's Principles of Internal Medicine. 19th ed. New York: McGraw Hill Education; 2015. p. 2283-308.
2. Winter WE, Schatz D, Bertholf RL. The Thyroid: Pathophysiology and Thyroid Function Testing. In: Burtis CA, Ashwood ER, Bruns DE, editor. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th ed. St. Louis, Missouri: Elsevier Saunders; 2012. p. 1905-44.
3. The Thyroid Gland. In: Barret KE, Barman SM, Boitano S, Brooks HL, editor. Ganong's Review of Medical Physiology. 25th ed. New York: McGraw Hill Education; 2016. p. 337-50.
4. Ridi RE, Tallima H. Physiological functions and pathogenic potential of uric acid: A review. J Adv Res. 2017;8(5):487-93.PMID: 28748115
5. Ralston SH, Penman I, Strachan MWJ, Hobson R, editors. Davidson's principles and practice of medicine. 23rd ed. London, England: Elsevier Health Sciences; 2021.
6. Burns CM, Wortmann RL. Disorders of Purine and Pyrimidine Metabolism. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, editor. Harrison's Principles of Internal Medicine. 19th ed. New York: McGraw Hill Education; 2012. p. 431e1-e6.
7. Grassi D, Ferri L, Desideri G, Giosia PD, Cheli P, Pinto RD, et al. Chronic Hyperuricemia, Uric Acid Deposit and Cardiovascular Risk. Curr Pharm Des. 2013;19(13): 2432–8.doi: 10.2174/1381612811319130011.
8. Giordano N, Santacroce C, Mattii G, Geraci S, Amendola A, Gennari C. Hyperuricemia and gout in thyroid endocrine disorders. Clin exp rheumatol. 2001;19(6):661-5. PMID: 11791637
9. See LC, Kuo CF, Yu KH, Luo SF, Chou IJ, Ko YS, et al. Hyperthyroid and hypothyroid status was strongly associated with gout and weakly associated with hyperuricaemia. PloS one. 2014;9(12):e114579. doi:https://doi.org/10.1371/journal.pone.0114579
10. Pandey R, Jaiswal S, Sah JP, Bastola K,Dulal S. Assessment of Serum Enzymes level in Patients with Thyroid Alteration attending Manipal Teaching Hospital, Pokhara. Research and Reviews: A Journal of Life Sciences. RRJoLS.2013; 3(1):1-9.
11. Basu G, Mohapatra A. Interactions between thyroid disorders and kidney disease. Indian J Endocrinol Metab. 2012 Mar-Apr; 16(2): 204-213.doi: 10.4103/2230-8210.93737
12. Emmanouel DS, Lindheimer MD, Katz AI. Mechanism of impaired water excretion in the hypothyroid rat. J Clin Invest.1974; 54: 926–34.doi: 10.1172/JCI107833
13. Leeper RD, Benua RS, Brener JL et al., Hyperuricemia in myxedema. J Clin Endocrinol Metab 1960 Nov; 20: 1457-66.doi: 10.1210/jcem-20-11-1457
14. Allon M, Harrow A, Pasque CB, et al., Renal sodium and water handling in hypothyroid patients: the role of renal insufficiency. J Am Soc Nephrol. 1990 Aug; 1(2):205-10.doi: 10.1681/ASN.V12205.
15. Jia D, Liang LB, Tang GH, He H, Zhang M, Li ZP, Li SQ. [The Association Between Serum Uric Acid and Creatinine in Patients with Hypothyroidism]. Sichuan Da XueXue Bao Yi Xue Ban. 2015 Sep;46(5):747-9. Chinese. PMID: 26619549.
16. Saini V, Yadav A, Arora MK, Arora S, Singh R, Bhattacharjee J. Correlation of creatinine with TSH levels in overt hypothyroidism - a requirement for monitoring of renal function in hypothyroid patients? Clin Biochem. 2012 Feb;45(3):212-4. doi: 10.1016/j.clinbiochem.2011.10.012. PMID: 22061337.
17. Marwah S, Mehta M, Shah H, Haridas N, Trivedi A. Corre-

lation of serum uric acid and serum creatinine in hypothyroidism. Natl J Physiol Pharm Pharmacol. 2015; 5(3): 232-5. doi: 10.5455/njppp.2015.5.1202201523.
18. Kaur V, Singh K, Verma M. Changes in biochemical markers of renal function in subclinical and overt hypothyroidism. Int. J. Bioassays. 2015.
19. Chaudhury H, Raihan K, Uddin M, Ansari S, Hasan M, Ahmed M, Hoque M. Renal function impairment in Hypothyroidism. Bangladesh J Med Biochem. 2013 Jan. 13;6(1):19-25. doi: https://doi.org/10.3329/bjmb.v6i1.13283
20. Jat A, Khare A, Patel N. A study of relationship of hyperuricemia in hypothyroid patients. Int J Med Res Rev. 2019Feb.28 [cited 2023Apr.13];7(1):19-3. doi: https://doi.org/10.17511/ijmrr.2019.i01.04
21. Satyajit K, Arindam S. Correlation of Altered Lipid Profile, Uric Acid and Fasting Plasma Glucose Levels in Females with Hypothyroidism. Endocrinol MetabSyndr. 2017; 6(6):2161-10175. doi: 10.4172/2161-1017.1000275
22. Sato A, Shirota T, Shinoda T, Komiya I, Aizawa T, Takemura Y, Yamada T. Hyperuricemia in patients with hyperthyroidism due to Graves' disease. Metabolism. 1995 Feb;44(2):207-11. doi: 10.1016/0026-0495(95)90266-x.
23. Yazar A, Döven O, Atis S, Gen R, Pata C, Yazar EE, Kanik A. Systolic pulmonary artery pressure and serum uric acid levels in patients with hyperthyroidism. Arch Med Res. 2003 Jan-Feb;34(1):35-40. doi: 10.1016/s0188-4409(02)00457-5.
24. Raber W, Vukovich T, Vierhapper H. Serum uric acid concentration and thyroid-stimulating-hormone (TSH): results of screening for hyperuricaemia in 2359 consecutive patients with various degrees of thyroid dysfunction. Wien KlinWochenschr. 1999 Apr 23;111(8):326-8. PMID: 10378314.