



## CORRELATION BETWEEN URIC ACID AND THYROID HORMONES IN PATIENTS WITH HYPOTHYROIDISM: A CASE CONTROL STUDY

<b>Himani Pundir</b>	Department of Biochemistry, Index Medical College, Hospital and Research, Indore
<b>Jaya Jain</b>	Department of Biochemistry, Index Medical College, Hospital and Research, Indore
<b>Sangeeta B Singh</b>	Department of Biochemistry, SHKM GMC, Nuh
<b>Shikha Mahajan</b>	Department of Biochemistry, SHKM GMC, Nuh
<b>Asha Kumari</b>	Department of Biochemistry, SHKM GMC, Nuh
<b>Yuthika Agrawal*</b>	Department of Biochemistry, SHKM GMC, Nuh *Corresponding Author

### ABSTRACT

**Background:** Thyroid disease influences the purine metabolism, which may increase serum uric acid (UA) level. Previous studies showed a high incidence of hyperuricemia in patients with hypothyroidism but with low thyroid stimulating hormone (TSH)-to-serum uric acid association. **Objective:** Aim of this work was to investigate the serum uric acid relationship to thyroid hormones in patients with hypothyroidism. **Subjects and Methods:** This case-control study included a total of 120 participants as control group and 120 patients with hypothyroidism, attending the outpatient department at Index Medical College, Hospital and Research Centre, Indore. TSH, T4 and T3, fasting blood sugar, fasting lipids, creatinine, and uric acid were evaluated. **Results:** There were significant statistical differences between the studied groups regarding uric acid, T. cholesterol, Triglycerides, HDL -C, LDL-C, creatinine, TSH, T3 and T4 ( $P < 0.001$ ). Serum UA, T3, T4, TSH were comparable in male and female in cases. Among hypothyroid patients, we did not find significant correlation between uric acid and age, kidney function tests, thyroid function tests. **Conclusion:** This study suggests the possible relation of uric acid and hypothyroidism.

**KEYWORDS :** Uric acid; Thyroid hormones; Hypothyroidism.

### INTRODUCTION

Uric acid (UA) is a water soluble and antioxidant compound which is mainly produced by the liver (1). It also protects cell membranes and DNA against the harm done by the free radicals (2). Uric acid is formed by purine metabolism which is affected by thyroid dysfunction (3).

There are few reports about the association of thyroid dysfunction and metabolism of UA, with contradictory evidence. There was a poor relationship between TSH and serum uric acid (SUA) levels (4,5). Previous research, however, documented a high prevalence of elevated levels of UA in hypothyroidism (6), which has been attributed to reduced renal perfusion and glomerular filtration rate (GFR) in primary hypothyroid patients (7).

As to thyroid dysfunction, the elevated levels of SUA are also accompanied with other co-morbid conditions including hypertension, metabolic syndrome, chronic kidney disease and type 2 diabetes mellitus (8). The elevated UA has been seen to regulate endocrine disorders that promote inflammation which can be an important factor leading to dyslipidemia and atherosclerosis (9).

Previous studies have attempted to discover the link between uric acid and hypothyroidism as both these conditions leads to other metabolic changes (6, 10). However, the results of such studies were inconsistent and the association between thyroid disease and SUA concentrations is still unclear.

So, this study was aimed at evaluating the connexion between uric acid and thyroid hormones in patients with hypothyroidism in order to close this gap in the literature.

### Subjects and Methods

This case-control study included a total of 240 patients aged 20 to 60 years, 120 healthy participants as a control group and 120 cases of hypothyroidism, attending at the outpatient department at Index Medical College, Hospital and Research

Centre, Indore. Written informed consent of all the subjects was obtained.

### This Study was Ethically Approved by Ethical Board.

Exclusion criteria included Patients with secondary thyroid dysfunction, pregnancy, history of Renal or Hepatic disease, history of other endocrine disorders and history of medications that can affect UA or thyroid hormones level.

Full medical history was taken from all subjects, emphasizing on age, gender, the duration of thyroid dysfunctions and family history of thyroid disease. Laboratory investigations: fasting blood sugar, Fasting lipids {total cholesterol (TC), triglycerides (TAG), low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C)}, creatinine, uric acid, T3, T4 and TSH, levels were assessed.

T3, T4 and TSH were analyzed by ELISA method.

### Statistical Analysis

Data between case and control group were assessed using t test and expressed as mean  $\pm$  SD. For correlations between quantitative variables, the Pearson correlation coefficient was used. P values  $< 0.05$  have been recognized as statistically important.

### RESULTS

Our study groups included 120 patients with hypothyroidism, 63 were males and 57 were females with their mean age ( $44.08 \pm 16.86$ ) years, and 120 healthy control, with mean age ( $38.20 \pm 14.28$ ) years. There were significant statistical differences between the studied groups regarding uric acid, fasting blood sugar, T. cholesterol, Triglycerides, HDL -C, LDL-C, creatinine, TSH, T3 and T4 ( $P < 0.001$ )(Table 1). All parameters were comparable in male and female in hypothyroid patients (table 2). Among hypothyroid patients, we did not find significant correlation between uric acid and age, kidney function tests, thyroid function tests. (Table 3).

**Table 1: Values And P Value Of Various Parameters In Cases And Controls**

S no	PARAMETER	CASES	CONTROLS	p VALUE
1	S URIC ACID (mg/dL)	7.92+4.13	5.56+4.65	<0.001
2	FASTING BLOOD SUGAR (mg/dL)	164.43+63.47	120.54+20.72	<0.001
3	S. CREATNINE (mg/dL)	1.12+ 0.71	0.68+0.34	<0.001
4	S. CHOLESTEROL (mg/dL)	252.08+27.64	175.43+40.51	<0.001
5	S. TRYGLYCERIDE (mg/dL)	226.93+52.49	121.34+22.93	<0.001
6	S. HDL-C(mg/dL)	42.81+10.69	37.48+4.70	<0.001
7	S.LDL-C(mg/dL)	163.88+29.84	113.80+40.00	<0.001
8	S.VLDL-C(mg/dL)	45.39+10.50	24.27+4.59	<0.001
9	T3(ng/dL)	0.71+0.45	1.25+0.37	<0.001
10	T4(µg/dL)	3.81+1.13	7.30+1.73	<0.001
11	TSH(mIU/L)	6.99+1.14	2.5+1.62	<0.001

**Table 2: Values And P Value Of Various Parameters In Males And Females In Cases Of Hypothyroidism**

S no	PARAMETER	MALES (63)	FEMALES (57)	p VALUE
1	S URIC ACID (mg/dL)	8.04+4.26	7.78+4.01	>0.05
2	FASTING BLOOD SUGAR(mg/dL)	159.43+64.70	170.07+62.17	>0.05
3	S. CREATNINE (mg/dL)	1.08+ 0.21	1.16+1.01	>0.05
4	S. CHOLESTEROL (mg/dL)	251.16+26.34	253.09+29.22	>0.05
5	S. TRYGLYCERIDE (mg/dL)	231.63+51.52	221.34+53.51	>0.05
6	S. HDL-C(mg/dL)	43.02+10.46	42.58+11.03	>0.05
7	S.LDL-C(mg/dL)	161.81+28.25	166.16+31.59	>0.05
8	S.VLDL-C(mg/dL)	46.33+10.30	44.35+10.70	>0.05
9	T3(ng/dL)	0.64+0.41	0.79+0.49	>0.05
10	T4(µg/dL)	3.80+1.12	3.84+1.17	>0.05
11	TSH(mIU/L)	7.02+1.14	6.96+1.16	>0.05

**Table 3: Association (Pearson's Coefficient And P Value) Of Various Parameters With Uric Acid In Hypothyroid Patients**

S no	PARAMETER	r	p VALUE
1	AGE	-.030	.74
2	FASTING BLOOD SUGAR	-.164	0.07
3	S. CREATNINE	.152	.09
4	S. CHOLESTEROL	-.098	.29
5	S. TRYGLYCERIDE	-.030	.74
6	S. HDL-C	-.097	.29
7	S.LDL-C	-.115	.21
8	S.VLDL-C	-0.30	.74
9	T3	-.043	.64
10	T4	-.54	.56
11	TSH	.072	.43

**DISCUSSION**

This case control study shows relationship between UA and thyroid hormones in patients with hypothyroidism. The results in previous studies were inconsistent. Our results supported our hypothesis that in subjects with hypothyroidism, UA levels were significantly higher than controls. Also, no significant association was recorded patients between UA and age, fasting blood sugar, lipid profile, thyroid hormones.

Our results are in agreement with studies by Rafat et al. (11), Khan et al. (12) and Giordano et al. (6). On the contrary, study by Abebe et al. (13) reported low serum UA levels in hypothyroid patients. A case-control study of Sato et al (14) found serum UA levels in overt hypothyroid patients to be decreased. The disagreement between these finding and our

results can be attributed by the differences in the studied population and in sample size.

The current study found that creatinine was significantly higher in hypothyroid patients than control as suggested in studies by Sidhu et al. (15), Rafat et al. (11), Saini et al. (4) and Khan and Majumder (16), while Rashead and Hamid(17) had contrary results.

Histological anomalies in nephrons, especially basement membrane thickening, have been demonstrated in both hypothyroid rats and humans. These changes may result in physiological effects including alterations in renal hemodynamics, decrements in renal blood flow and GFR and hence reduced clearance of creatinine and uric acid (18), in addition to hypothyroid myopathy. For chronic kidney disorders such patients should be closely monitored for hypothyroidism as well.

However, non-significant correlation was revealed between UA and thyroid function tests among our hypothyroid patients. The association between UA level and thyroid disorders has been investigated in many studies, which provided conflicting results. The link between TSH and UA serum has been poor by studies of See et al. (10), Saini et al. (4) and Raber et al. (5) and contrary results were shown by Arora et al. (19)

Our findings showed that in hypothyroid patients T. Cholesterol, triglycerides were significantly higher than controls. This is in agreement with finding of Rafat et al.(11). Abnormal lipid profile in thyroid disorders is common. LDL receptor function gets reduced in hypothyroidism resulting in reduced LDL and intermediate density lipoprotein catabolism and induction of cholesterol synthesis

**CONCLUSION**

It could be concluded that in subjects with hypothyroidism, UA levels were higher than controls. Serum creatinine levels were also higher in hypothyroid patients. No significant correlation was found between UA and other parameters in hypothyroidism patients. This research indicates a thyroid function test might be needed for patients with hyperuricemia.

**REFERENCES**

1. Becker B (1993): Towards the physiological function of uric acid. *Free Radical Biology & Medicine*, 14: 615-631.
2. Spitsin S, Scott G, Kean R et al. (2000): Protection of myelin basic protein immunized mice from free-radical mediated inflammatory cell invasion of the central nervous system by the natural peroxynitrite scavenger uric acid. *Neuroscience Letters*, 292:137-141, 2000.
3. Rodrigues S, Baldo M, Capingana P et al. (2012): Gender distribution of serum uric acid and cardiovascular risk factors: population based study. *Arq Bras Cardiol*, 98(1):13-21.
4. Saini V, Yadav A, Arora M et al. (2012): Correlation of creatinine with TSH levels in overt hypothyroidism—A requirement for monitoring of renal function in hypothyroid patients?. *Clinical Biochemistry*, 45(3): 212-214.
5. Raber W, Vukovich T, Vierhapper H (1999) Serum uric acid concentration and thyroid-stimulatinghormone: results of screening for hyperuricaemia in 2359 consecutive patients with various degrees of thyroid dysfunction. *Wien Klin Wochenschr*, 111: 326-328.
6. Giordano N, Santacroce C, Mattii G et al. (2001) Hyperuricemia and gout in thyroid endocrine disorders. *Clin Exp Rheumatol*, 19:661-665.
7. Khan A, Majumder I (2010): Serum creatinine and uric acid levels of hypothyroid patients. *Bangladesh Journal of Medical Biochemistry*, 3(2): 61-63.
8. Abeles A (2015): Hyperuricemia, gout, and cardiovascular disease: an update. *Curr Rheumatol Rep*, 17: 13-16.
9. Ali N, Rahman S, Islam S et al. (2019): The relationship between serum uric acid and lipid profile in Bangladeshi adults. *BMC Cardiovascular Disorders*, 19: 42-46.
10. See L, Kuo C, Yu K et al. (2014): Hyperthyroid and Hypothyroid Status Was Strongly Associated with Gout and Weakly Associated with Hyperuricaemia. *PLoS One*, 9(12): e114579.
11. Rafat M, Alsaryyad M, El Ghannam M et al. (2019): Study of Serum Uric Acid level in Thyroid Disorders : The Egyptian Journal of Hospital Medicine, 77: 5853-5857.
12. Khan A, Khan M, Ahkter S (2017): Prevalence of thyroid dysfunction in community of Duwakot. *Journal of Pathology of Nepal*, 7: 1184-87.
13. Abebe N, Kebede T, Wolde M (2016): Assessment of renal function and electrolytes in patients with thyroid dysfunction in Addis Ababa, Ethiopia: a cross sectional study. *The Pan African Medical Journal*, 24: 36-42.
14. Sato A, Shiota T, Shinoda T et al. (1995): Hyperuricemia in patients with

- hyperthyroidism due to graves' disease. *Metabolism*, 44:207-211.
15. Sidhu G, Malek R, Khubchandani A et al. (2016): A study of serum urea, creatinine and uric acid levels in hypothyroid patients. *Int J Res Med.*, 5 (2): 115-8.
  16. Khan A, Majumder I (2010): Serum creatinine and uric acid levels of hypothyroid patients. *Bangladesh Journal of Medical Biochemistry*, 3 (2): 61-63.
  17. Rasheed Q, Hamid D (2015): The effect of thyroid hormone on some biochemical factors of kidney. *International Journal of Advanced Research*, 3 (7): 290-297.
  18. Montenegro J, Gonzalez O, Saracho R et al. (1996): Changes in renal function in primary hypothyroidism. *Am J Kidney Dis.*, 27(2): 195-8.
  19. Arora S, Chawla R, Tayal D (2009): Biochemical markers of liver and kidney are influenced by thyroid function – a case – controlled follow up study in Indian hypothyroid subjects. *Indian Journal of Clinical Biochemistry*, 24: 370-374.