Original Article

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Biochemistry Section

Evaluation of Serum Creatinine and Serum Uric Acid in Hypothyroid Patients: A Cross-sectional Study

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ABSTRACT

Introduction: Hypothyroidism, a prevalent endocrine disorder, leads to a generalised metabolic slowdown due to insufficient thyroid hormone production, potentially resulting in elevated levels of serum uric acid and creatinine, thus affecting renal function and purine metabolism.

Aim: To assess serum creatinine and serum uric acid levels in hypothyroid patients while establishing correlations with their thyroid-stimulating hormone (TSH), Free Triiodothyronine (FT3), and Free Thyroxine (FT4) levels.

Materials and Methods: A comparative cross-sectional study was conducted in the Department of Biochemistry, Government Medical College, Kozhikkode, Kerala, India. The study involved 140 participants, including 70 recently diagnosed hypothyroid patients and 70 age- and sex-matched euthyroid individuals. Thyroid hormone levels (FT3, FT4) and TSH were quantified using the Cobas e411 electro-chemiluminescence technique. Serum creatinine levels were measured using the Modified Jaffe's method, and serum uric acid levels were assessed through the Uricase method (Enzokit). Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 21.0, and tables and graphs were generated using Microsoft Word and Excel.

Results: The mean age of study participants of control group was 39.02 years and of the hypothyroid group was 36.80 years. The comparative cross-sectional analysis revealed significantly higher levels of serum uric acid and serum creatinine in hypothyroid patients compared to euthyroid controls. Specifically, hypothyroid patients exhibited a mean serum uric acid level of 10.77±2.34 mg/dL, while euthyroid controls had a mean of 4.37±0.94 mg/dL. Mean serum creatinine levels for hypothyroid patients and euthyroid controls were 2.16±0.80 mg/dL and 0.75±0.14 mg/dL, respectively. Notably, a significant positive correlation was observed between serum uric acid and serum creatinine levels with TSH (r=0.42, p-value <0.001 and r=0.45, p=0.00, respectively).

Conclusion: The study identified significantly higher levels of serum uric acid and creatinine in hypothyroid patients compared to euthyroid individuals, potentially attributed to haemodynamic changes and disruptions in purine metabolism. Regular monitoring of these parameters is crucial for individuals with hypothyroidism.

Keywords: Euthyroid, Free triiodothyronine, Free thyroxine, Thyroid stimulating hormone

INTRODUCTION

The thyroid gland, located anterior to the trachea between the cricoid cartilage and the suprasternal notch, plays a pivotal role in maintaining thermogenic and metabolic homeostasis in adults by producing thyroxine (T4) and triiodothyronine (T3) hormones. These hormones act through thyroid hormone receptors, orchestrating vital physiological processes [1]. Thyroid Stimulating Hormone (TSH), secreted by thyrotrope cells in the anterior pituitary, serves as a key regulator of the thyroid axis and a valuable marker of thyroid hormone action. Hypothalamic Thyrotropin Releasing Hormone (TRH) stimulates pituitary TSH production, initiating thyroid hormone synthesis and secretion [1].

Among thyroid disorders, hypothyroidism is a prevalent condition, manifesting in both mild and severe forms, affecting 2% to 15% of the population. This disorder stems from a deficiency in thyroid hormone secretion and action. Primary hypothyroidism arises when the thyroid gland fails to produce sufficient hormones, while secondary hypothyroidism indicates inadequate function of the hypothalamic-pituitary-thyroid axis. Elevated serum TSH levels precede thyroid hormone decline, commonly attributed to iodine deficiency or autoimmune thyroid disease, marked by elevated anti-thyroid peroxidase antibodies [1]. Sub-clinical hypothyroidism manifests as biochemical evidence of thyroid hormone deficiency, often with minimal clinical symptoms [1].

Thyroid hormones exert a profound influence on kidney function, impacting growth, development, and renal structure and function. Hypothyroidism is associated with reduced Glomerular Filtration Rate (GFR), increased serum creatinine, and alterations in water excretion. Haemodynamic changes in hypothyroidism contribute to elevated serum creatinine levels. Furthermore, disruptions in thyroid hormone levels affect purine metabolism, leading to alterations in uric acid levels, resulting in hyperuricemia and its associated conditions, including gout. These changes can also be attributed to decreased renal plasma flow and impaired glomerular filtration [2-4]. Given the clinical relevance of these parameters in hypothyroidism, accurate estimation of these biochemical markers is crucial for patient management. Early diagnosis and treatment of hypothyroidism can mitigate complications associated with hypothyroid-induced renal dysfunction. Routine assessment of thyroid function is thus imperative [2-6].

The primary objectives of present study were to estimate serum creatinine and serum uric acid levels in hypothyroid patients and compare them with euthyroid individuals, as well as to estimate serum FT3, FT4, and TSH levels in the study subjects. Additionally, the study aimed to identify correlations between serum creatinine, serum uric acid, and serum FT3, FT4, and TSH levels in the study groups.

MATERIALS AND METHODS

The present comparative cross-sectional study was conducted among patients at the Government Medical College, Kozhikode, Kerala, India, including those attending the Endocrinology clinic or

admitted to the Medicine ward within a time period of one year. Study was approved from the Institutional Ethics Committee (IEC), Government Medical College Kozhikode (IEC No.-GMCKKD/RP2016/EC/207).

Inclusion criteria: Case group, Control group and patients attending the inpatient and outpatient units of Government Medical College, Kozhikode, Kerala, India, bystanders of other patients, medical-paramedical staff, and other willing to participate were included in the study

Exclusion criteria: Critical illness, renal failure, diabetes mellitus, systemic hypertension, coronary artery disease, pregnancy, malignancy, gout, chronic alcoholism, and patients unwilling to participate and students not matched to the age group and subjects not providing written consent were excluded from the study.

Study Procedure

Data was collected from 140 subjects, including age, sex, duration of illness, history of smoking, alcoholism, diabetes mellitus, systemic hypertension, blood pressure, pulse rate, and respiratory rate.

Blood parameters assessed: Serum FT3, FT4, and TSH levels using Cobas e411 (electro-chemiluminescence technique). Serum creatinine levels using Modified Jaffe's method. 3. Serum uric acid levels using the Uricase method.

Test principles: Serum FT3, FT4, and TSH estimation (Cobas e411-electro-chemiluminescence): Serum FT3, FT4, and TSH levels were assessed using the Cobas e411 system, which utilises the Electro-chemiluminescence technique. This method involves the use of specific antibodies labeled with a ruthenium complex. For TSH estimation, monoclonal antibodies directed against human TSH are employed, which are labeled with a ruthenium complex. The reaction occurs in multiple steps: first, a sandwich complex is formed with the sample, biotinylated monoclonal TSH-specific antibody, and a monoclonal TSH specific antibody labeled with a ruthenium complex. Then, after adding streptavidin-coated micro-particles, the complex binds to the solid phase via biotin-streptavidin interaction. Finally, chemiluminescent emission, induced by applying a voltage, is measured to determine TSH levels. This method ensures high sensitivity and specificity for thyroid function assessment [1].

Serum creatinine estimation (Modified Jaffe's method): Serum creatinine levels were determined using the Modified Jaffe's method. In this enzymatic colorimetric assay, creatinine forms a yellow-orange complex with picrate under alkaline conditions. The rate of dye formation is directly proportional to the creatinine concentration in the specimen. This method allows for the assessment of renal function as creatinine is freely filtered by the glomeruli and is not significantly re-absorbed or secreted by the renal tubules under normal conditions. The results are corrected for non specific reactions caused by serum/plasma pseudo-creatinine chromogens, ensuring accurate assessment of creatinine levels [3]. These test principles elucidate the biochemical processes underlying the quantification of thyroid hormones and creatinine levels, contributing to the accuracy and reliability of the study's measurements.

STATISTICAL ANALYSIS

Data analysis was performed using SPSS version 21.0. The results were expressed as mean±SD. Student's t-test was used to determine significance, with p-value <0.05 considered significant. Pearson's linear correlation was used to study correlations between parameters.

RESULTS

The study aimed to assess serum creatinine and uric acid levels in individuals with hypothyroidism and investigate their correlation with thyroid function tests. In present study of 140 participants, including 70 hypothyroid patients and 70 controls, demographic characteristics were analysed [Table/Fig-1]. The gender distribution revealed a roughly equal representation of males and females in both groups. However, there were differences in the mean age between the control group (mean age 39.02 years) and the hypothyroid group (mean age 36.80 years) [Table/Fig-2].

Category	Gender		Total n (%)
	Male n (%)	Female n (%)	
Controls	29 (41.4)	41 (58.6)	70 (50.0)
Cases	30 (42.9)	40 (57.1)	70 (50.0)
Total subjects	59 (42.1)	81 (57.9)	140 (100.0)

[Table/Fig-1]: Gender distribution among the study groups.

Study groups	Mean age	Standard deviation
Normal control (n=70)	39.02	8.19
Hypothyroid (n=70)	36.80	9.14

[Table/Fig-2]: Mean age distribution among the study groups.

Thyroid Function Tests (TFT): The study found a significant difference in thyroid function tests between the control and hypothyroid groups. The mean serum TSH levels were markedly elevated in hypothyroid individuals (8.83±3.23 mIU/mL) compared to the control group (1.87±0.98 mIU/mL), with a p-value <0.001 [Table/Fig-3]. Similarly, serum FT3 levels were significantly reduced in hypothyroid patients (2.58±1.16 pmol/L) compared to the control group (4.60±0.62 pmol/L), with a p-value <0.001 [Table/Fig-4]. Serum FT4 levels also showed a significant decrease in hypothyroidism (10.98±3.46 pmol/L) compared to the control group (16.70±2.10 pmol/L) with a p-value <0.001 [Table/Fig-5].

Study groups	Mean TSH (mIU/mL)	Standard deviation	p-value
Control (n=70)	1.87	0.98	<0.001
Hypothyroid (n=70)	8.83	3.23	

[Table/Fig-3]: Mean serum TSH value among the study groups.

Study groups	Mean FT3 (pmol/L)	Standard deviation	p-value
Normal	4.60	0.62	<0.001
Hypothyroid	2.58	1.16	

[Table/Fig-4]: Mean serum FT3 value among the study groups.

Study groups	Mean FT4 (pmol/L)	Standard deviation	p-value
Normal	16.70	2.10	<0.001
Hypothyroid	10.98	3.46	

[Table/Fig-5]: Mean serum FT4 value among the study groups.

Serum uric acid and creatinine levels: The study revealed that hypothyroid individuals had significantly higher mean serum uric acid levels (10.77±2.34 mg/dL) compared to euthyroid individuals (4.37±0.94 mg/dL), with a p-value <0.001 [Table/Fig-6]. Serum creatinine levels were also notably higher in the hypothyroid group (2.16±0.80 mg/dL) compared to the control group (0.75±0.14 mg/dL), with a p-value <0.001 [Table/Fig-7].

Study groups	Mean uric acid (mg/dL)	Standard deviation	p-value
Normal	4.37	0.94	<0.001
Hypothyroid	10.77	2.34	

[Table/Fig-6]: Mean serum uric acid value among the study groups.

Study groups	Mean creatinine (mg/dL)	Standard deviation	p-value
Normal	0.75	0.14	<0.001
Hypothyroid	2.16	0.80	

[Table/Fig-7]: Mean serum creatinine value among the study groups.

Correlation analysis: This demonstrated a significant positive correlation between serum TSH levels and both uric acid (r=0.42) and

creatinine (r=0.45) in hypothyroid patients [Table/Fig-8]. Scatter plots visually represented these correlations, showing a linear relationship between TSH levels and uric acid as well as TSH levels and creatinine in hypothyroidism.

Correlation of serum TSH with other parameters	Pearson's correlation (r)	p-value
Uric acid	0.42	<0.001
Creatinine	0.45	<0.001

[Table/Fig-8]: Correlation of serum TSH with uric acid and creatinine.

The study findings indicate that hypothyroidism is associated with alterations in serum creatinine and uric acid levels [Table/Fig-6,7]. Hypothyroid patients exhibited elevated levels of both uric acid and creatinine compared to euthyroid individuals. Additionally, there was a significant positive correlation between TSH levels and both uric acid and creatinine in hypothyroidism, suggesting a potential link between thyroid function and renal function in these patients [Table/Fig-8]. [Table/Fig-9] presents the correlation of serum FT3 levels with uric acid and creatinine. The analysis shows that there is no statistically significant correlation between serum FT3 and either uric acid (r=-0.005, p=0.970) or creatinine (r=-0.076, p=0.532). These results suggest that there is no meaningful linear relationship between serum FT3 levels and uric acid or creatinine in the studied population. [Table/Fig-10], on the other hand, displays the correlation of serum FT4 levels with uric acid and creatinine. Similar to the findings for serum FT3, there is no statistically significant correlation between serum FT4 and uric acid (r=-0.018, p=0.883) or creatinine (r=0.014, p=0.910). This indicates that there is no significant linear association between serum FT4 levels and uric acid or creatinine in the examined subjects. In summary, these results suggest that serum FT3 and FT4 levels do not appear to be strongly linked to uric acid or creatinine levels in the study population.

Correlation of serum FT3 with other parameters	Pearson's correlation (r)	p-value
Uric acid	-0.005	0.970
Creatinine	-0.076	0.532

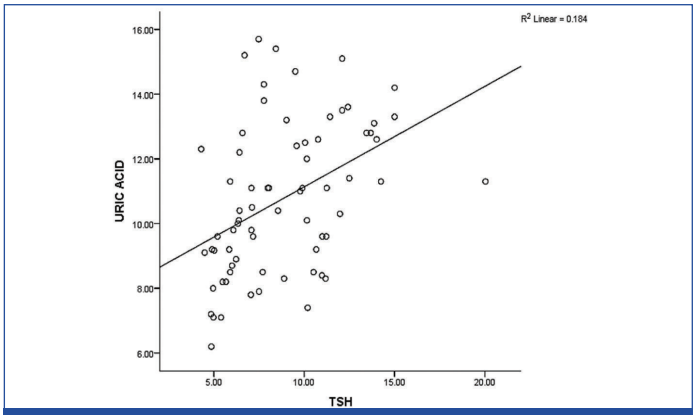
[Table/Fig-9]: Correlation of serum FT3 with other parameters.

Correlation of serum FT4 with other parameters	Pearson's correlation (r)	p-value
Uric acid	-0.018	0.883
Creatinine	0.014	0.910

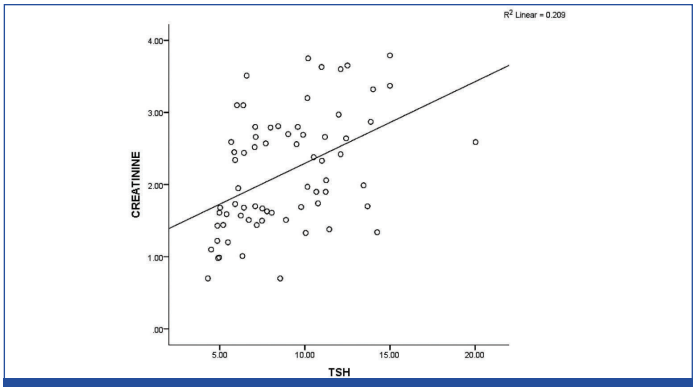
[Table/Fig-10]: Correlation of serum FT4 with other parameters.

Scatter plots:

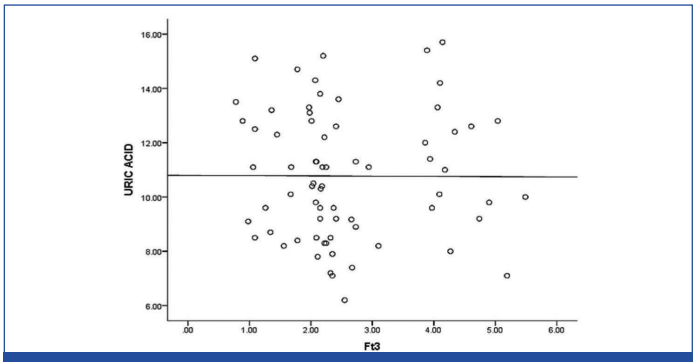
- Scatter Plot 1: Serum TSH with uric acid - This plot illustrates a significant positive correlation between serum TSH levels and uric acid in hypothyroid patients [Table/Fig-11].
- Scatter Plot 2: Serum TSH with creatinine - This plot demonstrates a significant positive correlation between serum TSH levels and creatinine in hypothyroid patients [Table/Fig-12].
- Scatter Plot 3: Serum FT3 with uric acid - This plot indicates an insignificant correlation between serum FT3 and uric acid in hypothyroid patients [Table/Fig-13].
- Scatter Plot 4: Serum FT3 with creatinine - This plot shows an insignificant negative correlation between serum FT3 and creatinine in hypothyroid patients [Table/Fig-14].
- Scatter Plot 5: Serum FT4 with uric acid - This plot reveals no significant association between serum FT4 and uric acid in hypothyroid patients [Table/Fig-15].
- Scatter Plot 6: Serum FT4 with creatinine - This plot displays an insignificant correlation between serum FT4 and creatinine in hypothyroid patients [Table/Fig-16].



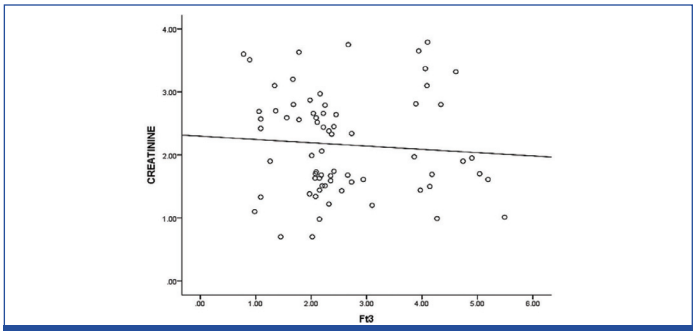
[Table/Fig-11]: Scatter Plot 1: Serum TSH with uric acid.



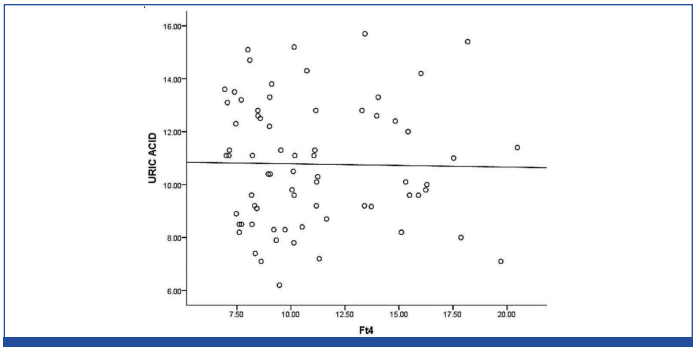
[Table/Fig-12]: Scatter Plot 2: Serum TSH with creatinine.



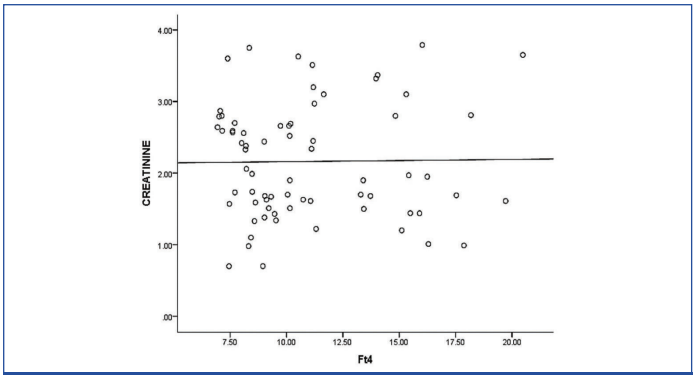
[Table/Fig-13]: Scatter Plot 3: Serum FT3 with uric acid.



[Table/Fig-14]: Scatter Plot 4: Serum FT3 with creatinine.



[Table/Fig-15]: Scatter Plot 5: Serum FT4 with uric acid.



[Table/Fig-16]: Scatter Plot 6:Serum FT4 with creatinine.

DISCUSSION

The current study aimed to assess serum uric acid and serum creatinine levels in hypothyroid patients and investigate potential relationships with thyroid function indicators. The participants in present study ranged in age from 20 to 60 years and included 70 hypothyroid patients and 70 healthy controls. The study concentrated on common symptoms of hypothyroidism, including fatigue, constipation, sensitivity to cold, menstrual cycle changes, weight gain, and hair loss. With the help of pertinent sources, this discussion thus provides a thorough examination of the findings and contextualises them.

Association between hypothyroidism and gender: The study found that 57.14% of hypothyroid patients were women, a considerable prevalence. This finding is in line with a number of earlier studies [7-10], which have repeatedly shown that women are more likely than men to experience thyroid problems, including hypothyroidism. The difference between men and women in their hormones, particularly estrogen's probable role in modifying thyroid function, is suggested to be responsible for this gender gap in thyroid problems [7,11,12].

Thyroid function parameters and hypothyroidism: The present study comparative cross-sectional analysis revealed significant differences between hypothyroid and euthyroid patients in several important thyroid function indicators, including TSH, FT3, and FT4.

Serum TSH: The mean TSH concentration for hypothyroid patients was significantly higher compared to the control group, indicating a clear correlation between elevated TSH levels and hypothyroidism [Table/Fig-3] [5]. This increase in TSH is a result of the body trying to compensate for low thyroid hormone levels by stimulating the thyroid gland to produce more thyroid hormones.

Serum FT3 and FT4: These levels were significantly lower in hypothyroid patients as compared to euthyroid individuals [Table/Fig-4-5]. Reduced levels of FT3 and FT4 are consistent with the main symptom of hypothyroidism, which is the thyroid gland's underproduction of thyroid hormones by the thyroid gland. These results support a number of earlier studies that have shown an association between hypothyroidism and lower FT3 and FT4 levels [5,7,13-15].

Serum uric acid and hypothyroidism: The study observed a noteworthy increase in serum uric acid levels in individuals with hypothyroidism [Table/Fig-6]. This result indicates a potential association between hypothyroidism and hyperuricemia. This finding aligns with earlier studies, including those conducted by Kuzell WC et al., (1955) [16], Giordano et al., (2001) [17], and Erickson et al., (1994)[13], which first suggested a link between hypothyroidism and hyperuricemia. For instance, Kuzell WC and colleagues examined gout patients and found that 20% of males and 30% of females had hypothyroidism [16]. Several variables could be responsible for the connection between hypothyroidism and hyperuricemia. Firstly, hypothyroidism may result in decreased renal plasma flow and glomerular filtration, which could raise blood uric acid levels [15]. Secondly, patients with hypothyroidism may experience worsening hyperuricemia due to poor renal excretion of uric acid, which may be brought on by a decreased GFR. Studies by Kreisman SH and Hennessey JV (1999) [18], Schmid et al., (2004) [14], and Jia et al., (2015) [19], which all revealed higher creatinine levels in hypothyroidism, support these theories. While this study's findings highlight a significant positive correlation between serum TSH and uric acid levels in hypothyroid patients [Table/Fig-8], the lack of a correlation between serum FT3 or FT4 and uric acid levels [Table/Fig-9,10] suggests that TSH might play a more direct role in influencing uric acid metabolism. However, the exact mechanisms underlying the relationship between thyroid function and uric acid metabolism warrant further investigation.

Serum creatinine and hypothyroidism: Similar to serum uric acid, the study observed a substantial increase in serum creatinine levels in individuals with hypothyroidism [Table/Fig-7]. Elevated serum creatinine levels are indicative of impaired renal function, which has been consistently associated with hypothyroidism in prior research [14,18-20]. Kreisman SH and Hennessey JV (1999) reported significantly higher mean creatinine values during hypothyroidism than during the euthyroid state, highlighting the impact of thyroid dysfunction on renal function [18]. Furthermore, studies by Schmid C et al., (2004) [14], Jia et al., (2015) [19], Sidhu et al., (2016) [20], and Taruna Bharti et al., (2017) [15] consistently reported elevated creatinine levels in hypothyroid patients. Additionally, Kumara DS et al., (2017) [21] and Nagarajappa et al., (2014) [20] demonstrated a significant relationship between hypothyroidism and increased creatinine levels. These findings underscore the clinical significance of evaluating renal function in hypothyroid patients.

Potential mechanisms underlying renal dysfunction in hypothyroidism: The observed alterations in serum uric acid and creatinine levels in hypothyroidism may be attributed to various mechanisms. Firstly, the reduction in renal plasma flow and GFR associated with hypothyroidism could lead to impaired clearance of both uric acid and creatinine [15]. Secondly, the association between hypothyroidism and muscle dysfunction could contribute to the increase in creatinine levels [18,22].

The results of present study highlight how crucial it is to keep an eye on thyroid function in those with abnormal renal function, and vice versa. This is especially important for people on kidney-clearing medications because thyroid hormones have a significant impact on renal function. Further demonstrating the relationship between thyroid function and renal health, Englund FI et al., (2016) found an inverse relationship between FT3 and FT4 levels and plasma creatinine concentration [23]. Additionally, the Mooraki and Basani (1998) study demonstrated how successfully treating hypothyroidism might result in a decrease in blood creatinine levels, indicating the possibility of reversible renal impairment in these patients [24]. The significance of early diagnosis and effective thyroid hormone replacement therapy is highlighted by this.

Hence, new understandings of the relationships between altered serum uric acid and creatinine levels and hypothyroidism can be deduced from present study. The clinical importance of thyroid assessment in patients presenting with renal failure, and vice versa, is highlighted by the observed gender predominance among hypothyroid patients and the considerable alterations in thyroid function measures. To understand the precise mechanisms behind these relationships and to investigate potential treatment strategies to lessen renal impairment in hypothyroidism, more study is still required. These findings highlight the need for a patient-centered holistic strategy that considers thyroid and renal function.

Limitation(s)

- Serum FT3, FT4, and TSH estimation: While the Electro-chemiluminescence technique offers high sensitivity and specificity for thyroid function assessment, it may be affected

by the presence of autoantibodies to thyroid hormones, which can interfere with the assay results.

- Serum creatinine estimation: The Modified Jaffe's method for creatinine assessment is generally reliable for evaluating renal function. However, it may be influenced by certain factors such as the presence of substances like bilirubin and haemoglobin, which can lead to potential interference in the results.

CONCLUSION(S)

The study has certain drawbacks, including a small sample size and a brief time frame, which could affect the generalisability of the results. There is no post-treatment analysis to determine reversibility, and the causes of hypothyroidism are not investigated. The study lacks thorough renal function tests and only examines hypothyroidism, ignoring variations among thyroid disorders. Furthermore, cardiovascular risk factors are not taken into account. Despite these drawbacks, the study demonstrates strong correlations between higher serum uric acid and creatinine levels and hypothyroidism, highlighting the clinical significance of assessing these parameters in individuals with hypothyroidism. These aspects of endocrine medicine require further study or a more comprehensive understanding.

REFERENCES

[1] Heuer H, Visser TJ. Minireview: Pathophysiological importance of thyroid hormone transporters. Endocrinology. 2009;150(3):1078-83. Doi: 10.1210/en.2008-1518. Epub 2009 Jan 29. PMID: 19179441.

[2] Sayari S, Molaei Z, Torabi Z. The relationship between subclinical hypothyroidism and serum levels of uric acid and creatinine in children aged 2-14 years. Ann Pediatr Endocrinol Metab. 2018;23(1):38-42. Doi: 10.6065/apem.2018.23.1.38. Epub 2018 Mar 22. PMID: 29609448; PMCID: PMC5894565.

[3] Sidhu GK, Malek RR, Khubchandani A, Mansuri SH, Patel MS, Oza RH. A study of serum urea, creatinine and uric acid levels in hypothyroid patients. International Journal Res Med. 2016;5(2):115-18.

[4] Katz AI, Lindheimer MD. Actions of hormones on the kidney. Annu Rev Physiol. 1977;39:97-133. Doi: 10.1146/annurev.ph.39.030177.000525. PMID: 192139.

[5] 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;45(3):212-14. Doi: 10.1016/j.clinbiochem.2011.10.012. Epub 2011 Oct 28. PMID: 22061337.

[6] Jaiswal N, Nirwan DS. Study of serum creatinine level in hypothyroidism. J Mahatma Gandhi Univ Med Sci Tech. 2018;3(3):79-81.

[7] Bar-Andziak E, Milewicz A, Jędrzejuk D, Arkowska A, Mieszczanowicz U, Krzyżanowska-Świniarska B. Thyroid dysfunction and thyroid autoimmunity in a large unselected population of elderly subjects in Poland-the 'PolSenior' multicentre crossover study. Endokrynol Pol. 2012;63(5):346-55. PMID: 23115067.

[8] Dariyerli N, Andican G, Catakoğlu AB, Hatemi H, Burçak G. Hyperuricemia in hypothyroidism: Is it associated with post-insulin infusion glycemic response? Tohoku J Exp Med. 2003;199(2):59-68. Doi: 10.1620/tjem.199.59. PMID: 12705351.

[9] Yokogoshi Y, Saito S. [Abnormal serum uric acid level in endocrine disorders]. Nihon Rinsho. 1996;54(12):3360-63. Japanese. PMID: 8976120.

[10] Isomäki H. Hyperuricaemia in northern Finland. An epidemiological study of serum uric acid in rural, urban and hospital populations. Ann Clin Res. 1969;1(Suppl 1):01-62. PMID: 5399387.

[11] Marwah S, Mehta M, Shah H, Haridas N, Trivedi A. Correlation of serum uric acid and serum creatinine in hypothyroidism. National Journal of Physiology, Pharmacy and Pharmacology. 2015;5(3):232.

[12] Khan AH, Majumder I. Serum creatinine and uric acid levels of hypothyroidpatients. Bangladesh Journal of Medical Biochemistry. 2013;3(2):61-63.

[13] Erickson AR, Enzenauer RJ, Nordstrom DM, Merenich JA. The prevalence of hypothyroidism in gout. Am J Med. 1994;97(3):231-34. Doi: 10.1016/0002-9343(94)90005-1. PMID: 8092171.

[14] Schmid C, Brändle M, Zwimpfer C, Zapf J, Wiesli P. Effect of thyroxine replacement on creatinine, insulin-like growth factor 1, acid-labile subunit, and vascular endothelial growth factor. Clin Chem. 2004;50(1):228-31. Doi: 10.1373/clinchem.2003.021022. PMID: 14709659.

[15] Bharti T, Vijaysimha M, Jayaswal RP, Praveen NM, Jha RK, Sah AK, et al. Serum Urea, Uric acid, and Creatinine levels in Thyroid dysfunctions patients in Gurgaon, India. Int J Innovative Res Sci Eng Technol. 2017;6(8):15964-67.

[16] Kuzell WC, Schaffarzick RW, Naugler WE, Koets P, Mankle EA, Brown B, et al. Some observations on 520 gouty patients. J Chronic Dis. 1955;2(6):645-69. Doi: 10.1016/0021-9681(55)90193-4. PMID: 13271515.

[17] 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):661-65. PMID: 11791637.

[18] Kreisman SH, Hennessey JV. Consistent reversible elevations of serum creatinine levels in severe hypothyroidism. Arch Intern Med. 1999;159(1):79-82. Doi: 10.1001/archinte.159.1.79. PMID: 9892334.

[19] Jia D, Liang LB, Tang GH, He H, Zhang M, Li ZP, et al. [The association between serum uric acid and creatinine in patients with hypothyroidism]. Sichuan Da Xue Xue Bao Yi Xue Ban. 2015;46(5):747-49. Chinese. PMID: 26619549.

[20] Nagarajappa K, Sushma BJ, Shweta R Hebbar. Study of thyroid stimulating hormone, serum creatinine and uric acid levels in patients with hypothyroidism. International Journal of Pure and Applied Bioscience. 2014;2(2):187-90.

[21] Kumara DS, Kumar BG, Krishna CS, Vishwanath HL. Circulating thyroid hormones with serum uric acid and creatinine in hypo and hyperthyroidism. International Journal. 2017;4(2):123-25.

[22] Dumitriu L, Bartoc R, Ursu H, Purice M, Ionescu V. Significance of high levels of serum malonyl dialdehyde (MDA) and ceruloplasmin (CP) in hyper- and hypothyroidism. Endocrinologie. 1988;26(1):35-38. PMID: 3387887.

[23] Englund Flodström I, Berggren K, Usener B, Broberg H, Larsson A, Brattsand G. The effect of thyroid dysfunction on plasma creatinine levels. Annals of Thyroid Research. 2016;2(2):82-86.

[24] Mooraki A, Bastani B. Reversible renal insufficiency, hyperuricemia and gouty arthritis in a case of hypothyroidism. Clin Nephrol. 1998;49(1):59-61. PMID: 9491289.

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