ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Evaluation of Uric acid, Creatinine, BMI, EGFR in hypothyroid patients and euthyroid controls

[1]Dr. N. Jyothi, [2]Dr. Goda Veena Murty, [3]Dr.V. Bhagyalakshmi, [4]Dr. Thumma Sankara Narayana,

[1,2]Assistant Professor, Dept. of Biochemistry, Rangaraya Medical College, Kakinada
[3] Professor & HOD, Dept. of Biochemistry, Rangaraya Medical College, Kakinada
[4]Associate professor, Dept. of Biochemistry, Rangaraya Medical College,Kakinada

Corresponding Author: Dr. Thumma Sankara Narayana

Abstract

Introduction

Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormone leading to generalised slowing down of metabolic process. 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. 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.

Material and Methods

This is a Case control study was conducted in the Department of Biochemistry at Rangaraya Medical College, Kakinada. 50 newly diagnosed hypothyroid patients attending department of General surgery were involved. Demographic information of cases and controls are noted in data collection Tables. BMI Is calculated. Sample collection: Study participants are advised to be on overnight fast and blood sample is collected in morning in labelled red top vacutainer for T3,T4,TSH.

Results

The mean level in cases (1.19 ng/mL) is higher compared to controls (0.73 ng/mL). The standard deviation in cases is also higher, indicating greater variability in T3 levels among cases. The mean level in cases (6.36 µg/dL) is significantly higher compared to controls (0.64 µg/dL), with a much larger standard deviation in cases. The mean TSH level in cases (33.92 µIU/mL) is considerably higher than in controls (1.77 µIU/mL). The standard deviation in cases is also larger, suggesting greater variability. The mean uric acid level in cases (6.28 mg/dL) is higher compared to controls (5.65 mg/dL). The standard deviation is slightly lower in cases (1.32) than in controls (1.55), suggesting that while cases have a higher average uric acid level, the variability among controls is somewhat greater. The mean creatinine level in cases (0.95 mg/dL) is higher compared to controls (0.58 mg/dL). The standard deviation is also higher in cases (0.27) compared to controls (0.24), indicating that creatinine levels vary more among cases. The mean eGFR level in cases (80.26 mL/min/1.73 m^2) is lower compared to controls (92.78 mL/min/1.73 m^2). The standard deviation is higher in cases (15.56) compared to controls (12.18), indicating greater variability in eGFR among cases.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Conclusion

Present study shows that there is increased uric acid levels and creatinine levels and decreased eGFR levels in study group as compared to control group. The prevalence of hyperuricemia is high in hypothyroidism. These changes in the biochemical values is because of the renal dysfunction evident by decrease in mean eGFR level as compared to mean eGFR level in control group. Thus, these findings are helpful in understanding the interaction between thyroid gland and kidney showing the detrimental effect of hypothyroid state on renal functioning.

Keywords: Hypothyroidism, Uric acid, Creatinine, Thyroid Profile.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

INTRODUCTION

Hypothyroidism is a clinical syndrome resulting from deficiency of thyroid hormone leading to generalised slowing down of metabolic process. 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 [2].

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 [3]. 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. [4-6]

Hypothyroidism is associated with many biochemical abnormalities including increased serum creatinine levels. The serum creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration. [7] The serum creatinine level may also be increased due to hypothyroid myopathy. In hypothyroidism, associated autoimmune diseases may also play a role in modifying the underlying renal problem.

Creatinine elevation was presumed to be due to reduction in GFR and decreased renal blood flow and decreased clearance of creatinine. The significant increase of both hyperuricemia and gout was found in the hypothyroid patients.

The objectives for this study are:

- TO estimate T3,T4,TSH in hypothyroid patients and euthyroid controls
- To Estimate uric acid, creatinine in hypothyroid patients and euthyroid controls.
- TO correlate T3, t4, TSH, PARAMETERS with uric acid, creatinine, In hypothyroid patients and euthyroid controls.

Material and Methods

This is a Case control study was conducted in the Department of Biochemistry at Rangaraya Medical College, Kakinada. 50 newly diagnosed hypothyroid patients attending department of General surgery were involved.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Inclusion criteria;

- Newly detected cases of Hypothyroidism
- Age ;21-45 years
- Both male and female

Exclusion Criteria ;

- Persons on thyroxine treatment
- Pregnancy and lactating mothers
- Renal disease, liver disease
- Cardiovascular Disease
- Hypertension, Diabetes mellitus, gout, muscular disorders, malignancy ,smoking, alcoholism Patients on Drugs (Hypolipidemic Drugs) antihypertensives, steroids, H/o of chemotherapy Or radio therapy for malignancy

Data collection

Demographic information of cases and controls are noted in data collection Tables. BMI Is calculated.

Sample collection: Study participants are advised to be on overnight fast and blood sample is collected in morning in labelled red top vacutainer for T3,T4,TSH.

After properly mixing the sample in vacutainer, it is left at a room temperature for 15-20. Minutes for clot formation. The red vacutainer is then centrifuged at 3000-5000rpm for 15 minutes for separation of serum. The serum is aliquoted in to labelled Eppendorf tubes. They are analysed immediately and stored at refrigeration at -4degree centigrade till completion of study process.

BIOCHEMICAL Analysis

Beckman coulter Access 2 immunoassay analyser and AU 480 Clinical chemistry analyser are used for analysis .The instruments are calibrated and calibration is checked by using appropriate controls.

T3, T4,TSH These are analysed in serum by chemiluminiscent, competitive immunoassay Instrument used for analysis is Access 2. Uric acid is estimated by using serum uricase method by using Beckman AU 480. Creatinine is estimated by using jaffes method by using Beckman AU480

Statistical ANALYSIS

All the participants data after collection and saved on the spread sheets in MS excel. SPSS Software is used for data analysis. After testing for normal distribution of data of Measured variables. Mean +SD is used to summarise this data.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Ethical Consideration:

Study proposal was submitted to Institutional ethical committee for approval before conduction of study.

Results

Table 1: Distribution of Age Group between Cases and Controls

Age Group in years	Cases n (%)	Controls n (%)
21-25	21 (42%)	19 (38%)
26-30	13 (26%)	16 (32%)
31-35	11 (22%)	9 (18%)
36-40	5 (10%)	6 (12%)
41-45	50 (100%)	50 (100%)

In table 1, total of 50 cases and 50 controls, but the percentages don't sum up to 100% for the cases or controls. The age group 21-25 has a higher percentage of cases (42%) compared to controls (38%). The age group 26-30 has a lower percentage of cases (26%) compared to controls (32%). The age group 31-35 has a higher percentage of cases (22%) compared to controls (18%). The age group 36-40 has a lower percentage of cases (10%) compared to controls (12%).

Table 2: Distribution of Gender between Cases and Controls

Gender	Cases n (%)	Controls n (%)
Male	5 (10%)	6 (12%)
Female	45 (90%)	44 (88%)
Total	50 (100%)	50 (100%)

In table 2, Male: 10% of cases are male, compared to 12% of controls. This suggests a slightly lower proportion of males among the cases compared to controls. Female: 90% of cases are female, compared to 88% of controls. This indicates a slightly higher proportion of females among the cases.

Table 3: Distribution of Height, Weight and BMI between Cases and Controls

Parameters	Cases Mean±SD	Controls Mean±SD
Height	159.44±9.53	157.94 ±9.24
Weight	64.52±10.29	63.10±8.59
BMI	25.07±5.60	25.32±3.77

Height: Cases have a slightly greater mean height (159.44 cm) compared to controls (157.94 cm). The standard deviations are similar, indicating a comparable variability in height. Weight: Cases have a slightly higher mean weight (64.52 kg) compared to controls (63.10 kg). Again, the standard deviations are comparable. BMI: Cases have a marginally lower mean BMI (25.07 kg/m^2) compared to controls (25.32 kg/m^2), with the controls showing slightly less variability in BMI in table 3.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Table 4: Distribution of Thyroid Profile between Cases and Controls

Thyroid Profile	Cases Mean±SD	Controls Mean±SD
T3	1.19±0.37	0.73 ±0.32
T4	6.36±3.08	0.64±0.40
TSH	33.92±16.78	1.77±0.99

In table 4, T3 (Triiodothyronine): The mean level in cases (1.19 ng/mL) is higher compared to controls (0.73 ng/mL). The standard deviation in cases is also higher, indicating greater variability in T3 levels among cases.

T4 (Thyroxine): The mean level in cases (6.36 µg/dL) is significantly higher compared to controls (0.64 µg/dL), with a much larger standard deviation in cases.

TSH (Thyroid Stimulating Hormone): The mean TSH level in cases (33.92 µIU/mL) is considerably higher than in controls (1.77 µIU/mL). The standard deviation in cases is also larger, suggesting greater variability.

Table 5: Distribution of Uric acid level between Cases and Controls

Biochemical Parameters	Cases Mean±SD	Controls Mean±SD
Uric acid	6.28±1.32	5.65 ±1.55

In table 5, the mean uric acid level in cases (6.28 mg/dL) is higher compared to controls (5.65 mg/dL). The standard deviation is slightly lower in cases (1.32) than in controls (1.55), suggesting that while cases have a higher average uric acid level, the variability among controls is somewhat greater.

Table 6: Distribution of Creatinine level between Cases and Controls

Biochemical Parameters	Cases Mean±SD	Controls Mean±SD
Creatinine Level	0.95±0.27	0.58 ±0.24

In Table 6, the mean creatinine level in cases (0.95 mg/dL) is higher compared to controls (0.58 mg/dL). The standard deviation is also higher in cases (0.27) compared to controls (0.24), indicating that creatinine levels vary more among cases.

Table 7: Distribution of EGFR level between Cases and Controls

Biochemical Parameters	Cases Mean±SD	Controls Mean±SD
EGFR	80.26±15.56	92.78 ±12.18

In table 7, the mean eGFR level in cases (80.26 mL/min/1.73 m^2) is lower compared to controls (92.78 mL/min/1.73 m^2). The standard deviation is higher in cases (15.56) compared to controls (12.18), indicating greater variability in eGFR among cases.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Discussion

Present study evaluated the effect of hypothyroidism on parameters of renal function and to compare it with euthyroid subjects and also to study the correlation of (TSH, T4 and T3) with uric acid, creatinine and e GFR. Person with age group 21–45 years were included in this study. Most of the people in study group belonged to the age group of 21 to 40 years and that of control group belonged to age group 21-30 years. In a study conducted by Chandhury H.S. et al., 2013, the most common age group 30-39 years. [8] The mean age of hypothyroid and controls were nearly same. However, hypothyroidism was found more common in 25-35 years age group.

In our study, male: 10% of cases are male, compared to 12% of controls. This suggests a slightly lower proportion of males among the cases compared to controls. Female: 90% of cases are female, compared to 88% of controls. This indicates a slightly higher proportion of females among the cases. Tejomani M et al. 2013 also observed the prevalence of hypothyroidism was higher among females. [9] The increased predisposition of females is observed in overt and subclinical hypothyroids. Also in Qahtan A. Rashead et al. 2015 study- distribution of study population had more percentage rate of females than the percentage rate of males. [10]

In this study, T3 (Triiodothyronine): The mean level in cases (1.19 ng/mL) is higher compared to controls (0.73 ng/mL). The standard deviation in cases is also higher, indicating greater variability in T3 levels among cases. T4 (Thyroxine): The mean level in cases (6.36 µg/dL) is significantly higher compared to controls (0.64 µg/dL), with a much larger standard deviation in cases. TSH (Thyroid Stimulating Hormone): The mean TSH level in cases (33.92 µIU/mL) is considerably higher than in controls (1.77 µIU/mL). The standard deviation in cases is also larger, suggesting greater variability. It is seen that the (T3, T4) level significantly decreased in study group when compared to control the finding is very similar to Singh et al. 2006, Nagarajappa et al. 2014. [11]

There is a significant difference in TSH value among study and control group which is very similar to study conducted by VI Indrajith. 6 Indrajith 2016 which showed decreased level of T3 and T4 and increased TSH in the study when compared to that of control group. This is due to decreased synthesis of thyroid hormones and loss of negative feedback control when compared to healthy individuals. [12]

In this study, the mean uric acid level in cases (6.28 mg/dL) is higher compared to controls (5.65 mg/dL). The standard deviation is slightly lower in cases (1.32) than in controls (1.55), suggesting that while cases have a higher average uric acid level, the variability among controls is somewhat greater. Very similar results were found in subsequent studies like Nagarajappa et al. 2014 showed increase in uric acid levels in cases as compared to controls and the increase is statistically highly significant, the hyperuricemia is secondary to decreased renal plasma flow and urate excretion. [13]

The changes in biochemical marker of renal function were found to be reversible after thyroxine replacement therapy. [14] A study done by Ajaykumar et al 2013, also showed increase in uric acid levels in newly diagnosed hypothyroid patients, which decreased with 6 months of thyroxine replacement therapy. [15] These studies suggest that increase in uric acid level is because of hypothyroid effect on kidneys leading to impaired urate excretion and once thyroxine

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

supplementation is done it is reversible. [16] Gagandeep Sidhu et al 2016, Vijayapriya I Indrajith 2016 these studies also showed serum uric acid level was significantly increased in hypothyroid patients than controls and hyperuricemia is secondary to a decreased renal plasma flow and impaired glomerular filtration.since 75% of uric acid is eliminated through kidneys, in patients with hypothyroidism impaired renal function is one of the etiology for hyperuricemia. [17]

In this study, the mean creatinine level in cases (0.95 mg/dL) is higher compared to controls (0.58 mg/dL). The standard deviation is also higher in cases (0.27) compared to controls (0.24), indicating that creatinine levels vary more among cases. It had been confirmed that the rise in creatinine levels in hypothyroid patients did not relate to abnormalities in other renal functions or creatine kinase levels suggesting that neither hypothyroid myopathy nor intrinsic renal disease contributed to the changes seen in creatinine levels. [18] In Sukrella Khalid et al. 2006 study, mean serum creatinine levels increased in hypothyroidism as compared to the control group. Tayal et al. 2009 found that mean serum creatinine concentrations were significantly increased in both patient groups i.e. sub-clinical and overt hypothyroid as compared to euthyroid subjects. [19]

All these Studies say that the elevated serum creatinine levels in hypothyroid patients are due to physiological effects including alterations in renal hemodynamics, decrease in GFR and reduced clearance of creatinine. Some argue that serum creatinine level may also be increased due to hypothyroid myopathy. [20] Sarika Arora et al. 2009 The levels of serum creatinine in hypothyroid subjects were within normal range (< 1.4 mg/dl) but significantly higher than in the euthyroid subjects ($p < 0.001$).

Thus, the increase in creatinine in hypothyroid patients, though on the higher side of physiological range is high then the controls and is statistically significant and is mainly because of alterations in renal hemodynamics leading to decrease in GFR, reduced creatinine secretion, thus decreased creatinine excretion. [21]

In this study the mean eGFR level in cases (80.26 mL/min/1.73 m^2) is lower compared to controls (92.78 mL/min/1.73 m^2). The standard deviation is higher in cases (15.56) compared to controls (12.18), indicating greater variability in eGFR among cases. In Anne et al 2008 study, eGFR was calculated using the simplified Modification of Diet in Renal Disease Study equation and it was found that the mean e GFR value is low in hypothyroid as compared to euthyroid and stated that in hypothyroidism, decreased eGFR probably reflects a true reduction in GFR. [22] The mechanism of this is thought to be the decreased cardiac output caused by the reduced cardiac heart rate, stroke volume and contractibility all of which are caused by low thyroid hormone status. [23] Although there is an increased systemic vascular resistance, overall there is a decrease in systemic blood volume and consequently a reduction in GFR. When a low eGFR is encountered, hypothyroidism should be considered as a possible cause. Sukrella Khalid et al 2006, in hypothyroid patients mean estimated GFR was decreased as compared to mean estimated GFR control group and the difference is statistically significant. [24]

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

Conclusion

Present study shows that there is increased uric acid levels and creatinine levels and decreased eGFR levels in study group as compared to control group. The prevalence of hyperuricemia is high in hypothyroidism. These changes in the biochemical values is because of the renal dysfunction evident by decrease in mean eGFR level as compared to mean eGFR level in control group. Thus, these findings are helpful in understanding the interaction between thyroid gland and kidney showing the detrimental effect of hypothyroid state on renal functioning. This renal impairment is often overlooked but is readily reversible by prompt treatment leading to normalization of biochemical markers. Hence, it is suggested to assess the renal status of the patient at the time of diagnosis of Hypothyroidism.

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. Dariyerli N, Andican G, Catakog˘ lu 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.
3. Yokogoshi Y, Saito S. [Abnormal serum uric acid level in endocrine disorders]. Nihon Rinsho. 1996;54(12):3360-63. Japanese. PMID: 8976120.
4. 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.
5. 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.
6. Khan AH, Majumder I. Serum creatinine and uric acid levels of hypothyroidpatients. Bangladesh Journal of Medical Biochemistry. 2013;3(2):61-63.
7. 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.
8. 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.
9. 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.
10. 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.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

11. 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.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. 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.
20. 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.
21. Jaiswal N, Nirwan DS. Study of serum creatinine level in hypothyroidism. J Mahatma Gandhi Univ Med Sci Tech. 2018;3(3):79-81.
22. Karanikas G, Schutz M, Szabo M, et al. Isotopic renal function studies in severe hypothyroidism and after thyroid hormone replacement therapy. Am J Nephrol 2004;24(1):41–45. DOI: 10.1159/000075628.

ISSN: 0975-3583, 0976-2833 VOL 15, ISSUE 08, 2024

23. 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.
24. 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.