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A STUDY ON SERUM UREA AND CREATININE IN DIAGNOSED CASES OF SUBCLINICAL HYPOTHYROIDISM

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ABSTRACT: Hypothyroidism is a progressive disorder characterized by varying degrees of thyroid failure, metabolic consequences, and hemodynamic changes that decrease renal plasma flow and glomerular filtration rate, increasing serum creatinine level. Therefore, the present study aimed to evaluate and analyse the level of serum urea, creatinine and thyroid function tests in cases of subclinical hypothyroidism and apparently healthy controls and determine whether thyroid dysfunction has detrimental effects on serum creatinine and urea levels in subclinical hypothyroidism cases. Both thyroid function tests (TSH, T3, and T4), serum urea, and creatinine were analyzed in 45 cases with subclinical hypothyroidism and 45 healthy subjects. Patients with subclinical hypothyroidism had a statistically significant rise in creatinine levels compared to controls. In contrast, there was no significant difference in serum urea levels between patients and controls. There was likewise a positive correlation between creatinine and urea in patients with subclinical hypothyroidism. The study results indicate that renal function should be regularly monitored in patients with subclinical hypothyroidism.

INTRODUCTION: Subclinical hypothyroidism is defined as a rise in serum thyroid-stimulating hormone (TSH) level above the upper limit of the reference range while serum free thyroxine (FT4) levels remain within the range¹. In India, various epidemiological studies reveal a prevalence percentage of Subclinical hypothyroidism ranging from 9% to 11.4%².

Subclinical hypothyroidism (SCH) is a laboratory diagnosis due to its asymptomatic nature and its link to the kidney. The function isn't well-defined. The thyroid and renal functions have a well-known relationship³. The presence of hypothyroidism is linked to considerable changes in biochemical indicators of renal function^{4,5}.

Thyroid dysfunction has been shown to impair renal physiology and development^{6,7}. Hypothyroidism is accompanied by a decrease in glomerular filtration, an increase in serum creatinine, and a change in water excretion ability^{7,8}. Thyroid hormone (TH) deficiency reduces cardiac output, resulting in a generalized hypodynamic state of the circulatory system, which

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causes these renal abnormalities^{6,9}. Several studies have worked in assessing kidney function test in hypothyroidism, but very few studies have reported the effect of hypothyroidism on renal function tests, especially creatinine^{7,10,11}. Some studies have also reported hyperuricemia leading to gout in hypothyroid subjects^{12,13}. Marwah *et al.*, in their study, discovered that thyroid hormone has a significant impact on renal function. This knowledge would help patients with elevated creatinine or gout who have an unknown thyroid status avoid unneeded testing, treatment costs, and anxiety. Furthermore, Reversibility of renal failure after thyroxine supplementation remains the most consistent way of demonstrating a possible cause-and-effect relationship between hypothyroidism and renal failure¹⁴. In accordance with the result of a previous study, Mohamed Ali *et al.*, in their study have reported that Patients who received appropriate thyroid disease treatment have a lower risk of developing renal dysfunction. Renal dysfunction has been observed to coexist with specific thyroid hormone levels¹⁵. While early studies hypothesized that thyroid hormone deficiency might be a physiologic adaptation in kidney disease patients¹⁶.

Multiple case series have shown that severe hypothyroidism leads to creatinine elevations, reduced plasma flow and decreases GFR^{17,11}. The decrease in renal plasma flow and glomerular filtration rate (GFR) that accompany hypothyroidism are thought to be related to the generalized hypodynamic state of the cardiovascular system in hypothyroidism, which is associated with a consistent elevation in serum creatinine levels. Changes in serum creatinine levels appear to be reversible and occur quickly. It may be clinically important to understand this association because it could account for creatinine elevation in a hypothyroid patient. It may be clinically relevant to understand this association therein it could account for creatinine elevation in a patient with hypothyroidism¹¹. There is very limited available data related to the impact of subclinical hypothyroidism on renal function tests in this region. As a result, the current study was designed to investigate changes in serum urea and creatinine levels in patients with subclinical hypothyroidism and how these values correlate with the patient's thyroid profile.

MATERIALS AND METHODS: The present case-control study was conducted in the Department of Biochemistry, Integral Institute of Medical Sciences & Research, Lucknow, Uttar Pradesh. 90 subjects (45 cases of sub-clinical hypothyroidism and 45 apparently healthy controls) in age group 20-59 years were selected for the study with written informed consent. Cases of subclinical hypothyroidism were selected from patients attending the medicine OPD of IIMS & R. Subjects with a history of renal disease, individuals on a high-protein diet, and pregnant women were excluded from the study. Clinical history was obtained from each study participant with the help of a data collection proforma.

Sample Collection and Serum Separation: 3ml of venous blood was collected from the subjects in a plain vial under aseptic conditions. The blood sample was allowed to clot at room temperature before centrifugation. The serum was further used to estimate urea, creatinine, and thyroid function tests (TSH, T3, and T4).

Estimation of Thyroid Profile and Serum Urea and Creatinine: Serum Creatinine and urea was estimated by using commercially available kits with ERBA CHEM 7 semi autoanalyser.

Thyroid profile was estimated by using commercially available kits with Biomerieux mini vidas immunoanalyzer.

Statistical Analysis: Statistical analysis was done using Microsoft excel and GraphPad. All data were expressed as mean \pm standard deviation. An unpaired t-test was performed to compare the study parameters between cases and controls. Pearson's correlation coefficient was employed to determine the relationship between variables. p-value <0.05 was considered statistically significant.

RESULTS: A total of 90 subjects were enrolled in this case-control study. The results of the statistical analysis have been summarized in the tables. **Table 1** shows the comparison of clinical parameters between the study groups. According to statistical analysis, there was no significant difference between cases and controls with regard to T3, T4, and Urea. However, it was found that levels of TSH and creatinine were raised significantly in cases compared to controls (p=0.0001 & p=0.0001

respectively). **Table 2** shows Pearson’s correlation coefficient between variables in subjects with subclinical hypothyroidism.

A significant positive correlation between urea and creatinine levels was observed.

TABLE 1: CLINICAL PARAMETERS OF THE STUDY GROUPS

Parameters	Cases (Mean±SD) N=45	Controls (Mean±SD) N= 45	p- value
T3	1.25± 0.59	1.20± 0.29	0.64
T4	6.50± 1.22	6.43± 1.36	0.81
TSH	7.48± 2.34	2.45± 1.07	0.0001
UREA	28.84± 7.57	28.47± 6.59	0.82
CREATININE	0.88± 0.30	0.56± 0.17	0.0001

T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone

TABLE 2: CORRELATION BETWEEN VARIABLES IN CASES OF SUBCLINICAL HYPOTHYROIDISM

Parameters	T3	T4	TSH	UREA	Creatinine
T3	1	.184	.345	-.050	.093
T4	-	1	-.016	-.047	.142
TSH	-	-	1	-.209	.041
UREA	-	-	-	1	.519*
CREATININE	-	-	-	-	1

* Correlation is significant at the 0.01 level (2-tailed).

T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormone

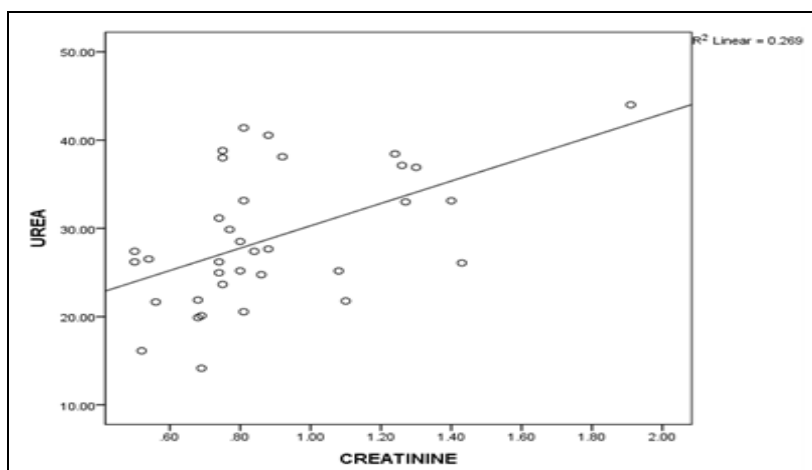


FIG. 1: SCATTER DIAGRAM SHOWING CORRELATION BETWEEN SERUM UREA AND SERUM CREATININE AMONG SUBCLINICAL HYPOTHYROIDISM CASES

DISCUSSION: The current study aimed to assess the effect of subclinical hypothyroidism on renal function parameters, compare it to healthy controls, and investigate the correlation of TSH, T4, T3 urea and creatinine among subclinical hypothyroidism cases. Our study shows that subclinical hypothyroidism may alter renal functions. Urea and creatinine are considered the key markers of glomerular function. In this case-control study, we observed that the level of serum creatinine was significantly increased in patients with subclinical hypothyroidism compared to healthy controls, whereas there was no significant change observed in serum level of urea. A positive correlation has been observed between urea and creatinine in patients with subclinical hypothyroidism.

The results of this study were similar to that of Torkian *et al.* In a case-control study; they reported that serum creatinine is significantly increased in patients with subclinical hypothyroidism. In contrast, they too found no difference in serum urea levels between cases and controls¹⁸. Thyroid hormones impact renal development, kidney hemodynamics, glomerular filtration rate, sodium and water homeostasis, and so on¹⁹. Hypothyroidism affects renal function by systemic hemodynamic, metabolic and cardiovascular effects. Hypothyroidism has been linked to higher serum creatinine levels and a lower glomerular filtration rate. The data presented here clearly show how alteration in thyroid hormone levels affects kidney function in subclinical hypothyroidism.

CONCLUSION: Multiple studies have linked subclinical hypothyroidism to worsening renal function. Our study found that serum creatinine levels were significantly elevated in cases of subclinical hypothyroidism. In conclusion, it is prudent that patients with subclinical hypothyroidism monitor their renal function. However, further studies are required to comprehend the impact of hypothyroidism on renal function fully.

Ethical Review: For human participant enrolment and blood sample collection, approval was taken from the Institutional Ethics Committee (IEC approval number: IEC/IIMS&R/2019/38), Integral Institute of Medical Sciences and research, Lucknow, Uttar Pradesh.

Declaration:

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REFERENCES:

1. Patil VP, Shilpasree AS, Patil VS, Pravinchandra KR, Ingleshwar DG and Vani AC: Evaluation of renal function in subclinical hypothyroidism. *J of Laboratory Physicians* 2018; 10(01): 050-5.
2. Deshmukh V, Behl A, Iyer V, Joshi H, Dholye JP and Varthakavi PK: Prevalence, clinical and biochemical profile of subclinical hypothyroidism in normal population in Mumbai. *Indian Journal of Endocrinology and Metabolism* 2013; 17(3): 454.
3. Patil VP, Shilpasree AS, Patil VS, Pravinchandra KR, Ingleshwar DG and Vani AC: Evaluation of renal function in subclinical hypothyroidism. *Journal of Laboratory Physicians* 2018; 10(01): 050-5.
4. Basu G and Mohapatra A: Interactions between thyroid disorders and kidney disease. *Indian Journal of Endocrinology and Metabolism* 2012; 16(2): 204.
5. Pan Q, Gao S, Gao X, Yang N, Yao Z, Hu Y, Miao L, Chen Z and Wang G: Relation of kidney function and

homocysteine in patients with hypothyroidism. *Endocrine Connections* 2021; 10(5): 502-10

6. Jankauskas SS, Morelli MB, Gambardella J, Lombardi A and Santulli G: Thyroid hormones regulate both cardiovascular and renal mechanisms underlying hypertension. *Journal of Clinical Hypertension Greenwich Conn* 2021; 23(2): 373.
7. Torkian P, Mansournia MA and Mansournia N: Evaluation of biochemical markers of kidney function in patients with subclinical hypothyroidism in comparison with euthyroid people. *Journal of Family Medicine and Primary Care* 2020; 9(8): 4234.
8. Semwal M and Gupta AK: An Overview on the sign of the interaction between thyroid and kidney disease. *Asian Pacific Journal of Nursing and Health Sciences* 2019; 2(2): 25-31.
9. Moses MA and Scheinman SJ: The kidneys and electrolyte metabolism in hypothyroidism; Werner and Ingbar's *The Thyroid*. Lippincott-Raven Philadelphia Edition 1996; 7: 812-815.
10. Arora S, Chawla R and Tayal D: Biochemical markers of liver and kidney function are influenced by thyroid function- A case controlled follow up study in Indian hypothyroid subjects. *Indian Journal of Clinical Biochemistry* 2009; 24(4): 370-74.
11. Dhivya S, Gangopadhyay S, Pradeep Kumar S and Sarkar G: Serum creatinine and eGFR are affected in female hypothyroid patients with poor Thyroid control. *Age Years* 2020; 36(5.45): 33-4.
12. Bhargavi SK, Kumar S and Prasad M: Study of uric acid levels in hypothyroid patients. *Inflammation* 2019; 6(1): 64-66.
13. Rafat MN, Alsayyad MM, El Ghannam MZ and Rafat ME: Study of Serum Uric Acid level in Thyroid Disorders. *The Egyptian J of Hospital Medicine* 2019; 77(6): 5853-7.
14. Rao NS, Chandra A and Malhotra KP: Severe hypothyroidism-associated acute renal failure—A case series from North India and review of literature. *Thyroid Research and Practice* 2019; 16(3): 121.
15. Mohamed Ali M, Reddy Maddika S, Vyas A, Iyer V and Cheriya P: Thyroid disorders and chronic kidney disease. *International Journal of Nephrology* 2014; 2014.
16. Rhee CM, Kalim S. Thyroid Status in Chronic Renal Failure Patients. In *Textbook of Nephro-Endocrinology Academic Press* 2018; 477-492.
17. Karanikas G, Schütz M, Szabo M, Becherer A, Wiesner K, Dudczak R and Kletter K: Isotopic renal function studies in severe hypothyroidism and after thyroid hormone replacement therapy. *American Journal of Nephrology* 2004; 24(1): 41-5.
18. Torkian P, Mansournia MA and Mansournia N: Evaluation of biochemical markers of kidney function in patients with subclinical hypothyroidism in comparison with euthyroid people. *Journal of Family Medicine and Primary Care* 2020; 9(8): 4234.
19. Iglesias P, Bajo MA, Selgas R and Díez JJ: Thyroid dysfunction and kidney disease: an update. *Reviews in Endocrine and Metabolic Disorders* 2017; 18(1): 131-44.

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