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# Early identification of thyroid illness and its intricate relationship to renal function may be crucial for therapy planning

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ABSTRACT

**Introduction:** An epidemiological shift has occurred in India, where the burden of chronic illnesses is increasing, and communicable diseases are declining. Chronic diseases such as diabetes mellitus, cancer, and chronic respiratory disorders are on the rise, and this trend has been attributed to unhealthy lifestyles, increased urbanization, and changes in society and the environment. Such a category did not include chronic kidney disease (CKD). End-stage renal disease (ESRD) is defined as glomerular filtration rate (GFR) <15 ml/min/1.73 m2, while chronic kidney disease (CKD) is defined as a sustained eGFR of <60 ml per minute per 1.73 m2 of body-surface area for more than three months irrespective of the underlying cause while glomerular filtration rate (GFR) <15 ml/min/1.73 m2 is considered as end-stage renal disease (ESRD). CKD is classified into five stages ranging from mild dysfunction to complete failure. Globally, CKD is a significant cause of morbidity and death and there is a 38% increase in mortality linked to renal failure in developing nations like India. It has been shown that the epidemiology of CKD in India differs from that in the West; patients in India were, on average, five to twenty years younger Pregnancy-related malnutrition, environmental variables, genetics, or postponed medical care that accelerates the course of CKD are among the likely reasons and birth weight.

**Materials and Methods:** The present hospital-based, cross-sectional, observational study was conducted in the a tertiary care teaching hospital in South India from December 2020 to January 2024.

The study comprised 50 patients of CKD between 30 and 70 years of age of both sexes with no previous history of any thyroid dysfunction, while 50 apparently healthy age and sex-matched individuals from the same ethnic population with normal renal function and no past history of thyroid disorders served as a control group.

**Result:** The results of this study and most others, there is a possibility that abnormal thyroid hormone activity may result in a decline in renal function. Early identification of thyroid illness and its intricate relationship to renal function may be crucial for therapy planning.

**Conclusion:** The current cross-sectional hospital-based observational study discovered that uremic patients had considerably lower mean TT3 and TT4 and higher mean TSH when compared to healthy controls, regardless of the kind of medication or duration of the disease. Based on the results of this study and most others, there is a possibility that abnormal thyroid hormone activity may result in a decline in renal function. Early identification of thyroid illness and its intricate relationship to renal function may be crucial for therapy planning.



## 1. Introduction

India has experienced an epidemiological transition with a decline in communicable diseases and a growing burden

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of chronic diseases.[1] Unhealthy lifestyles, increasing urbanization, and societal and environmental changes have been implicated in the rapid rise in chronic diseases like cardiovascular disease, diabetes mellitus, cancer, and chronic respiratory diseases.[1] Notably, chronic kidney disease (CKD) was not included in that category.

CKD is characterized by a sustained estimated glomerular filtration rate (eGFR) of <60 ml per minute per 1.73 m2 of body-surface area for more than three months irrespective of the underlying cause while glomerular filtration rate (GFR) <15 ml/min/1.73 m2 is considered as end-stage renal disease (ESRD).[2] CKD is classified into five stages ranging from mild dysfunction to complete failure.[3] CKD has been identified as a leading cause of morbidity and mortality worldwide.[4] In developing countries like India, there was a rise of 38% in mortality attributed to renal failure.[5] The epidemiology of CKD in India has been found that the patients with CKS+D were relatively younger by 5 to 20 years.[6] The probable causes include malnutrition during pregnancy, environmental factors, genetic factors, or delayed medical attention leading to faster progression of CKD.[7] Low birth weight has also been attributed to the increased risk of CKD.[8]

Thyroid hormones are important for the development of kidneys and the maintenance of the internal environment of the body.[9] The thyroid hormones and kidney function are interrelated with each other.[10] The kidney not only participates in thyroid hormone metabolism and elimination, but it also serves as an important site for thyroid hormone action. Thyroid hormone secretion is disturbed in CKD patients as the hypothalamic pituitary thyroid axis gets influenced.[11] Alternatively, thyroid disturbance leads to altered kidney function by affecting water and electrolyte balance, GFR, kidney architecture, renal blood flow, and tubular function.[12]

Low triiodothyronine (T3) is the most common laboratory finding in CKD patients. Factors like metabolic acidosis and protein loss in uremic patients affect the functioning of the iodothyronine deiodinase enzyme, leading to reduced conversion of thyroxine (T4) to T3.[13] Inflammatory cytokines like tumor necrosis factor (TNF)-$\alpha$ and interleukin (IL)-1 get accumulated due to decreased clearance inhibiting the expression of 1 5'-deiodinase leading to low T3.[14] Thyroid-stimulating hormone (TSH) levels may be normal or elevated in CKD patients, but usually, pituitary receptors are reduced in response to the thyrotropin-releasing hormone (TRH). They have both altered TSH circadian rhythm and glycosylation.

Moreover, there is reduced clearance of TSH leading to increased half-life so the response of TSH to TRH gets blunted.[13] In CKD patients, T4 levels may be normal or reduced because of monodeiodinase action in the inner benzene ring, leading to reverse T3, which passes from the vascular space to extravascular and intracellular spaces.[13] Hyperthyroidism is usually not associated with CKD. In fact, it may enhance CKD.[15]

Because of the interrelationship between kidney function and thyroid hormone status and their variability, it is crucial for clinicians to understand their correlation. Despite a large number of available studies, there is a paucity of Indian data, especially in the northeastern region of India, regarding their correlation. So, the present study was planned on CKD patients either on conservative management or hemodialysis to determine their thyroid profile status. To the best of our knowledge, no such study has been conducted in the Barak Valley region of the northeastern state of Assam. The outcome of our study may help to understand the comorbid conditions associated with CKD.

## 2. Materials and Methods

The present hospital-based, cross-sectional, observational study was conducted in the a tertiary care teaching hospital in South India from December 2020 to January 2024

The study comprised 50 patients of CKD between 30 and 70 years of age of both sexes with no previous history of any thyroid dysfunction, while 50 apparently healthy age and sex-matched individuals from the same ethnic population with normal renal function and no past history of thyroid disorders served as a control group. There were 40 males (80%) and 10 females (20%) in each group. Patients were recruited from both the inpatient and outpatient departments of the medicine department, as well as those attending the dialysis unit of the hospital. CKD patients with serum creatinine >5.5 mg/dl and urea level >55 mg/dl and a dipstick test positive for protein were included in the study based on their history, clinical signs, and symptoms. eGFR was calculated using a modification of diet in renal disease (MDRD) 4 variable formula.[16] All the cases were in stage 5 of CKD with eGFR < 15 ml/min/m2, of which 24 (48%) cases were on conservative management, while 26 (52%) were on hemodialysis. The study subjects participated voluntarily after the study's nature and purpose were explained. The written informed consent was obtained from the participants, and their confidentiality was maintained.

Exclusion criteria included patients less than 30 years of age, family history of goiter or thyroid dysfunction, and those receiving conpresent treatment for thyroid disease and drugs known to affect thyroid hormone. All the participants included in the study underwent estimation for serum total triiodothyronine (T3), total thyroxine (T4), TSH, blood urea, and serum creatinine.

## 3. Statistical analysis

The data collected were entered into Microsoft ExcelSheet and analysed using SPSS 27 Version. The data were expressed as mean, standard deviation (SD), standard error of the mean (SEM), and confidence interval (CI). The

significance between different variables was tested using Student's t-test. The chi-square test was used to analyze discrete variables. A two-tailed p-value of less than 0.05 was considered statistically significant.

## 4. Results

The study comprised 50 patients of CKD between 30 and 70 years of age of both sexes with no previous history of any thyroid dysfunction, while 50 apparently healthy age and sex-matched individuals from the same ethnic population with normal renal function and no past history of thyroid disorders served as a control group. There were 40 males (80%) and 10 females (20%) in each group The mean age of the case and control groups was 52.32 ± 8.12 years and 56.38 ± 8.13 years, respectively. The maximum number of subjects in each of the two groups was in the age group of 55 years and 60 years. All the subjects were investigated for blood urea, serum creatinine, T3, T4, and TSH. The eGFR was calculated using the 4-variable MDRD formula. All the cases were in stage 5 of CKD (eGFR < 15 ml/min/m2), out of which 36 (72%) had eGFR ≤ 10 ml/min/m2.

The mean blood urea level was 123.84 ± 68.18 (mg/dl) in cases and 23.81 ± 6.36 (mg/dl) in controls, while the mean serum creatinine level was 12.76 ± 4.48 (mg/dl) in cases and 0.62 ± 0.21 (mg/dl) in controls. In the unpaired t-test between the case and control groups, the two-tailed p-value was <0.0001 for both blood urea and serum creatinine.

The mean blood level of T3, T4, and TSH in cases was 43.17 ± 8,64 (ng/dl), 7.10 ± 2.98 ($\mu$g/dl), and 15.92 ± 7.9 ($\mu$IU/ml), respectively, while in control, it was 109.18 ±18.98 (ng/dl), 9.02 ± 2.31 ($\mu$g/dl), and 2.19 ± 0.49 ($\mu$IU/ml), respectively. The unpaired t-tests between the case and control groups in both T3 and T4 were extremely significant with a two-t8iled p-value <0.0001, while for TSH, it was significant with a two-tailed p-value of 0.0002.

The mean levels of TT3, TT4, and TSH in cases on conservative treatment were 41.82 ± 18.34 (ng/dl), 8.30 ± 3.81 ($\mu$g/dl), and 5.92 ± 2.07 ($\mu$IU/ml), respectively, while in cases on hemodialysis, the mean levels were 32.83 ± 12.11 (ng/dl), 5.21 ± 1.9 ($\mu$g/dl), and 22.15 ± 10.76 ($\mu$IU/ml), respectively. In the unpaired t-test between cases on conservative treatment and cases on hemodialysis, the two-tailed p-value was 0.002, 0.003, and 0.04, respectively.

In the present investigation, low TT3, which was present in all CKD patients and whose mean TT3 was considerably lower than that of healthy control, was the most common anomaly related to thyroid function. While most CKD patients in this research had normal or decreased TT4 levels, there was a statistically significant decrease in the mean TT4 when compared to the healthy controls. In the present study, it was discovered that most TSH levels were raised or normal, but that CKD patients' mean TSH levels were substantially higher than those of the control group. Falhi et al. found similar outcomes when they looked at 50 CKD patients between the ages of 20 and 50. They found that the TSH level increased and the T3 and T4 levels decreased significantly ($P < 0.01$).

In contrast, the study by Khatiwada et al. found that CKD patients had a substantial increase in TSH levels but a non-significant drop in T3 and T4 levels.[16] In comparison to controls, Rajagopalan et al discovered a substantial drop in T3 and T4 and an unaltered TSH in CKD patients Prior research conducted in Iraq on patients with chronic kidney disease (CKD) either conservative care or routine hemodialysis revealed a significant decrease in TT3 and TT4, but no discernible changes in TSH levels when compared to the control group Toda et al found a statistically significant association whereas Alshammari et al found a non-significant correlation between the incidence of hypothyroidism and a decline in GFR.

## 5. Conclusion

The current cross-sectional hospital-based observational study discovered that uremic patients had considerably lower mean TT3 and TT4 and higher mean TSH when compared to healthy controls, regardless of the kind of medication or duration of the disease. Based on the results of this study and most others, there is a possibility that abnormal thyroid hormone activity may result in a decline in renal function. Early identification of thyroid illness and its intricate relationship to renal function may be crucial for therapy planning.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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