International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

A Study of Thyroid Function Tests in Chronic Kidney Disease Patients

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Abstract: ***Background**: Chronic kidney disease (CKD) is a progressive disorder characterized by declining renal function and metabolic disturbances. Thyroid hormones regulate renal growth, glomerular filtration, and electrolyte balance, whereas impaired kidney function alters thyroid hormone synthesis, metabolism, and clearance. **Objective**: To evaluate thyroid function abnormalities in CKD patients and determine their correlation with disease severity. **Methods**: A cross-sectional study was conducted on 52 CKD patients at Government General Hospital, Jayanagar, Bengaluru, excluding those with known thyroid disorders or on dialysis. Serum T3, fT4, and TSH were analyzed by electro-chemiluminescence immunoassay, and eGFR was calculated using the MDRD formula. Thyroid dysfunctions were categorized as low T3 syndrome, subclinical or overt hypothyroidism, and hyperthyroid states. Statistical analysis was performed using SPSS v17, with $p < 0.05$ considered significant. **Results**: Mean age was 61.96 ± 13.59 years; 65.4% were in stage 4 CKD. Thyroid dysfunction was present in 88.5%, predominantly subclinical hypothyroidism (50%) and low T3 syndrome (23.1%). Serum T3 and TSH showed significant correlations with CKD stage ($p = 0.007$, $p < 0.001$). **Conclusion**: Thyroid dysfunction, especially subclinical hypothyroidism and low T3 syndrome, is highly prevalent in CKD and worsens with disease progression. Routine thyroid function screening is recommended to enable timely intervention and improve outcomes.*

Keywords: chronic kidney disease, thyroid dysfunction, subclinical hypothyroidism, low T3 syndrome, renal function

1. Introduction

Chronic kidney disease (CKD) represents a progressive and irreversible deterioration of renal function resulting in the accumulation of metabolic waste products and disturbances in endocrine homeostasis. The estimated global prevalence of CKD ranges from 10–15%, and in India it is approximately 17.2%, with stages 3–5 comprising nearly 10% of cases [1]. The bidirectional interaction between renal and thyroid function is clinically significant: the kidney contributes to the metabolism and excretion of thyroid hormones, while thyroid hormones influence renal growth, glomerular filtration rate (GFR), and sodium-water balance [2]

Thyroid dysfunction in CKD results from multiple mechanisms such as uremic toxin accumulation, metabolic acidosis, iodine retention, altered deiodinase activity, and pituitary–thyroid axis disturbances [3]. Reduced conversion of thyroxine (T4) to triiodothyronine (T3) due to impaired type I 5′-deiodinase activity is a hallmark biochemical alteration [4]. Low T3 syndrome and subclinical hypothyroidism are the most frequently reported abnormalities, whereas overt hypothyroidism and hyperthyroidism are relatively uncommon.

Several studies have demonstrated an inverse relationship between GFR and thyroid-stimulating hormone (TSH) levels, suggesting that subclinical hypothyroidism becomes more prevalent as CKD progresses [5]. However, the reported frequency of thyroid dysfunction in CKD varies widely, ranging from 20% to 80%, possibly due to differences in population demographics, iodine intake, diagnostic thresholds, and severity of renal impairment [6].

Beyond its biochemical significance, thyroid dysfunction in CKD has important clinical implications. Hypothyroidism may exacerbate cardiovascular morbidity, dyslipidemia, and anemia, while hyperthyroidism may accelerate protein catabolism and worsen renal perfusion [7]. Moreover, thyroid hormone abnormalities have been independently linked with increased mortality and reduced quality of life in end-stage renal disease [8]. Despite this, thyroid testing is often underutilized in routine nephrology practice. Therefore, evaluating thyroid function in CKD is critical for comprehensive patient management. The present study aimed to determine the prevalence and pattern of thyroid dysfunction in CKD patients and to assess its correlation with CKD stage, thereby contributing to a better understanding of renal–endocrine interactions.

2. Materials and Methods

2.1 Study design and participants

This was a hospital-based cross-sectional observational study conducted on 52 adult patients diagnosed with chronic kidney disease (CKD) as per the Kidney Disease: Improving Global Outcomes (KDIGO) 2012 criteria (eGFR < 60 mL/min/1.73 m² for ≥3 months or evidence of structural/functional renal damage). Patients were recruited from the in-patient and out-patient departments of General Medicine, Government General Hospital, Jayanagar, Bengaluru, between January 2023 and December 2023.

Ethical clearance was obtained from the Institutional Ethics Committee, and written informed consent was taken from all participants prior to inclusion. The study was conducted in accordance with the Declaration of Helsinki.

2.2 Inclusion criteria

- Adults aged ≥ 18 years with clinically and biochemically proven CKD on conservative management.
- Estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², calculated using the Modified Diet in Renal Disease (MDRD) formula.

2.3 Exclusion criteria

1) Known thyroid disorder or current use of thyroxine, anti-thyroid drugs, or iodine-containing medications/contrast agents within the past 3 months.
2) Patients on maintenance hemodialysis or peritoneal dialysis.
3) Acute illness, infection, recent surgery, or trauma.
4) Known diabetes mellitus, pregnancy, or malignancy.
5) Use of nephrotoxic or thyroid-affecting drugs such as lithium, amiodarone, or corticosteroids.

2.4 CKD staging and diagnostic confirmation

The severity of CKD was categorized according to KDIGO (2012) guidelines based on eGFR estimated by the MDRD formula:

Patients were grouped as follows:
- Stage 3a: eGFR 45–59 mL/min/1.73 m²
- Stage 3b: eGFR 30–44 mL/min/1.73 m²
- Stage 4: eGFR 15–29 mL/min/1.73 m²
- Stage 5: eGFR < 15 mL/min/1.73 m² (excluded if on dialysis).

Only stages 3 and 4 CKD were included to ensure uniformity. Diagnosis of CKD was confirmed by persistently elevated serum creatinine levels (> 3 months) and ultrasonographic evidence of chronic parenchymal disease—such as increased cortical echogenicity, loss of corticomedullary differentiation, or bilaterally shrunken kidneys.

2.5 Data collection

All participants underwent a detailed clinical evaluation and systemic examination, emphasizing renal symptoms (fatigue, edema, oliguria) and thyroid-related manifestations (weight change, cold intolerance, lethargy). Anthropometric data such as height, weight, body-mass index (BMI), and blood pressure were recorded.

Laboratory investigations included complete urine examination, serum urea, creatinine, electrolytes, fasting glucose, and abdominal ultrasonography for kidney morphology and cortical echotexture.

Comorbid conditions, duration of CKD, and ongoing medications were documented to exclude confounding factors influencing thyroid status.

2.6 Laboratory measurements

Venous blood samples (5 mL) were collected from each participant in the morning between 8:00 a.m. and 10:00 a.m. after an overnight fast of 8–10 hours to minimize diurnal variation in thyroid hormone secretion. Samples were collected under aseptic precautions, allowed to clot, and centrifuged at 3000 rpm for 10 minutes to obtain clear serum.

Serum was analyzed immediately or stored at 2–8 °C for a maximum of 24 hours before testing. Hemolyzed or lipemic samples were excluded to avoid assay interference.

Serum TSH, total T3, and free T4 were estimated by electro-chemiluminescence immunoassay (ECLIA) using the Roche Cobas e411 analyzer (Roche Diagnostics, Germany) with manufacturer-supplied calibrators and reagents. The analyzer was calibrated daily using two-point calibration and verified by internal quality control sera at both low and high concentration levels (Bio-Rad Laboratories, USA). The analytical coefficient of variation (CV) for intra-assay and inter-assay precision was maintained below 5% for all three parameters.

The assay's analytical sensitivity was 0.005 µIU/mL for TSH, 0.2 ng/mL for T3, and 0.1 ng/dL for fT4.

Normal reference ranges:
- TSH: 0.45 – 4.50 µIU/mL
- Total T3: 80 – 220 ng/dL
- Free T4: 0.93 – 1.70 ng/dL

In addition to thyroid hormones, routine biochemical investigations were performed to characterize renal function and metabolic status:
- Serum urea and creatinine were measured by the kinetic UV method (Jaffe's reaction) using an automated analyzer (Beckman Coulter AU480).
- Serum sodium and potassium were estimated by ion-selective electrode (ISE) method.
- eGFR was calculated using the MDRD formula for CKD staging.

All assays were carried out in the Department of Biochemistry, Government General Hospital, Jayanagar, following standard internal quality control (IQC) and external quality assurance (EQAS) protocols.

2.7 Classification of thyroid dysfunction

Thyroid status was classified based on serum T3, fT4, and TSH values as follows:
- Low T3 syndrome: Low T3 with normal TSH and fT4.
- Subclinical hypothyroidism: TSH > 4.5 µIU/mL with normal fT4.
- Overt hypothyroidism: TSH > 4.5 µIU/mL with fT4 < 0.93 ng/dL.
- Subclinical hyperthyroidism: TSH < 0.05 µIU/mL with normal T3 and fT4.
- Overt hyperthyroidism: TSH < 0.05 µIU/mL with elevated T3 and/or fT4.

2.8 Statistical analysis

All data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics v17.0 (SPSS Inc., Chicago, IL). Continuous variables were expressed as mean ± standard deviation (SD), while categorical data were summarized as

frequencies and percentages. Differences between categorical variables were assessed using the Chi-square test or Fisher's exact test as appropriate. Pearson's correlation coefficient was applied to assess relationships between thyroid parameters (T3, T4, TSH) and CKD stages/eGFR values. A two-tailed $p < 0.05$ was considered statistically significant.

3. Results

3.1 Sociodemographic and clinical characteristics

A total of 52 patients with chronic kidney disease (CKD) were included in the study. The mean age of the participants was **61.96 ± 13.59 years** (range: 36–86 years). The number of males and females were **23 (44.2%)** and **29 (55.8%)**, respectively. The mean creatinine clearance among the study population was **28.04 ± 10.11 mL/min/1.73 m²**, with a median of 26.5 mL/min (range: 15–52 mL/min). Based on estimated GFR, the distribution of CKD stages showed that the majority of patients were in **Stage 4 (65.4%)**, followed by **Stage 3b (25.0%)** and **Stage 3a (9.6%)**. Anemia was a common finding, observed in **80.8%** of participants, and ultrasonography revealed **bilaterally shrunken kidneys** in **82.7%** of cases. The baseline characteristics of the study participants are summarized in **Table I**.

Table I: Demographic and clinical characteristics of study participants

Variable	Category	n (%)	Mean ± SD / Range
Age (years)	≤ 40 yrs	3 (5.8)	61.96 ± 13.59 (36–86)
	41–50 yrs	11 (21.2)	
	51–60 yrs	12 (23.1)	
	61–70 yrs	8 (15.4)	
	71–80 yrs	14 (26.9)	
	> 80 yrs	4 (7.7)	
Gender	Male	23 (44.2)	
	Female	29 (55.8)	
Creatinine clearance (mL/min)			28.04 ± 10.11 (15–52)
Anemia	Present	42 (80.8)	
	Absent	10 (19.2)	
USG findings	Bilateral shrunken kidneys	43 (82.7)	
	Normal	5 (9.6)	

3.2 Serum thyroid hormone levels

The mean serum **TSH** level among CKD patients was **6.18 ± 5.10 µIU/mL**, with a median of 4.50 µIU/mL (range 0–24.1). Mean total **T3** was **0.94 ± 0.49 ng/mL** (median 0.78), and mean total **T4** was **7.52 ± 2.11 µg/dL** (median 7.11). More than half of the patients (**55.8%**) had low serum T3, and a similar proportion (**55.8%**) had elevated TSH levels. Serum T4 levels were within the normal range in the majority (**90.4%**) of patients. The overall distribution of thyroid hormone status is shown in **Table II**.

Table II: Serum thyroid profile of CKD patients

Parameter	Mean ± SD	Median	Range	Interpretation
Serum T3 (ng/mL)	0.94 ± 0.49	0.78	0.3–3.5	Low in 55.8%
Serum T4 (µg/dL)	7.52 ± 2.11	7.11	1.4–11.0	Normal in 90.4%
Serum TSH (µIU/mL)	6.18 ± 5.10	4.50	0–24.1	High in 55.8%

3.3 Pattern of thyroid dysfunction and its correlation with CKD stages

Overall, **46 of 52 patients (88.5%)** exhibited some form of thyroid dysfunction.

Subclinical hypothyroidism was the most frequent abnormality, occurring in **26 (50.0%)** patients, followed by **low T3 syndrome** in **12 (23.1%)**, **overt hypothyroidism** in **3 (5.8%)**, and **subclinical hyperthyroidism** in **2 (3.8%)**. Only 6 patients (11.5%) had normal thyroid function.

The detailed distribution is presented in **Table III**.

Table III: Types of thyroid dysfunction among CKD patients

Type of dysfunction	Present n (%)	Absent n (%)
Low T3 syndrome	12 (23.1)	40 (76.9)
Subclinical hypothyroidism	26 (50.0)	26 (50.0)
Hypothyroidism	3 (5.8)	49 (94.2)
Subclinical hyperthyroidism	2 (3.8)	50 (96.2)

When correlated with CKD stage, a clear trend was observed:

- **Serum T3** levels declined significantly with worsening CKD stage ($p = 0.007$).
- **TSH** levels increased significantly with disease progression ($p < 0.001$).
- **T4** levels showed no significant association ($p = 0.59$).

The frequency of **subclinical hypothyroidism** and **low T3 syndrome** increased markedly in stage 4 CKD, while **subclinical hyperthyroidism** was restricted to stage 3a. The correlations are summarized in **Table IV**.

Table IV: Correlation of thyroid parameters and dysfunction with CKD stages

Parameter	Stage 3a (n = 5)	Stage 3b (n = 13)	Stage 4 (n = 34)	*p*-value
Serum T3 (low)	0 (0%)	5 (38.5%)	24 (70.6%)	0.007 *
Serum T4 (low)	0 (0%)	2 (15.4%)	3 (8.8%)	0.59
Serum TSH (high)	0 (0%)	6 (46.2%)	23 (67.6%)	< 0.001 *
Low T3 syndrome	0 (0%)	8 (23.5%)	4 (30.8%)	0.09
Subclinical hypothyroidism	0 (0%)	5 (38.5%)	21 (61.8%)	0.02 *
Hypothyroidism	0 (0%)	1 (7.7%)	2 (5.9%)	0.82
Subclinical hyperthyroidism	2 (40.0%)	0 (0%)	0 (0%)	0.01 *

* Statistically significant ($p < 0.05$)

In summary, thyroid dysfunction was strongly associated with CKD severity. Patients in stage 4 showed the highest prevalence of subclinical hypothyroidism and low T3 syndrome, while overt hypothyroidism remained relatively uncommon. The findings indicate that as renal function declines, disturbances in thyroid hormone metabolism and regulation become more pronounced.

4. Discussion

The present study investigated thyroid function abnormalities among patients with chronic kidney disease (CKD) and demonstrated a remarkably high prevalence (88.5%) of thyroid dysfunction. Subclinical hypothyroidism and low T3 syndrome were the predominant abnormalities, and their frequency increased proportionally with the severity of renal impairment. These findings reinforce the intricate bidirectional relationship between thyroid and renal physiology.

4.1 Pathophysiological interplay between thyroid and kidney

The kidney is involved in the metabolism, degradation, and excretion of thyroid hormones, while thyroid hormones in turn regulate renal development, glomerular filtration rate (GFR), and tubular sodium reabsorption. Reduced renal mass and uremic toxin accumulation in CKD impair the activity of type-I 5′-deiodinase, leading to decreased peripheral conversion of thyroxine (T4) to triiodothyronine (T3). Furthermore, iodine retention, metabolic acidosis, inflammation, and altered hypothalamic–pituitary–thyroid axis contributes to the complex hormonal disturbances observed in CKD.

4.2 Comparison with previous studies

Our findings are consistent with those reported by Chonchol et al. (2008), who observed that the prevalence of subclinical hypothyroidism increased from 7% in patients with eGFR > 90 mL/min/1.73 m² to 17.9% when eGFR declined below 60 [9]. Similarly, Lo et al. (2005) found a significant rise in subclinical hypothyroidism from 5.4% to 23% as eGFR dropped below 30. In the present study, the proportion of patients with subclinical hypothyroidism increased from 38.5% in stage 3b to 61.8% in stage 4, showing a similar trend [10].

The prevalence of low T3 syndrome (23.1%) in our cohort aligns with studies by Basu and Mohapatra (2012) and Aminuddin et al. (2023), which described the “low T3 state” as the most common biochemical abnormality in CKD, resulting from impaired T4-to-T3 conversion. Chronic metabolic acidosis, elevated interleukin-1 and TNF-α levels, and reduced hepatic deiodinase activity are recognized mechanisms underlying this alteration [11,12].

Overt hypothyroidism, observed in 5.8% of our patients, was less frequent compared to subclinical forms but comparable to the findings of Kaptein et al. (1988) and Raj et al. (2025), who reported 3–5% prevalence in ESRD populations. Subclinical hyperthyroidism was rare (3.8%) and detected only in early CKD (stage 3a), suggesting that thyroid overactivity may occur transiently before progressive functional decline [13,14].

4.3 Correlation with CKD severity

A statistically significant inverse correlation was observed between CKD stage and serum T3 ($p = 0.007$) and a positive correlation between CKD stage and TSH ($p < 0.001$). These findings indicate that thyroid dysfunction worsens with declining renal function. Reduced clearance of iodine and TSH, along with altered TSH glycosylation and pituitary feedback mechanisms, may explain the gradual rise in TSH despite near-normal free T4 levels. The lack of significant change in serum T4 across stages suggests preserved thyroid synthetic capacity, while the observed hormonal pattern reflects altered peripheral metabolism rather than primary gland failure.

4.4 Clinical significance

Subclinical hypothyroidism and low T3 syndrome in CKD have important clinical implications. Several studies have shown that low T3 levels correlate with higher cardiovascular mortality and inflammation in end-stage renal disease. The low T3 state may represent an adaptive mechanism to reduce energy expenditure and protein catabolism; however, prolonged thyroid dysfunction can exacerbate dyslipidemia, anemia, and atherosclerosis, worsening overall prognosis. Early recognition and correction of thyroid dysfunction in CKD could therefore improve metabolic balance, delay disease progression, and enhance quality of life.

4.5 Comparison with Indian data

Indian studies by Avasthi et al. (2001), Rao et al. (1986), and Basu et al. (2012) have reported thyroid abnormalities in 70–90% of CKD patients, with low T3 and subclinical hypothyroidism being the most common findings. The present study corroborates these results, demonstrating a similar distribution pattern. Minor variations may arise from differences in sample size, assay methodology, and regional nutritional iodine status.

4.6 Limitations

The study's cross-sectional design precludes establishing causality between CKD and thyroid dysfunction. The absence of a healthy control group limits comparison with baseline population levels. Moreover, thyroid autoantibodies and reverse T3 were not assessed, which could have provided a deeper understanding of underlying mechanisms. A larger, longitudinal study would be beneficial to evaluate the progression and prognostic impact of thyroid dysfunction in CKD.

5. Conclusion

The current study demonstrates that thyroid dysfunction is highly prevalent among patients with chronic kidney disease, with subclinical hypothyroidism and low T3 syndrome being the most common abnormalities. The severity of thyroid dysfunction increases with advancing CKD stage, reflecting a strong interrelation between renal failure and endocrine dysregulation. The distribution of CKD stages among the study patients revealed that the majority of participants were in Stage 4, comprising a substantial proportion of the sample. Stage 3b was the second most prevalent stage, while Stage 3a accounted for the smallest group. This indicates that a significant number of patients were in the more advanced stages of chronic kidney disease

Regular thyroid function assessment should be incorporated into the evaluation of CKD patients, even in the absence of clinical symptoms, to facilitate early diagnosis and intervention. Correction of thyroid imbalance may help stabilize metabolic parameters, reduce cardiovascular risk, and improve overall outcomes in CKD management.

Further large-scale, prospective studies are required to clarify whether active treatment of subclinical thyroid dysfunction can modify renal and cardiovascular outcomes in this population.

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