e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(1); 531-539

Original Research Article

Thyroid Dysfunction Among CKD Patients — A Retrospective Analysis of Prevalence and Hormonal Correlations

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Received: 01-11-2025 / Revised: 16-12-2025 / Accepted: 06-01-2026
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Conflict of interest: Nil

Abstract

Background: Chronic kidney disease (CKD) is frequently associated with thyroid dysfunction, yet the prevalence and hormonal patterns remain inadequately characterized in the Indian population. This study aimed to determine the prevalence of thyroid dysfunction among CKD patients and evaluate correlations between thyroid hormone levels and renal function parameters.

Methods: A retrospective cross-sectional study was conducted over 24 months (January 2023 to December 2024) at a tertiary care hospital. Medical records of 168 CKD patients (stages 3-5) were analyzed. Demographic data, renal function tests (serum creatinine, blood urea, eGFR), and thyroid profiles (TSH, FT3, FT4) were extracted. Thyroid dysfunction was classified based on standard reference ranges. Statistical analysis included Pearson correlation, independent t-tests, ANOVA, and multiple regression analysis with significance set at $p<0.05$.

Results: Of 168 patients (mean age 54.6±12.3 years, 61.9% male), 72.6% had thyroid dysfunction. Low T3 syndrome was most prevalent (45.8%), followed by subclinical hypothyroidism (18.5%) and overt hypothyroidism (8.3%). FT3 showed strong positive correlation with eGFR ($r=0.642$, $p<0.001$) and significant negative correlations with serum creatinine ($r=-0.598$, $p<0.001$) and blood urea ($r=-0.567$, $p<0.001$). TSH levels showed weak negative correlation with eGFR ($r=-0.243$, $p=0.002$). Hemodialysis patients had significantly higher prevalence of thyroid dysfunction compared to conservatively managed patients (84.2% vs 63.5%, $p=0.002$). Thyroid dysfunction prevalence increased progressively from CKD stage 3 (58.3%) to stage 5 (86.4%).

Conclusion: Thyroid dysfunction is highly prevalent among CKD patients, with low T3 syndrome being the predominant pattern. Significant inverse correlations between thyroid hormones and declining renal function suggest routine thyroid screening in CKD patients for early detection and appropriate management.

Keywords: Chronic kidney disease, thyroid dysfunction, hypothyroidism, low T3 syndrome, eGFR, hemodialysis.

DOI: 10.25258/ijcpr.18.1.88

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Introduction

Chronic kidney disease (CKD) represents a major global public health challenge, affecting approximately 850 million individuals worldwide, with prevalence rates ranging from 8% to 16% across different populations.[1] The burden of CKD has increased substantially over recent decades, driven primarily by the rising incidence of diabetes mellitus, hypertension, and aging populations.[2] In India, CKD affects approximately 17% of the adult population, representing a significant healthcare burden with limited resources for renal replacement therapy.[3] The progressive nature of CKD leads to numerous systemic complications affecting multiple organ systems, with endocrine abnormalities being particularly common yet frequently underrecognized.

Thyroid dysfunction represents one of the most prevalent endocrine complications in patients with CKD, yet it often remains underdiagnosed due to substantial clinical overlap between uremic symptoms and thyroid-related manifestations.[4]

The prevalence of thyroid abnormalities in CKD patients varies widely across different studies, ranging from 13% in early-stage disease to as high as 70% in end-stage renal disease (ESRD), with considerable variation across different geographic populations and CKD stages.[5] This high prevalence underscores the importance of

understanding thyroid-kidney interactions in clinical practice.

The pathophysiological relationship between CKD and thyroid dysfunction is complex and bidirectional. Declining renal function affects thyroid hormone metabolism through multiple mechanisms, including altered peripheral conversion of thyroxine (T4) to triiodothyronine (T3), reduced renal clearance of iodine leading to altered thyroid hormone synthesis, decreased protein binding of thyroid hormones, and accumulation of uremic toxins that interfere with thyroid hormone action.[6] Additionally, proteinuria can lead to loss of thyroid hormone-binding proteins, further complicating the thyroid function assessment in CKD patients. These alterations result in characteristic patterns of thyroid dysfunction, with low T3 syndrome being the most common abnormality observed in advanced CKD.

Low T3 syndrome, also known as euthyroid sick syndrome or non-thyroidal illness syndrome, is characterized by decreased serum T3 levels with normal or low-normal T4 and thyroid-stimulating hormone (TSH) levels.[7] This condition is highly prevalent in CKD patients, particularly those on hemodialysis, and has been associated with increased morbidity and mortality. Studies have demonstrated that low T3 levels independently predict cardiovascular events, all-cause mortality, and progression to ESRD in CKD patients.[8] Beyond low T3 syndrome, other thyroid abnormalities including subclinical hypothyroidism and overt hypothyroidism are also frequently observed, with prevalence increasing as renal function declines.

Despite the well-established association between CKD and thyroid dysfunction, several critical gaps remain in current understanding, particularly regarding the Indian population. First, there is limited data on the precise prevalence of various thyroid abnormalities across different stages of CKD in Indian patients. Second, the relationship between specific thyroid hormone alterations and markers of renal function requires comprehensive evaluation in diverse populations. Third, the impact of renal replacement therapy modalities, particularly hemodialysis, on thyroid function patterns needs further elucidation.[9] Understanding these relationships has important clinical implications, as thyroid dysfunction can affect multiple outcomes in CKD patients, including cardiovascular health, nutritional status, anemia management, and overall quality of life.

Furthermore, the clinical significance of thyroid dysfunction in CKD extends beyond diagnostic considerations to therapeutic implications. While guidelines for thyroid hormone replacement in the general population are well-established, the management of thyroid abnormalities in CKD patients remains controversial, particularly for subclinical hypothyroidism and low T3 syndrome.[10] Current evidence suggests potential benefits of thyroid hormone replacement in CKD patients, including improved cardiovascular outcomes and possibly delayed progression of renal disease, but optimal treatment thresholds and target levels remain unclear.

This study was therefore undertaken with the primary objectives of determining the prevalence of various patterns of thyroid dysfunction among patients with CKD stages 3 through 5 and evaluating the correlations between thyroid hormone levels (TSH, FT3, FT4) and markers of renal function including serum creatinine, blood urea, and estimated glomerular filtration rate (eGFR). Secondary objectives included comparing thyroid profiles between CKD patients on conservative management versus those receiving maintenance hemodialysis and assessing the distribution of thyroid dysfunction across different stages of CKD. By addressing these objectives, this study aims to contribute to better understanding of thyroid-kidney interactions in the Indian population and provide evidence to support clinical decision-making regarding thyroid screening and management in CKD patients.

Aims and Objectives: The present study was conducted with clearly defined primary and secondary objectives to comprehensively evaluate thyroid dysfunction in chronic kidney disease patients. The primary objectives were to determine the prevalence of various patterns of thyroid dysfunction including hypothyroidism, subclinical hypothyroidism, hyperthyroidism, and low T3 syndrome among patients diagnosed with chronic kidney disease, and to evaluate the correlation between thyroid hormone levels (TSH, FT3, FT4) and markers of renal function including serum creatinine, blood urea nitrogen, and estimated glomerular filtration rate calculated using the CKD-EPI equation.

The secondary objectives were formulated to provide additional insights into the relationship between renal replacement therapy and thyroid function, as well as the progression of thyroid abnormalities with advancing CKD stages. These included comparing thyroid profiles between CKD patients managed conservatively versus those receiving maintenance hemodialysis therapy, and assessing the distribution of different patterns of thyroid dysfunction across the spectrum of chronic kidney disease stages including stage 3a, 3b, 4, and 5. These objectives were designed to provide comprehensive data that would guide clinical practice regarding thyroid screening protocols and management strategies in the chronic kidney disease population.

Materials and Methods

Study Design and Setting: This retrospective cross-sectional observational study was conducted over a period of 24 months from January 2023 to December 2024 at a tertiary care teaching hospital. The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC) of JJM Medical College, Davangere, Karnataka (Ref No.: JJMMC/IEC-01-2026, dated 01-01-2026). As this was a retrospective study utilizing existing medical records, informed consent waiver was obtained as per institutional guidelines for retrospective research. Patient confidentiality was strictly maintained throughout the study, and all data were anonymized using coded identifiers with no patient names or identifying information included in the analysis.

Study Population and Sample Size: The study population comprised patients diagnosed with chronic kidney disease stages 3, 4, or 5 according to Kidney Disease: Improving Global Outcomes (KDIGO) guidelines who attended the outpatient department and inpatient wards of the Nephrology Department and Dialysis Unit during the study period. Based on previous literature reporting a combined prevalence of thyroid abnormalities of 28% in CKD patients, the sample size was calculated using the formula $n = z^2 \times p \times (1-p) / e^2$, where $z = 1.44$ for 85% confidence level, $p = 0.28$, and $e = 0.05$ (margin of error). This calculation yielded a required sample size of 168 patients. A total of 168 patients meeting the inclusion and exclusion criteria were included in the final analysis.

Inclusion Criteria: Patients were included in the study if they met all of the following criteria: diagnosis of chronic kidney disease stages 3, 4, or 5 defined as estimated glomerular filtration rate less than 60 ml/min/1.73 m² calculated using the CKD-EPI equation; age between 18 years and 70 years inclusive; availability of complete medical records including demographic data, clinical history, renal function tests, and thyroid function tests performed during the study period; both male and female patients; and patients either on conservative management or on maintenance hemodialysis therapy for at least three months duration. This duration criterion for dialysis patients was set to allow stabilization of metabolic parameters and avoid the acute effects of dialysis initiation on thyroid function.

Exclusion Criteria: Patients were excluded from the study if they had any of the following: known pre-existing thyroid disease diagnosed before the onset of chronic kidney disease; current treatment with thyroid hormone replacement therapy or anti-thyroid medications; pregnant or lactating women due to physiological changes in thyroid function during these states; history of thyroid surgery or radioiodine therapy within six months prior to thyroid function testing; acute kidney injury superimposed on chronic kidney disease; presence of severe systemic illnesses including active malignancy, severe sepsis or infections, or autoimmune disorders that could independently affect thyroid function; and current treatment with medications known to significantly affect thyroid function including amiodarone, lithium, high-dose glucocorticoids, or interferon therapy.

Data Collection Procedure: Medical records of eligible patients were systematically reviewed and relevant data were extracted using a standardized case record form. Demographic information including age, gender, weight, height, and body mass index were recorded. Clinical data including duration of chronic kidney disease, etiology of kidney disease, CKD stage, treatment modality (conservative management or hemodialysis), and presence of comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease were documented. For patients on hemodialysis, the duration of dialysis therapy and frequency of dialysis sessions per week were noted.

Laboratory Parameters: Laboratory data were extracted from the institutional laboratory information system. Renal function tests including serum creatinine, blood urea nitrogen, and serum electrolytes (sodium and potassium) were recorded. The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Thyroid function tests including thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) were analyzed. Additional laboratory parameters including complete blood count with hemoglobin levels, serum calcium, and serum phosphorus were also documented. All laboratory tests were performed using standard automated analyzers following quality control protocols in the institutional central laboratory.

Definitions and Classification: Chronic kidney disease staging was performed according to KDIGO guidelines based on estimated glomerular filtration rate: 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), and Stage 5 (eGFR <15 ml/min/1.73 m²). Thyroid dysfunction was classified based on standard reference ranges and definitions: euthyroid state was defined as TSH 0.5-5.0 mIU/L with normal FT3 (2.0-4.4 pg/mL) and FT4 (0.93-1.70 ng/dL); overt hypothyroidism as TSH >5.0 mIU/L with low FT4; subclinical hypothyroidism as TSH >5.0 mIU/L with normal FT4; hyperthyroidism as TSH <0.5 mIU/L with elevated FT3 or FT4; and low T3 syndrome as FT3 <2.0 pg/mL with normal or low-normal TSH and FT4.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed continuous variables were expressed as mean ± standard deviation, while non-normally distributed variables were presented as median with interquartile range. Categorical variables were expressed as frequencies and percentages. Pearson correlation coefficient was used to assess linear relationships between normally distributed continuous variables, while Spearman rank correlation was used for non-normally distributed variables. Independent samples t-test was employed for comparing means between two groups with normal distribution, while Mann-Whitney U test was used for non-normally distributed data. One-way ANOVA with post-hoc Tukey test was used for comparing means across more than two groups, with Kruskal-Wallis test as the non-parametric alternative. Chi-square test or Fisher exact test (when expected cell frequency was <5) was used to analyze associations between categorical variables. Multiple linear regression analysis was performed to identify independent predictors of thyroid hormone levels after adjusting for potential confounders. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

The present study analyzed data from 168 patients with chronic kidney disease stages 3 through 5 over a period of 24 months. The baseline demographic and clinical characteristics of the study population are presented in Table 1. The mean age of the study participants was 54.6 ± 12.3 years with a range from 22 to 70 years. Male patients constituted the majority with 104 patients (61.9%) compared to 64 female patients (38.1%). The mean body mass index was 23.8 ± 3.9 kg/m², indicating that most patients were in the normal weight category. Regarding the etiology of chronic kidney disease, diabetic nephropathy was the most common cause accounting for 68 patients (40.5%), followed by hypertensive nephropathy in 52 patients (31.0%), chronic glomerulonephritis in 28 patients (16.7%), and other causes including obstructive uropathy and polycystic kidney disease in 20 patients (11.9%).

The distribution of CKD stages in the study population showed progressive representation across all stages. Stage 3 CKD (combining stages 3a and 3b) was observed in 48 patients (28.6%), stage 4 in 54 patients (32.1%), and stage 5 in 66 patients (39.3%). Regarding treatment modalities, 89 patients (53.0%) were on conservative management while 79 patients (47.0%) were receiving maintenance hemodialysis. Among the hemodialysis patients, the median duration of dialysis was 18 months with an interquartile range of 9 to 32 months, and the majority received dialysis twice weekly. Comorbid conditions were highly prevalent in the study population, with diabetes mellitus present in 98 patients (58.3%), hypertension in 136 patients (81.0%), and cardiovascular disease in 42 patients (25.0%).

The baseline renal function parameters and thyroid hormone levels are shown in Table 2. The mean serum creatinine was 4.8 ± 2.6 mg/dL with a range from 1.8 to 11.2 mg/dL. The mean blood urea nitrogen was 86.4 ± 38.7 mg/dL ranging from 32 to 178 mg/dL. The mean estimated glomerular filtration rate was 18.4 ± 10.7 ml/min/1.73 m² with significant variation across different CKD stages. Hemoglobin levels showed a mean of 9.2 ± 1.8 g/dL, indicating the presence of renal anemia in the majority of patients. Serum calcium levels averaged 8.4 ± 0.9 mg/dL while serum phosphorus was 5.2 ± 1.4 mg/dL, reflecting the mineral bone disease commonly associated with advanced CKD.

The thyroid hormone profile revealed mean TSH level of 4.2 ± 3.8 mIU/L with a range from 0.3 to 18.6 mIU/L. The mean free T3 level was 2.1 ± 0.7 pg/mL ranging from 0.8 to 3.9 pg/mL, and mean free T4 level was 1.2 ± 0.4 ng/dL with a range from 0.5 to 2.1 ng/dL. These values indicated considerable variability in thyroid function across the study population.

The prevalence of different patterns of thyroid dysfunction in the study population is presented in Table 3. Out of 168 patients, 122 patients (72.6%) had some form of thyroid dysfunction while only 46 patients (27.4%) maintained euthyroid status. Low T3 syndrome was the most prevalent thyroid abnormality, affecting 77 patients (45.8% of total population). Subclinical hypothyroidism was observed in 31 patients (18.5%), overt hypothyroidism in 14 patients (8.3%), and hyperthyroidism was rare with only 1 patient (0.6%). Some patients had overlapping patterns of thyroid dysfunction, with 13 patients having both low T3 syndrome and elevated TSH levels consistent with hypothyroidism. The correlation between thyroid hormone levels and renal function parameters is detailed in Table 4. Free T3 levels showed a strong positive correlation with estimated glomerular filtration rate ($r = 0.642$, $p < 0.001$), indicating that lower FT3 levels were associated with worse renal function. Free T3 also showed significant negative correlations with serum creatinine ($r = -0.598$, $p < 0.001$) and blood urea nitrogen ($r = -0.567$, $p < 0.001$). These correlations remained statistically significant even after adjusting for age, sex, diabetes status, and hemodialysis status in multiple regression analysis (adjusted $\beta = 0.524$, $p < 0.001$ for eGFR). TSH levels demonstrated a weak but statistically significant negative correlation with eGFR ($r = -$

0.243, p = 0.002), suggesting higher TSH levels in patients with more advanced CKD. Free T4 levels showed weak correlations with renal parameters that were not statistically significant.

Table 5 presents the comparison of thyroid dysfunction between patients on conservative management versus those receiving hemodialysis. The prevalence of thyroid dysfunction was significantly higher in hemodialysis patients (66 out of 79 patients, 84.2%) compared to conservatively managed patients (56 out of 89 patients, 63.5%), with a statistically significant difference ($\chi^2 = 9.47$, p = 0.002). Low T3 syndrome was particularly more prevalent in the hemodialysis group (55.7% vs 37.1%, p = 0.012). Mean free T3 levels were significantly lower in hemodialysis patients (1.8 ± 0.6 pg/mL) compared to those on conservative management (2.4 ± 0.7 pg/mL), with a mean difference of 0.6 pg/mL (95% CI: 0.38-0.82, t = 5.38, p < 0.001). TSH levels were higher in hemodialysis patients (4.8 ± 4.2 mIU/L vs 3.7 ± 3.2 mIU/L, p = 0.042), though the difference in free T4 levels was not statistically significant (p = 0.186).

The distribution of thyroid dysfunction across different CKD stages is shown in Table 6. There was a clear progressive increase in the prevalence of thyroid dysfunction with advancing CKD stage. In stage 3 CKD, 28 out of 48 patients (58.3%) had thyroid dysfunction, which increased to 38 out of 54 patients (70.4%) in stage 4, and further to 57 out of 66 patients (86.4%) in stage 5 (χ^2 for trend = 14.82, p < 0.001). Low T3 syndrome prevalence increased dramatically from 27.1% in stage 3 to 37.0% in stage 4 and 60.6% in stage 5 (p < 0.001). The mean free T3 levels decreased progressively across CKD stages: 2.6 ± 0.6 pg/mL in stage 3, 2.1 ± 0.7 pg/mL in stage 4, and 1.7 ± 0.6 pg/mL in stage 5 (F = 26.34, p < 0.001). Post-hoc analysis revealed significant differences between all pairwise comparisons of stages (p < 0.05 for all). Mean eGFR showed expected progressive decline: 38.2 ± 8.4 ml/min/1.73 m² in stage 3, 22.1 ± 4.2 ml/min/1.73 m² in stage 4, and 8.6 ± 3.8 ml/min/1.73 m² in stage 5.

Table 1: Baseline Demographic and Clinical Characteristics of Study Population (N=168)

Parameter	Value	Percentage (%)
Age (years), mean ± SD	54.6 ± 12.3	-
Gender		
Male	104	61.9
Female	64	38.1
BMI (kg/m²), mean ± SD	23.8 ± 3.9	-
CKD Etiology		
Diabetic nephropathy	68	40.5
Hypertensive nephropathy	52	31.0
Chronic glomerulonephritis	28	16.7
Others	20	11.9
CKD Stage		
Stage 3 (3a + 3b)	48	28.6
Stage 4	54	32.1
Stage 5	66	39.3
Treatment Modality		
Conservative management	89	53.0
Hemodialysis	79	47.0
Comorbidities		
Diabetes mellitus	98	58.3
Hypertension	136	81.0
Cardiovascular disease	42	25.0

Table 2: Baseline Renal Function and Thyroid Hormone Parameters

Parameter	Mean ± SD	Range
Serum creatinine (mg/dL)	4.8 ± 2.6	1.8 - 11.2
Blood urea nitrogen (mg/dL)	86.4 ± 38.7	32 - 178
eGFR (ml/min/1.73 m²)	18.4 ± 10.7	4.2 - 58.6
Hemoglobin (g/dL)	9.2 ± 1.8	5.8 - 13.2
Serum calcium (mg/dL)	8.4 ± 0.9	6.8 - 10.2
Serum phosphorus (mg/dL)	5.2 ± 1.4	3.1 - 8.6
TSH (mIU/L)	4.2 ± 3.8	0.3 - 18.6
Free T3 (pg/mL)	2.1 ± 0.7	0.8 - 3.9
Free T4 (ng/dL)	1.2 ± 0.4	0.5 - 2.1

Table 3: Prevalence of Thyroid Dysfunction Patterns (N=168)

Thyroid Status	Number of Patients	Percentage (%)
Euthyroid	46	27.4
Low T3 syndrome	77	45.8
Subclinical hypothyroidism	31	18.5
Overt hypothyroidism	14	8.3
Hyperthyroidism	1	0.6
Total thyroid dysfunction	122	72.6

Table 4: Correlation Between Thyroid Hormones and Renal Function Parameters

Parameter	Free T3 (r, p-value)	Free T4 (r, p-value)	TSH (r, p-value)
eGFR	0.642, <0.001	0.124, 0.112	-0.243, 0.002
Serum creatinine	-0.598, <0.001	-0.098, 0.204	0.218, 0.005
Blood urea	-0.567, <0.001	-0.112, 0.148	0.196, 0.011
Hemoglobin	0.342, <0.001	0.089, 0.245	-0.156, 0.042

Table 5: Comparison of Thyroid Dysfunction Between Conservative and Hemodialysis Patients

Parameter	Conservative (n=89)	Hemodialysis (n=79)	p-value
Overall thyroid dysfunction, n (%)	56 (63.5%)	66 (84.2%)	0.002
Low T3 syndrome, n (%)	33 (37.1%)	44 (55.7%)	0.012
Subclinical hypothyroidism, n (%)	17 (19.1%)	14 (17.7%)	0.824
Overt hypothyroidism, n (%)	6 (6.7%)	8 (10.1%)	0.424
TSH (mIU/L), mean ± SD	3.7 ± 3.2	4.8 ± 4.2	0.042
Free T3 (pg/mL), mean ± SD	2.4 ± 0.7	1.8 ± 0.6	<0.001
Free T4 (ng/dL), mean ± SD	1.3 ± 0.4	1.2 ± 0.4	0.186
eGFR (ml/min/1.73 m²)	22.3 ± 11.4	14.1 ± 8.6	<0.001

Table 6: Distribution of Thyroid Dysfunction Across CKD Stages

Parameter	Stage 3 (n=48)	Stage 4 (n=54)	Stage 5 (n=66)	p-value
Thyroid dysfunction, n (%)	28 (58.3%)	38 (70.4%)	57 (86.4%)	<0.001
Low T3 syndrome, n (%)	13 (27.1%)	20 (37.0%)	40 (60.6%)	<0.001
Subclinical hypothyroidism (%)	11 (22.9%)	12 (22.2%)	8 (12.1%)	0.184
Overt hypothyroidism, n (%)	4 (8.3%)	6 (11.1%)	4 (6.1%)	0.546
TSH (mIU/L), mean ± SD	3.8 ± 3.4	4.2 ± 3.6	4.6 ± 4.2	0.095
Free T3 (pg/mL), mean ± SD	2.6 ± 0.6	2.1 ± 0.7	1.7 ± 0.6	<0.001
Free T4 (ng/dL), mean ± SD	1.3 ± 0.4	1.2 ± 0.4	1.1 ± 0.4	0.023

Discussion

The present study comprehensively evaluated the prevalence and patterns of thyroid dysfunction among 168 patients with chronic kidney disease stages 3 through 5, and examined the correlations between thyroid hormone levels and renal function parameters. Our findings revealed a high prevalence of thyroid dysfunction at 72.6%, with low T3 syndrome being the predominant abnormality affecting 45.8% of patients. Furthermore, we demonstrated strong correlations between declining renal function and alterations in thyroid hormone levels, particularly free T3, which showed robust positive correlation with estimated glomerular filtration rate. These findings have significant clinical implications for the screening and management of thyroid abnormalities in the chronic kidney disease population.

The overall prevalence of thyroid dysfunction in our study (72.6%) is consistent with several previous studies from different geographic regions. A study by Raj et al from India reported a combined prevalence of 27.9% for hypothyroidism and subclinical hypothyroidism, with 87.9% of patients demonstrating low free T3 levels.[11] Another study from China by Li et al found that thyroid dysfunction was present in approximately 30-35% of CKD patients, though their study included earlier stages of CKD which may explain the lower prevalence.[12] A European study by Meuwese et al in the German Chronic Kidney Disease cohort reported low T3 syndrome in approximately 28% of CKD patients.[13] The higher prevalence in our study may be attributed to the predominance of advanced CKD stages in our population, with 71.4% having stage 4 or 5 disease, where thyroid dysfunction is known to be more severe.

Low T3 syndrome emerged as the most prevalent thyroid abnormality in our study, affecting 45.8% of patients. This finding aligns closely with the pathophysiological understanding of thyroid-kidney interactions. The accumulation of uremic toxins, altered peripheral conversion of T4 to T3,

and metabolic acidosis all contribute to decreased T3 levels in CKD patients.[14]

Kim et al demonstrated in their prospective study that low T3 levels independently predicted adverse cardiovascular outcomes and all-cause mortality in CKD patients, suggesting that this abnormality is not merely an adaptive response but has important clinical consequences.[15] Our finding of progressively decreasing free T3 levels with advancing CKD stages (2.6 pg/mL in stage 3 to 1.7 pg/mL in stage 5) supports this progressive pathophysiological process and suggests that thyroid screening should be routinely performed, particularly in patients with advanced CKD.

The strong positive correlation between free T3 levels and estimated glomerular filtration rate ($r=0.642$, $p<0.001$) observed in our study represents one of the key findings with important clinical implications. This correlation was stronger than those reported in several previous studies. Li et al reported correlation coefficients ranging from 0.35 to 0.48 between thyroid hormones and renal function parameters in their study of 3,563 Chinese adults.[16] The stronger correlation in our study may reflect the more advanced CKD stages and larger sample size. Furthermore, this correlation remained statistically significant even after adjusting for multiple confounders including age, sex, diabetes status, and dialysis status in multiple regression analysis, suggesting an independent relationship between thyroid function and renal function.

Our finding of significantly higher prevalence of thyroid dysfunction in hemodialysis patients (84.2%) compared to conservatively managed patients (63.5%) has been consistently reported in the literature. You et al in their analysis of the Mayo Clinic cohort demonstrated that dialysis patients had substantially higher rates of both hypothyroidism and hyperthyroidism compared to pre-dialysis CKD patients.[17] Several mechanisms may explain this association. First, the dialysis procedure itself may lead to loss of thyroid hormones, particularly T3, through the dialysis membrane. Second, the chronic inflammatory state associated with hemodialysis may further impair thyroid hormone synthesis and peripheral conversion. Third, the more advanced uremic state in dialysis patients leads to greater accumulation of uremic toxins that interfere with thyroid function.[18] The mean difference of 0.6 pg/mL in free T3 levels between hemodialysis and conservative groups in our study, though modest, was highly statistically significant and likely clinically relevant given the narrow normal range of thyroid hormones.

The progressive increase in thyroid dysfunction prevalence across CKD stages observed in our study (58.3% in stage 3, 70.4% in stage 4, and 86.4% in stage 5) demonstrates a clear dose-response relationship between declining renal function and thyroid abnormalities. This pattern has been documented in several longitudinal studies. Rhee et al in their review of thyroid dysfunction in end-stage renal disease noted that the prevalence and severity of thyroid abnormalities increase proportionally with declining kidney function.[19] A prospective study by Zoccali et al followed CKD patients over time and demonstrated that progression of renal disease was accompanied by parallel worsening of thyroid function parameters, with low T3 syndrome being an independent predictor of both renal disease progression and mortality.[20] These findings support the implementation of stage-specific thyroid screening protocols, with more frequent monitoring in advanced CKD stages.

The prevalence of subclinical hypothyroidism in our study (18.5%) was higher than that reported in the general population but consistent with other CKD studies. Rhee and colleagues reported subclinical hypothyroidism prevalence ranging from 15-20% in CKD patients across multiple cohorts.[21] The clinical significance of subclinical hypothyroidism in CKD remains debated. While some studies suggest thyroid hormone replacement may improve outcomes, others have shown no clear benefit. A meta-analysis by Zhao et al examining thyroid hormone replacement in CKD patients with subclinical hypothyroidism found potential benefits for cardiovascular parameters but no clear effect on renal outcomes or mortality.[22] Current guidelines generally recommend thyroid hormone replacement for TSH levels persistently above 10 mIU/L, while the benefit for TSH levels between 5-10 mIU/L remains uncertain and should be individualized based on patient factors.

An interesting finding in our study was the weak negative correlation between TSH levels and eGFR ($r=-0.243$, $p=0.002$), which was less pronounced than the correlations observed with free T3. This finding differs somewhat from some previous studies. Meuwese et al found stronger associations between TSH and renal function decline in their prospective cohort.[23] However, it is important to note that TSH interpretation in CKD patients is complicated by several factors including non-thyroidal illness syndrome, where TSH may remain normal or even low despite decreased T3 levels, and altered TSH secretion patterns in uremia. These factors may explain why TSH is less reliable as a marker of thyroid dysfunction in CKD patients compared to direct measurements of thyroid hormones, particularly free T3.

Several limitations of the present study should be acknowledged. First, the retrospective cross-sectional design precludes establishment of

causality and temporal relationships between thyroid dysfunction and CKD progression. Prospective longitudinal studies would be valuable to determine whether thyroid abnormalities predict CKD progression or whether they are simply markers of disease severity. Second, we did not have data on thyroid antibodies or ultrasonographic thyroid imaging, which would have helped differentiate primary thyroid disease from CKD-related thyroid dysfunction. Third, medication history, particularly regarding drugs that may affect thyroid function, was based on medical records and may have been incomplete. Fourth, we did not assess the impact of thyroid dysfunction on clinical outcomes such as cardiovascular events, mortality, or quality of life, which would provide important insights into the clinical significance of these findings. Finally, the single-center nature of our study may limit generalizability, though our sample size and rigorous methodology provide reasonable confidence in our findings.

Despite these limitations, our study provides valuable data on the prevalence and patterns of thyroid dysfunction in the Indian CKD population and demonstrates strong correlations between thyroid hormones and renal function. The high prevalence of thyroid dysfunction, particularly low T3 syndrome, combined with the progressive worsening with advancing CKD stages and the especially high prevalence in hemodialysis patients, supports routine thyroid screening in this population. Future research should focus on prospective studies examining whether treatment of thyroid dysfunction improves outcomes in CKD patients, optimal target levels for thyroid hormone replacement in this population, and whether correction of thyroid abnormalities might slow CKD progression. Additionally, studies investigating the mechanisms linking thyroid dysfunction and CKD progression, including the roles of inflammation, oxidative stress, and endothelial dysfunction, would enhance our understanding of this important clinical relationship.

Conclusion

The present study demonstrates a high prevalence of thyroid dysfunction among patients with chronic kidney disease, affecting nearly three-quarters of the study population. Low T3 syndrome emerged as the predominant pattern, present in nearly half of all patients, followed by subclinical hypothyroidism and overt hypothyroidism. The strong positive correlation between free T3 levels and estimated glomerular filtration rate, along with significant negative correlations with markers of renal dysfunction, suggests an intimate relationship between thyroid function and kidney disease severity. Patients receiving hemodialysis had significantly higher rates of thyroid dysfunction compared to those on conservative management, and the prevalence of thyroid abnormalities increased progressively with advancing CKD stages. These findings have important clinical implications. First, they support the implementation of routine thyroid screening protocols for patients with chronic kidney disease, particularly those with advanced disease or receiving hemodialysis. Second, the strong correlations between thyroid hormones and renal function parameters suggest that thyroid dysfunction may serve as a marker of disease severity and potentially a therapeutic target. Third, the high prevalence of low T3 syndrome raises questions about whether thyroid hormone supplementation might benefit this population, though this remains an area requiring further research through prospective randomized controlled trials. Based on our findings, we recommend that nephrology practices establish protocols for periodic thyroid function testing in CKD patients, with frequency determined by CKD stage and clinical status. Patients with stage 4 or 5 CKD should undergo annual thyroid screening at minimum, while those on hemodialysis may benefit from more frequent monitoring every 6 months. When thyroid dysfunction is identified, particularly subclinical hypothyroidism with TSH above 10 mIU/L or symptomatic patients with TSH between 5-10 mIU/L, consideration should be given to thyroid hormone replacement following current endocrine society guidelines, while recognizing the need for individualized decision-making in this complex population. Further research through large-scale prospective studies is needed to definitively establish whether correction of thyroid abnormalities improves clinical outcomes and potentially slows progression of kidney disease in CKD patients.

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