ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 8, Issue – 3, May - 2025, Page No.: 79 – 86

Decoding Thyroid Function Test in Chronic Kidney Disease Patients

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How to citation this article: Dr. Karanveer Singh Khangurha, Dr. Navneet Saxena, Dr. Ashish Shukla, Dr Japneet Sidhu, "Decoding Thyroid Function Test in Chronic Kidney Disease Patients", IJMACR- May - 2025, Volume – 8, Issue - 3, P. No. 79 – 86.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Chronic Kidney Disease (CKD) is a major public health concern linked to high morbidity and mortality, particularly due to cardiovascular diseases. Thyroid dysfunction is a common comorbidity in CKD patients and may accelerate disease progression. **Objectives**: To assess thyroid function among admitted CKD patients and study its association with CKD staging

Methods: This hospital-based, cross-sectional observational study was conducted on 130 CKD patients at Jaipur National University. Patients were categorized into CKD stages III-V based on eGFR. Thyroid function tests (T3, T4, TSH) were assessed and analysed statistically.

Results: Among the 130 patients, 84.6% had hypothyroidism and 14.6% had subclinical hypothyroidism. Significant differences in thyroid function (using parameters like Free T4, Free T3, Mean TSH) were observed across progressing CKD stages. **Conclusion**: Thyroid dysfunction is highly prevalent among CKD patients, particularly in advanced stages. Routine screening and management of these metabolic derangements may slow CKD progression and reduce cardiovascular risk.

Keywords: CKD, Thyroid, Cross-sectional, T4, T3

Introduction

Chronic kidney disease (CKD) is a significant global health concern and a chronic, non-communicable disease that affects populations worldwide, including India. It is marked by the progressive and irreversible decline in kidney function, leading to impairments in excretory, metabolic, and endocrine activities. This deterioration is associated with a gradual reduction in the glomerular

filtration rate (GFR), ultimately resulting in the clinical condition known as uremia.[1,2,3]

In India, the percentage of deaths due to kidney failure escalated by 38% between 2001–2003 and 2010–2013. Furthermore, CKD is a significant risk factor for cardiovascular disease, which continues to be the leading cause of premature deaths and disability-adjusted life years. In developing countries like India, there is often limited emphasis on secondary and tertiary prevention strategies for CKD. Consequently, patients typically seek medical attention only when symptoms manifest, which is frequently during the advanced stages of the disease.[4,5]

The early stages of chronic kidney disease (CKD) are primarily managed by primary care physicians, who play a crucial role in slowing the progression of CKD to end-stage renal disease (ESRD). This is achieved by identifying and addressing associated comorbidities at an early stage. Among these, lipid dysfunction and thyroid dysfunction are particularly significant in patients with CKD.[6,7]

Thyroid hormone dysfunction is recognized comorbidity in CKD patients. CKD affects the synthesis, secretion, metabolism, and elimination of thyroid hormones. Under normal physiological conditions, iodine, being an essential component for thyroid hormone synthesis—is removed from the circulation via glomerular filtration. However, as GFR progressively declines in CKD, iodine accumulates in the bloodstream. This leads to reduced thyroid hormone synthesis due to the 'Wolff-Chaikoff effect.' Consequently, patients with CKD often exhibit subnormal levels of serum total and free T3, normal levels of reverse T3 and free T4, while TSH levels typically remain unchanged. Clinical symptoms of hypothyroidism may also present in CKD patients.[8]

Historical studies have documented various thyroid abnormalities in CKD, including hypothyroidism, hyperthyroidism, and euthyroidism. The prevalence of hypothyroidism among ESRD patients has been reported as 0.9%. Additionally, goiter has been observed in some CKD patients, further emphasizing the impact of thyroid dysfunction in this population.[8]

Thyroid hormones are essential for cellular growth and protein synthesis, significantly influencing renal development. The kidney-to-body mass ratio, a measure of functional renal mass, is directly affected by thyroid hormone levels. Hypothyroidism reduces this ratio, whereas hyperthyroidism increases it, although severe hyperthyroidism leads to protein breakdown and, ultimately, renal atrophy.

Thyroid hormones impact renal function through both direct and indirect mechanisms. Indirectly, they enhance renal blood flow by modulating cardiovascular function. Directly, they influence glomerular filtration rate (GFR), tubular secretory and reabsorptive functions, and hormonal activities within the kidney. They also regulate tubular potassium permeability and calcium reabsorption. Through adrenergic pathways, thyroid hormones affect the renin-angiotensin-aldosterone system (RAAS) by stimulating renin release, further highlighting their critical role in renal physiology.[9] The present study was conducted to assess the Thyroid function tests in admitted Patients of Chronic Kidney Disease in a Tertiary Care Teaching Hospital.

Objectives

1. To study thyroid function profile (T3, T4, TSH) in CKD patients.
2. To find out correlation between thyroid dysfunction and CKD staging

Materials and Methods

Study area: This proposed study was conducted in Institute for medical sciences and research Centre Jaipur

Study type and Design- A Hospital-based Cross-Sectional Observational Study

Study Population –included 130 Patients of Chronic Kidney Disease >18 years admitted in Dept. of Medicine and Nephrology at JNU Hospital.

Sample Size

A sample size of 130 subjects was calculated to verify significant positive correlation between serum creatinine and TSH values (r=0.248), at 95% confidence level and 5% allowable error considering 10% attrition as per article (Swati Srivastava, et al. in 2018)[10]

Inclusion Criteria

1. Patients with age >18 years
2. Patients who were diagnosed as CKD due to any aetiology evidenced radiologically (bilateral shrunken kidney/loss of corticomedullary differentiation) or biochemically (elevated blood urea, serum creatinine) for more than 3 months
3. Patients who gave consent to participate in the study

Exclusion criteria

1. Those who were on drugs altering thyroid profile such as amiodarone, steroids, dopamine, phenytoin, estrogen pills, and iodine-containing drugs.
2. Critically ill patients.
3. Pregnant women

CKD patients were categorized in stages I to V according to eGFR using the following formula

$$eGFR=\frac{\{140-age(years)\} \times ideal\ weight(kg)}{[(Creatinine\ (mg/dl)] \times 72)} \times 0.85\ (if\ female)$$

Lab Analysis

The thyroid profile was determined using a competitive immunoassay method for measuring levels of triiodothyronine (T3) and thyroxine (T4), which were crucial for assessing thyroid gland function. This technique involved the competition between the thyroid hormones in the sample and a labeled hormone for a fixed number of binding sites, allowing for precise quantification. Additionally, thyroid-stimulating hormone (TSH) levels were assessed using enhanced chemiluminescence. This method involved triggering a light-emitting chemical reaction when the hormone in the sample interacted with specific reagents, providing sensitive and accurate measurements of TSH.

Statistical Analysis

Qualitative variables were expressed in percentage (%) and proportion. Quantitative variables were expressed in Mean ± SD. Significance of difference of proportion was inferred by Chi-square test. Significance of difference in >2 means was inferred by ANOVA test. P-value <0.05 was considered significant for all statistical purposes.

Results

The demographic profile of participants indicated an average age of 47.98±14.60 years, with 65.38% males and 34.62% female participants. Table 1 includes distribution of participants as per age group and as per various grades of CKD. Majority 68.46% (89 patients) of participants, had Stage 5 CKD, indicating the most severe level of kidney dysfunction followed by Stage 4, comprising 30.77% (40 patients) of participants with and Stage 3 CKD comprising of 0.77% (1 patient) of the participants. None of the participants were classified as Stage 1 or Stage 2 CKD, reflecting that the study population predominantly comprised of individuals with advanced stages of chronic kidney disease.

Table 1: Demographic data and different grades of CKD among study participants

Variables	Frequency	Percentage (%)
Age group (in years)		
<30	13	10
31-40	31	23.85
41-50	31	23.85
51-60	24	18.46
>60	31	23.84
Gender		
Male	85	65.38
Female	45	34.62
CKD Stage		
Stage 3	1	0.77
Stage 4	40	30.77
Stage 5	89	68.46

Figure 1 represents that there is high prevalence of hypothyroidism among the participants, with only 0.77% (1 patient) exhibiting normal thyroid function. Majority of participants, 84.62% (110 patients), were classified as having hypothyroidism**.** Subclinical hypothyroidism was observed in 14.62% (19 patients).

Figure 1:

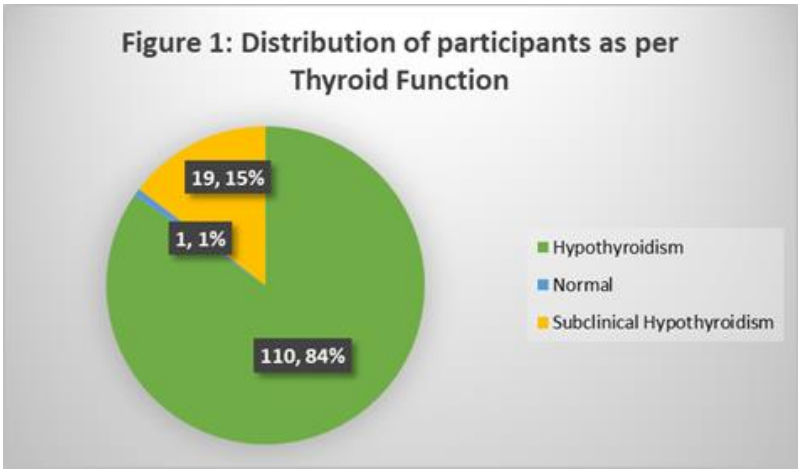

Table 2: Thyroid function distribution in various CKD grades

Thyroid Function	CKD Stage						
	Stage 3	%	Stage 4	%	Stage 5	%	Total
Hypothyroidism	0	0.00	21	16.15	89	68.46	110
Normal	1	0.77	0	0.00	0	0.00	1
Subclinical	0	0.00	19	14.62	0	0.00	19

Hypothyroidism							
Total	1	0.77	40	30.77	89	68.46	130
χ^2	180						
p-value	<0.001						

Table 2 depicts that the prevalence of hypothyroidism increased with CKD severity, with 68.46% of cases occurring in Stage 5 and 16.15% in Stage 4. Subclinical hypothyroidism was observed in 14.62% of participants, all of whom were in Stage 4. Only one participant with normal thyroid function was identified, and they were in Stage 3. Upon analysis with Chi-square test, the findings suggest a statistically significant relationship between higher burden of thyroid dysfunction in advanced CKD stages (p-value<0.001)

Table 3: Mean Free T4 value in different stages of CKD

	CKD Stage	N	Mean	SD	F value	P value
Free T4	Stage 3	1	1.93	NaN	7.81	<0.001
	Stage 4	40	4.74	1.56		
	Stage 5	89	3.5	1.78		

Table 3 show variations in Free T4 levels with CKD progression. In Stage 3, the mean Free T4 level is 1.93 (based on a single participant). In Stage 4, the mean Free T4 level rises to 4.74 with a standard deviation of 1.56. However, in Stage 5, the mean Free T4 level decreases to 3.5 with a standard deviation of 1.78. The level of Free T4 showed a significant decline in the mean values from Grade 4 to Grade 5. (F-value-7.81 and p-value<0.001)

Table 4: Mean Free T3 value in different stages of CKD

	CKD Stage	N	Mean	SD	F value	p-value
Free T3	Stage 3	1	2.98	NaN	0.552	0.557
	Stage 4	40	2.15	1.34		
	Stage 5	89	1.99	1.17		

Table 4 presents the mean Free T3 levels across different stages of CKD. The F-value of 0.552 and a p-value of 0.557 suggest that the differences in Free T3 levels across CKD stages are not statistically significant.

Table 5: Mean TSH value in different stages of CKD

	CKD Stage	N	Mean	SD	F value	p-value
TSH	Stage 3	1	13.4	NaN	12.9	<0.001
	Stage 4	40	6.24	4.41		
	Stage 5	89	10.44	4.42		

Table 5 presents the mean Thyroid Stimulating Hormone (TSH) levels across different stages of CKD. The mean TSH level in Stage 3 is 13.4 (based on a single participant). In Stage 4, the mean TSH level decreases to 6.24 with a standard deviation of 4.41, whereas in Stage 5, it rises again to 10.44 with a standard deviation of 4.42. The level of Free T4 showed a significant increase in the mean values from Grade 4 to Grade 5. (F-value-7.81 and p-value<0.001)

Table 6: eGFR Correlation with TSH and total cholesterol

	Pearson's r	p-value
TSH	-0.304	< .001

A significant negative correlation was observed between eGFR and TSH ($r = -0.304$, $p < 0.001$) indicating that as kidney function declines (lower eGFR), levels of TSH tend to increase, implying a potential link between worsening renal function and thyroid dysfunction. (Table 6)

Discussion

This study assessed thyroid dysfunction and lipid abnormalities in chronic kidney disease (CKD) patients. Participants ranged from 18 to 82 years old, with a mean age of 47.98 ± 14.60 years. Most were middle-aged or older, comprising 65.38% males and 34.62% females.

Gupta et al.[11] reported similar age distribution, with the majority in the 40–50 age group (31%), followed by those aged 30–40 (22%) and 50–60 (21%). Their study included 56% males and 44% females. Similarly, EaWha Kang et al[12]. found a high rate of subclinical hypothyroidism among CKD patients over 18 years old, diagnosed through clinical and lab evaluations. Khatiwada et al.[13] also observed comparable demographics, with 53.8% male participants and an average age of 44.1 ± 16.4 years. A study by EaWha Kang et al.[12] on CKD patients over 18 years of age reported a high incidence of subclinical hypothyroidism. Similarly, Khatiwada et al.[13] found 53.8% male participants, with a mean age of 44.1 ± 16.4 years.

In the current study, most participants (68.46%) had Stage 5 CKD, followed by 30.77% with Stage 4, and only 0.77% with Stage 3. By contrast, Khatiwada et al.[13]in 2015 observed a higher proportion in earlier stages, with 40% in Stage 3, 43.3% in Stage 4, and 16.6% in Stage 5.

Thyroid analysis in the present research revealed that only 0.77% had normal thyroid levels. Hypothyroidism was present in 84.62%, including 4.6% with subclinical hypothyroidism. In Khatiwada's study[13], thyroid disorders were found in 38.6% of CKD patients, predominantly subclinical hypothyroidism (27.2%). Similarly, Shantha GPS et al.[14] found a 24.8% prevalence in ESRD patients, while Ng et al.[15] reported 15.6% subclinical hypothyroidism and 4.1% subclinical hyperthyroidism among peritoneal dialysis patients in Taiwan.

The mean Free T4 levels show a slight decrease with advancing CKD stages: Stage 3 shows 2.41 pg/mL, Stage 4 shows 2.15 pg/mL, and Stage 5 shows 1.99 pg/mL. The F-value of 0.3547 and the P-value of 0.729 indicate that there is no statistically significant difference in mean Free T4 values across the different CKD stages. The mean Free T3 levels were 2.98 pg/mL in Stage 3, 2.15 pg/mL in Stage 4, and 1.99 pg/mL in Stage 5 with no statistically significant difference in Free T3 levels across CKD stages.but the mean TSH levels in the present study show a statistically significant difference in mean TSH values across the different CKD stages($p<0.001$), with increasing TSH across the CKD stages as Stage 4 shows 6.34 µIU/mL and Stage 5 shows 10.44 µIU/mL. Similar results were observed in a study done by G. Ayyappan et al.[16] where significant differences in thyroid (T3, T4, and TSH) were observed across CKD grades 2-5, with ($p < 0.0001$).In the current study, pearson's correlation estimated a significant negative correlation between eGFR and TSH ($r = -0.304$, $p < 0.001$), indicating that as kidney function declines

(lower eGFR), levels of TSH tend to increase, implying a potential link between worsening renal function and thyroid dysfunction. Similar results were observed in a study done by Swati Srivastava et al.[10] in which significant positive correlation between serum creatinine and TSH values (r=0.248, p=0.049)

Conclusion

This study emphasises the significant association between thyroid dysfunction and the progression of CKD. The findings underscore the critical importance of routine screening for hypothyroidism in patients with CKD. Further research should focus on a larger and diverse population to better understand these relationships and their implications in managing the patients of CKD.

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