Section: General Medicine

Original Research Article

STUDY OF THYROID FUNCTION TEST IN PATIENTS WITH CHRONIC KIDNEY DISEASE AT A TERTIARY CARE TEACHING HOSPITAL : A CROSS SECTIONAL STUDY

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is a characterised by declining renal function and is commonly seen in patients with diabetes, hypertension and aging. CKD is known to affect multiple systems including cardiovascular, haematological and endocrine functions. Thyroid dysfunction is common in CKD and he most common reported thyroid function abnormality in CKD is subclinical hypothyroidism which may contribute to metabolic disturbances, enhanced cardiovascular risk and overall poor health outcomes in CKD patients.
Materials and Methods: This comparative cross-sectional study was conducted at Adichunchanagiri Institute of Medical Sciences, India. The aim of this study was to assess thyroid function abnormalities in CKD patients versus healthy controls. Forty CKD patients and 40 age-matched healthy individuals were included. Demographic data, clinical history and laboratory tests (RFT, CBC, lipid profile, and TFT) were analyzed. Statistical comparisons were performed using SPSS 23. p-value less than 0.05 was considered statistically significant.
Results: Gender distribution was similar between the CKD group (52.5% males, 47.5% females) and controls (55% males, 45% females). The mean age was 48.88 ± 13.42 years for CKD patients. Thyroid function abnormalities were more common in CKD patients (56%) as compared to control group (32%) (p=0.006). CKD patients had lower T3 (2.32 vs. 2.69, p=0.0073) and T4 (1.02 vs. 1.22, p=0.018) but higher TSH (5.96 vs. 3.25, p<0.0001). Thyroid abnormalities increased with CKD severity and reached 72.7% in Stage 5.
Conclusion: Regular thyroid function monitoring in CKD is important as thyroid dysfunction worsens with disease progression. Early detection of thyroid function abnormalities can help manage metabolic and cardiovascular risks and improve patient outcomes. Routine screening allows timely interventions, reduces complications and may improve the quality of life in CKD patients.
Keywords: Chronic Kidney Disease, Thyroid Dysfunction, Thyroid Function Tests, Metabolic Complications.

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant public health problem and is characterized by a progressive decline in renal function over time. It is defined by a reduction in glomerular filtration rate (GFR) below 60 mL/min/1.73m² for at least three months duration or by the presence of kidney damage markers such as albuminuria.[1] The prevalence of CKD is increasing due to increasing prevalence of diabetes mellitus, hypertension and obesity.[2]
CKD is known to affect multiple systems including cardiovascular, haematological, neurological, and endocrine systems. Cardiovascular manifestations in

patients with thyroid dysfunction include accelerated atherosclerosis, vascular calcification, and left ventricular hypertrophy. Anemia of chronic disease due to erythropoietin deficiency and iron dysregulation is also commonly seen in these patients. The other abnormalities such as renal osteodystrophy, and vascular calcification, uremic encephalopathy, peripheral neuropathy and cognitive dysfunction is also commonly seen in patients with CKD. Disturbances in the hypothalamic-pituitary axis, altered insulin metabolism, and thyroid dysfunction is the common metabolic abnormalities seen in these individuals.3

Kidney plays an important role in thyroid hormone metabolism. The processes such as clearance of iodide, degradation of thyroxine (T4) and conversion of T4 to the active triiodothyronine (T3) via deiodinases are mainly handled by kidneys. CKD disrupts these processes leading to alterations in thyroid functions that may not necessarily indicate primary thyroid disease. Reduced renal clearance of iodine and accumulation of uremic toxins can interfere with thyroid hormone synthesis, secretion as well as metabolism. These alterations can have significant implications for thyroid functions in cases of CKD.[4] Subclinical hypothyroidism, with mildly elevated TSH and normal free T4 levels is common in CKD patients particularly those on dialysis.[5] Additionally, nonthyroidal illness syndrome (NTIS), also known as euthyroid sick syndrome is frequently observed where alterations in thyroid function tests occur in the absence of primary thyroid pathology. In contrast overt hypothyroidism and hyperthyroidism are less common but can occur.[6]

Assessing thyroid function in CKD patients is clinically important as it has been associated with adverse cardiovascular outcomes, metabolic derangements and is known to adversely affect quality of life. Hypothyroidism (clinical as well as subclinical) is linked to increased cardiovascular risk, endothelial dysfunction, dyslipidemia and higher mortality in CKD and dialysis patients.[7] Moreover thyroid dysfunction may also cause anemia, muscle wasting and impaired immune function. Because of significant overlap in symptoms between CKD and thyroid disorders an accurate analysis of thyroid function is important for optimal patient care. Early diagnosis and appropriate management of thyroid abnormalities in CKD patients can improve clinical outcomes, reduce cardiovascular morbidity and improve overall quality of life.[8]

Association between CKD and thyroid dysfunction has been reported by many authors. However, several gaps remain in our understanding of the exact mechanisms and clinical significance of thyroid function abnormalities in these patients. Current guidelines on the interpretation and management of thyroid dysfunction in CKD are also limited.[9] Additionally, most existing studies have been conducted in Western populations with limited data available from developing countries such as India where the burden of CKD is rising. Furthermore, variations in thyroid function patterns across different CKD stages not been extensively studied. This study aims to bridge these gaps by evaluating thyroid function abnormalities in CKD patients at a tertiary care teaching hospital and particularly analyse the effects of increasing CKD stages on thyroid functions. The findings will contribute to improving diagnostic approaches, guiding management strategies, and enhancing the overall care of CKD patients with thyroid dysfunction.

MATERIALS AND METHODS

This was a comparative cross sectional study conducted in the Department of Department of General Medicine Adichunchanagiri Institute of Medical Sciences, India which is a tertiary care medical college located in a rural area. The study aimed to evaluate thyroid function abnormalities among patients with Chronic Kidney Disease (CKD) as compared to healthy age matched healthy individuals. On the basis of pilot study, the minimum sample size was determined to be 40 patients when 90% power with 95% confidence interval was assumed. So, 40 diagnosed cases of chronic kidney disease (fulfilling Improving Global Outcomes (KDIGO) 2012 guidelines criteria for diagnosis of chronic kidney disease) were included on the basis of inclusion and exclusion criteria. 40 healthy individuals with no systemic illnesses were included in this study as control group

Group A (Cases): 40 patients diagnosed with CKD on the basis of improving Global Outcomes (KDIGO) 2012 guidelines criteria for diagnosis of chronic kidney disease10.

Group B (Controls): 40 age-matched individuals with no systemic illnesses.

Demographic information such as age, gender and body mass index (BMI) were noted for both cases and controls. In the CKD group, details regarding the duration of kidney disease, current treatment (dialysis status, use of erythropoietin, phosphate binders, and other medications) and presence of any systemic illnesses (e.g., diabetes mellitus, hypertension, cardiovascular disease) were noted. A detailed history was taken with a particular focus on signs and symptoms suggestive of thyroid dysfunction. Medication history was carefully asked and noted to exclude individuals taking medications which are known to interfere with thyroid hormone metabolism. A detailed general and systemic examination was done in all cases. The presence of CKD-related complication such as anemia and cardiovascular involvement was assessed through laboratory and clinical evaluation. Laboratory tests including renal function tests (blood urea and serum creatinine) were done in all cases. Thyroid function tests (TFT) were performed by measuring serum levels of T3, T4, and Thyroid-Stimulating Hormone (TSH) in all participants. Based on TFT results patients were categorized into thyroid dysfunction groups.

Following reference range for thyroid function test were used T3 (0.9–2.4 ng/dL), T4 (5.5–12.4 µg/dL), and TSH (0.6–5.5 IU/mL).

Data was entered into Microsoft Excel and SPSS software (version 23.0) was used for statistical analysis. Quantitative variables (e.g., TSH, T3, T4, blood urea, serum creatinine) were depicted as mean ± standard deviation (SD). Qualitative variables (e.g., presence of thyroid dysfunction, comorbid conditions) were expressed as frequency and percentages. Comparisons between the two groups (CKD vs. healthy controls) were performed using the chi-square test for categorical variables and an independent t-test for continuous variables. A p-value <0.05 was considered statistically significant.

Inclusion Criteria

1. Patients diagnosed with Chronic Kidney Disease (CKD) as per KDIGO 2012 guidelines.10
2. Patients in any stage of CKD (Stage 1 to 5), whether on dialysis or not.
3. Age above 18 years.
4. Willing to give informed written consent to be part of study.
5. Similar number of age matched healthy individuals without any systemic illnesses will be included as control group.

Exclusion Criteria

1. Age less than 18 years.
2. Refusal to give consent to be part of study.
3. History of thyroid disorders (previously diagnosed hyperthyroidism, hypothyroidism, or thyroidectomy).
4. Patients taking medications known to affect thyroid function (e.g., amiodarone, lithium etc).
5. Pregnant or lactating women.
6. Individuals with significant psychiatric disorders.

RESULTS

The analysis of gender distribution among patients with chronic kidney disease (CKD) and the control group showed a relatively balanced representation of males and females in both groups. Among CKD patients, there were 21 males (52.5%) and 19 females (47.5%), whereas in the control group, there were 22 males (55%) and 18 females (45%). The gender distribution in both the groups was found to be comparable (P>0.05) (Figure 1).

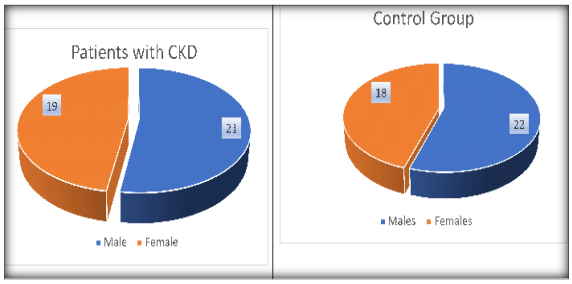

Figure 1: Gender Distribution of the studied cases

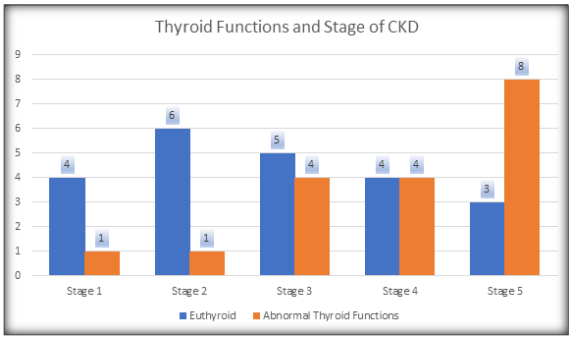

Figure 2: Correlation of thyroid Functions and stages of CKD

The analysis of age distribution among the CKD and control groups showed that the most common age group in both groups was 51-60 years (35.00%) in the CKD group as well as in the control group (37.50%). The mean age was 48.88 ± 13.42 years for the CKD group and 51.45 ± 11.46 years for the control group. The mean age of individuals in CKD group and control group was found to be comparable with no statistically significant difference (P=0.3599). [Table 1]

The analysis of thyroid function across CKD stages showed a rising prevalence of abnormal thyroid function as CKD progressed. In the early stages, euthyroid status was more common, with 80.0% in Stage 1 and 85.7% in Stage 2. However, in Stage 3, euthyroid cases dropped to 55.6%, while abnormal thyroid function increased to 44.4%. By Stage 4, both conditions were equally prevalent (50.0%). In Stage 5, abnormal thyroid function became predominant at 72.7%, with only 27.3% remaining euthyroid. [Figure 2]

Subclinical hypothyroidism was more common in the CKD group (26.0%) as compared to healthy individuals (10.0%). Overt hypothyroidism was present in 3 (6.0%) and 1 individual (2.0%) in CKD and control group respectively. Subclinical hyperthyroidism was observed in 2 individuals (4.0%) in the CKD group, whereas it was not present in the control group. No cases of overt hyperthyroidism were reported in either group. The thyroid function abnormalities were more common in CKD group as compared to healthy individuals and the difference was found to be statistically significant. [Table 2]

Mean T3 levels were lower in the CKD group (2.32 ± 0.59 pg/mL) as compared to the control group (2.69 ± 0.61 pg/mL) and the difference was found to be statistically significant (P>0.05). Similarly, the mean T4 levels were lower in the CKD group (1.02 ± 0.36 ng/dL) than in the control group (1.22 ± 0.38 ng/dL) with statistically significant difference (P=0.018). similarly mean TSH levels were significantly higher in the CKD group (5.96 ± 2.12 mIU/L) compared to the control group (3.25 ± 1.26 mIU/L) and the difference was found to be statistically highly significant (P<0.0001). [Table 3]

Table 1: Age distribution of cases in both the groups

Age groups	CKD group (n=40)	CKD group (%)	Control (n=40)	Control (%)
18 - 30 years	5	12.50%	2	5.00%
31 - 40 years	4	10.00%	3	7.50%
41 - 50 years	10	25.00%	12	30.00%
51 - 60 years	14	35.00%	15	37.50%
61 - 70 years	5	12.50%	6	15.00%
≥ 71 years	2	5.00%	2	5.00%
Total	40	100.0 %	41	100.0
Mean Age	48.88 +/- 13.42		51.45 +/- 11.46	
P = 0.3599 (Not significant)				

Table 2: Thyroid function tests in CKD vs healthy individuals

Thyroid Status	CKD Group		Control Group		P Value
	No of Patients	Percentage	No of Patients	Percentage	
Euthyroid	22	44.0%	34	68.0%	0.006
Subclinical Hypothyroidism	13	26.0%	5	10.0%	
Overt Hypothyroidism	3	6.0%	1	2.0%	
Subclinical Hyperthyroidism	2	4.0%	0	0.0%	
Overt Hyperthyroidism	0	0.0%	0	0.0%	
Total	40	100%	40	100%	

Table 3: Comparison of Mean T3,T4 and TSH levels in studied cases

Parameter	CKD Group - Mean ± SD	Control Group - Mean ± SD	P Value
Mean T3 Levels (pg/mL)	2.32 ± 0.59	2.69 ± 0.61	0.0073*
Mean T4 Levels (ng/dL)	1.02 ± 0.36	1.22 ± 0.38	0.018*
Mean TSH Levels (mIU/L)	5.96 ± 2.12	3.25 ± 1.26	< 0.0001*

DISCUSSIONS

The prevalence of subclinical and overt hypothyroidism is higher in CKD patients compared to the general population and this dysfunction tends to worsen with advancing stages of CKD. Since thyroid dysfunction in CKD can contribute to cardiovascular complications and metabolic imbalances it is crucial to monitor thyroid function in these patients.[11]

In our study among CKD patients, there were 21 males (52.5%) and 19 females (47.5%), whereas in the control group, there were 22 males (55%) and 18 females (45%). The mean age was 48.88 ± 13.42 years for the CKD group and 51.45 ± 11.46 years for the control group. The mean age as well as gender distribution was comparable in both the groups. Nivedita et al conducted a cross-sectional study to study the uric acid levels in different stages of chronic kidney disease (CKD) and its association with age, sex, and other comorbidities.[12] For this purpose, the authors undertook a study comprising 140 patients with CKD. Their serum uric acid levels were analyzed, considering a uric acid level above 7 mg/dl as hyperuricemia. The study received approval from the Institutional Ethics Committee, and informed consent was obtained from all participants. The study found that the median age of the participants was 55±13.47 years, with an age range of 19-80 years. The mean uric acid levels were 4.4±1.9 mg/dl in stage 3 CKD, 6.5±4.1 mg/dl in stage 4 CKD, and 8.8±3.1 mg/dl in stage 5 CKD ($p<0.05$). Males comprised 69.6% of the study population, while females comprised 31.4%, with a male-to-female ratio of 2.2:1. Similar age and gender distribution of cases with CKD has also been reported by the authors such as Zhang QL et al,[13] and Kovesdy CP et al.[14]

Subclinical hypothyroidism was more prevalent in the CKD group, affecting 13 individuals (26.0%), compared to 5 individuals (10.0%) in the control group. Overt hypothyroidism was present in 3 individuals (6.0%) in the CKD group and 1 individual (2.0%) in the control group. Subclinical hyperthyroidism was observed in 2 individuals (4.0%) in the CKD group, whereas it was not present in the control group. Patients in CKD group were having more thyroid function abnormalities as compared to healthy individuals and the difference was statistically significant ($P<0.05$). Gomba VE et al conducted a cross-sectional study to determine the prevalence and pattern of thyroid dysfunction in dialysis-naïve chronic kidney disease (CKD) patients.[15] For this purpose, the authors undertook a study comprising 100 CKD patients and 100 age- and sex-matched healthy controls. The study found that among the 200 participants, 93 were males and 107 were females, with mean ages of 46.3±15.9 years for CKD patients and 45.7±14.9 years for controls ($p=0.7587$). The prevalence of thyroid dysfunction was 45% in CKD patients compared to 4% in the control group. Sick euthyroid syndrome was the most common thyroid dysfunction (23%), followed by subclinical hypothyroidism (14%). Thyroid dysfunction increased with CKD severity, though this association was not statistically significant. On the basis of these findings, the authors concluded that thyroid dysfunction was highly prevalent in dialysis-naïve CKD patients. The high prevalence of thyroid function abnormalities seen in this study was similar to our study. Similar higher prevalence of thyroid dysfunction in cases of chronic kidney disease has

also been reported by the authors such as Mohamedali M et al,[16] and Kashif M et al.[17]

In this study thyroid hormone levels in CKD and control groups revealed significant differences with CKD patients exhibiting lower mean T3 (2.32 ± 0.59 pg/mL vs. 2.69 ± 0.61 pg/mL, p = 0.0073) and T4 (1.02 ± 0.36 ng/dL vs. 1.22 ± 0.38 ng/dL, p = 0.018) levels, while mean TSH levels were significantly higher (5.96 ± 2.12 mIU/L vs. 3.25 ± 1.26 mIU/L, p < 0.0001). Thyroid dysfunction worsened with CKD progression, with euthyroid status being more prevalent in early stages (80.0% in Stage 1 and 85.7% in Stage 2), decreasing to 55.6% in Stage 3, and equalling abnormal thyroid function at 50.0% in Stage 4. In Stage 5, abnormal thyroid function predominated at 72.7%, indicating a progressive decline in thyroid function as CKD severity increased. Ansari I et al conducted a cross-sectional study to highlight thyroid dysfunction and its relation to the severity and different stages of chronic kidney disease (CKD).[18] For this purpose, the authors undertook a study comprising 200 CKD patients. The study found that 181 (91.5%) patients had thyroid abnormalities. Among them, 57% had low T3 syndrome, 23% had low T4 syndrome, and 10.5% had primary hypothyroidism. Additionally, as CKD stages advanced, TSH levels increased significantly (p=0.04).On the basis of these findings, the authors concluded that as kidney function progressively deteriorated, particularly in stage five, the likelihood of hypothyroidism increased. Similar correlation between severity of CKD and thyroid dysfunction was also reported by the authors such as Hafed AB et al,[19] and Raj R et al.[20]

CONCLUSION

Thyroid dysfunction is common in chronic kidney disease (CKD) and worsens as the disease progresses, with a higher prevalence of subclinical and overt hypothyroidism among CKD patients compared to healthy individuals. This study found significantly lower T3 and T4 levels and elevated TSH levels in CKD patients, indicating altered thyroid function. As thyroid abnormalities can contribute to metabolic disturbances, cardiovascular complications, and overall disease burden, routine thyroid function monitoring in CKD patients is crucial for early detection and timely management. Regular screening and appropriate interventions may improve clinical outcomes and quality of life in individuals with CKD.

Conflict of Interest: None.

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