Section: Physiology

Original Research Article

THYROID DYSFUNCTION IN CHRONIC KIDNEY DISEASE PATIENTS

G. Swati Lakshmi[1], P. Pratima[2], Ch. B. S. Srinivas[3], M. Padma Geetanjali[4]

[1]Senior Resident, Department of Physiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.
[2]Associate Professor, Department of Physiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.
[3]Assistant Professor, Department of Physiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.
[4]Professor & HOD, Department of Physiology, Andhra Medical College, Visakhapatnam, Andhra Pradesh, India.

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Corresponding Author:
Dr. Ch. B. S. Srinivas,
Email: saisrinivaschennupati@gmail.com

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ABSTRACT

Background: Thyroid dysfunction is a prevalent comorbidity in patients with chronic kidney disease (CKD), with significant implications for disease progression and patient outcomes. The complex interplay between thyroid function and renal disease is multifaceted, involving alterations in thyroid hormone metabolism, hypothalamic pituitary-thyroid axis dysfunction, and systemic inflammation. This study aimed to assess the frequency and association between thyroid dysfunction and chronic kidney disease (CKD), with a primary focus on determining the prevalence of thyroid function abnormalities in CKD patients and exploring the correlation between CKD and thyroid dysfunction. **Materials and Methods:** This study included 160 patients with chronic kidney disease (CKD), all of whom underwent clinical examination. Laboratory investigations included complete blood count (CBC), serum electrolytes (sodium and potassium), urine routine and microscopy, renal function tests, and thyroid profile (free T3, free T4, and TSH). Results were collected and data was analyzed statistically. **Result:** Among patients with chronic kidney disease (CKD), thyroid function tests—specifically FT3, FT4, and TSH—were more frequently altered. Variations in serum creatinine levels were observed to affect the concentrations of FT3, FT4, and TSH. **Conclusion:** A comprehensive understanding of the relationship between chronic kidney disease (CKD) and thyroid dysfunction can enhance diagnosis, treatment, and overall management, ultimately leading to improved patient care and outcomes. Thyroid dysfunction, especially hypothyroidism and subclinical hypothyroidism, is more common in individuals with chronic kidney disease (CKD) than in the general population.

INTRODUCTION

Chronic kidney disease (CKD) is a common and progressive condition that affects millions of individuals worldwide.[1] Thyroid dysfunction is also prevalent issue that can impact various aspects of health and wellbeing.[2] The interplay between chronic kidney disease (CKD) and thyroid dysfunction is complex and multifactorial, with each condition capable of influencing the other and presenting with overlapping symptoms. Both the thyroid gland and the kidneys are integral to maintaining homeostasis in the human body, and their interactions have significant implications for health and disease.[3-6] The thyroid gland, produces hormones essential for the regulation of metabolism, energy balance, and the functioning of various organs. The two primary hormones, thyroxine (T4) and triiodothyronine (T3), influence cellular processes and energy expenditure throughout the body. Thyroid hormone secretion is tightly controlled by the hypothalamus-pituitary-thyroid (HPT) axis. The kidneys play a crucial role in filtering blood, eliminating waste products, and maintaining electrolyte and fluid balance. Renal function is crucial for maintaining blood pressure, acid-base balance, and overall homeostasis. The kidneys also play a crucial role in eliminating metabolic waste products and drugs from the body. The link between thyroid and kidney function has been recognized for decades, with early observations of altered renal function in individuals with thyroid disorders7. However, the understanding of the intricate mechanisms involved in this relationship has evolved over time, especially with advancements in endocrinology and nephrology.

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Epidemiological studies have identified a higher prevalence of thyroid dysfunction in individuals with chronic kidney disease and vice versa.[8,9] The coexistence of these conditions creates difficulties in diagnosis, clinical management, and determining prognosis. The prevalence of thyroid disorders may vary across different stages of kidney disease, emphasizing the need for a nuanced approach in clinical practice. The rationale for investigating the interplay between thyroid dysfunction and kidney disorders lies in the clinical significance of these conditions when they coexist.[10] Patients with both thyroid and kidney disorders may experience complex clinical presentations, altered responses to medications, and challenges in achieving optimal treatment outcomes.[11] Understanding the underlying mechanisms and clinical implications is essential for delivering comprehensive and tailored healthcare.

MATERIALS AND METHODS

This was a hospital-based cross-sectional study aimed to evaluate the frequency and relationship between thyroid dysfunction and chronic kidney disease mainly to determine the prevalence of thyroid functional abnormalities in CKD patients and to explore the correlation between CKD and thyroid dysfunction. This study was conducted between September 2022 to August 2023. The study population comprised of CKD patients admitted in Nephrology ward, KGH, Visakhapatnam. CKD was diagnosed based on history, clinical examination and on NKF (National Kidney Foundation) criteria. Sample size: 160 (based on formula: 4PQ/L2; P: Prevalence, Q: 100-P, L: Absolute provision). Prior approval was obtained from the Institutional Ethics Committee of Andhra Medical College. A written informed consent was taken from each individual of the study in English and Telugu. Confidentiality was strictly maintained.

Inclusion Criteria

- All the CKD patients willing to participate in the study and gave informed written consent.
- Patients between 18 and 60 years of age.
- Kidney disease of 3 or more than 3 months duration.
- Patients with no family history of any thyroid disease.
- Patients who have not undergone any surgical/radiological intervention to thyroid gland.
- Patients not receiving drugs altering thyroid profile like amiodarone, phenytoin, beta blocker, steroids, estrogen, iodine compounds.

Exclusion criteria:

- Patients who did not provide valid informed consent.
- Patients with family history of thyroid disorders or past history of thyroid medication use.
- History of any surgery or radiological intervention to thyroid gland, pregnancy.
- Patients receiving medications such as amiodarone, phenytoin, beta blockers, steroids, estrogen, or iodine compounds.
- Patients under 18 years of age or over 60 years of age were excluded.

Data collection: Data was collected from CKD patients in Nephrology wards, KGH, Visakhapatnam with their consent. Detailed history of patient was taken. Samples collected from the patient were sent to lab and data from reports were collected. Clinical and systemic examination was done on the patient.

Data analysis: Data entry and statistical analysis was performed with the help of Microsoft Excel and SPSS28. The statistical significance level was fixed at p value less than 0.05.

RESULTS

The mean age of the study population was 38.28 ± 5.6 years. The mean age among Group 1 with normal TFT was 37.7 ± 13.01 and the mean age among group 2 with altered TFT was 38.9 ± 11.4 years. The difference between both groups was not statistically significant at p=0.3.

Table 1: Age distribution of the study population

Age group	Count of Age	%
<20	5	3%
20-29	42	26%
30-39	35	22%
40-49	40	25%
50-60	38	24%
Grand Total	160	

Table 2: Gender distribution of study population.

Row Labels	Count of Sex	%
F	135	84%
M	25	16%
Grand Total	160	

Table 3: Weight distribution in the study population

Weight group	Normal Thyroid	Thyroid dysfunction	Grand Total
55-64	46	-	46
65-74	40	13	53
75-84	2	39	41

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85-94	-	20	20
Grand Total	88	72	160

The mean weight in group 1 was 80.5 ± 5.8 kgs. The mean weight in group 2 was 65.4 ± 5.4 kgs.

Table 4: Serum Creatinine levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of s.creatinine (mg/dl)	4.6	6.8	5.6
SD	1.5	1.1	1.7

The difference between both the groups in s. creatinine is significant at p<0.0001.

Table 5: Blood Urea levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of Blood Urea (mg/dl)	99.8	120.5	109.1
SD	10.5	11.8	15.2

The difference between both the groups in blood urea levels is statistically significant at p <0.0001

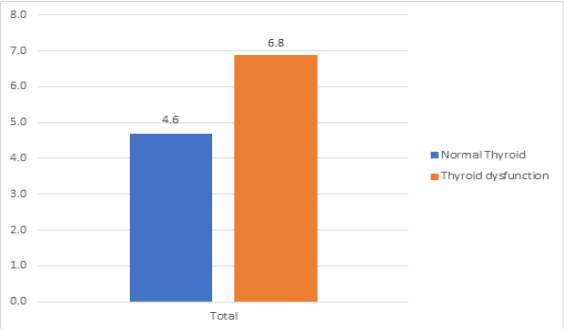

Figure 1: Bar diagram showing s.creatinine levels in study population

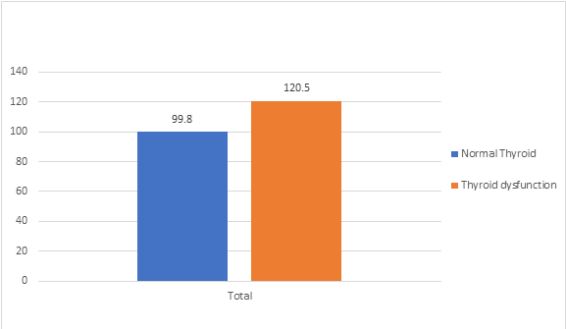

Figure 2: Bar diagram showing blood urea levels in study population

Table 6: Serum uric acid levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of S.Uric acid (mg/dl)	5.0	10.3	7.4
SD	1.4	1.3	2.9

The difference in both the groups in uric acid value is statistically significant at p<0.00001

Table 7: eGFR value in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of eGFR (ml/min)	44.2	30.9	38.2
SD	15.8	24.8	22.3

The difference in eGFR in both the groups is statistically significant at p<0.0001

Table 8: Stage of CKD among the subjects

Row Labels	Normal Thyroid	Thyroid dysfunction	Grand Total
2	29	-	29
3	23	33	56
4	27	28	55
5	9	11	20
Grand Total	88	72	160

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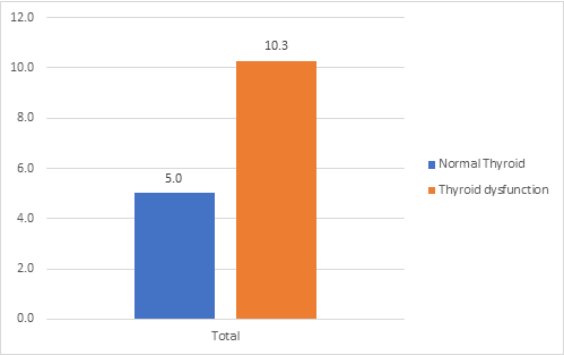

Figure 3: Bar diagram showing serum uric acid levels in study population

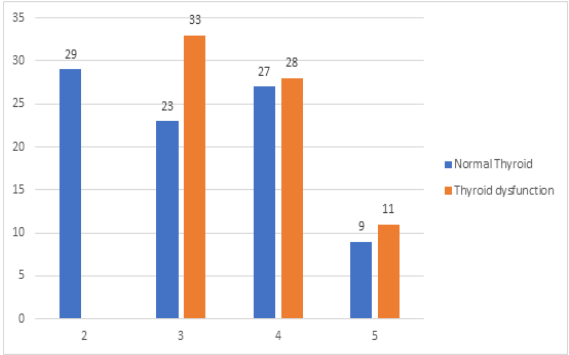

Figure 4: Bar diagram showing stage of CKD among subjects

Table 9: Free T3 levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of FT3 (pg/mL)	3.4	6.3	4.7
SD	0.8	0.9	1.6

The difference in FT3 between both the groups is statistically significant at $p<0.0001$

Table 10: Free T4 levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of FT4 ng/dL	1.1	3.8	2.3
SD	1.3	0.5	1.6

The difference in FT4 between both the groups is statistically significant at $p<0.0001$

Table 11: TSH levels in study population

	Normal Thyroid	Thyroid dysfunction	Grand Total
Average of TSH IU/L	2.6	9.5	5.7
SD	2.5	1.5	4.0

The difference in TSH between both the groups is statistically significant at $p<0.0001$

Table 12: Comparison between normal TFT group and altered TFT group

	Normal Thyroid	Thyroid dysfunction
TSH IU/L	2.6	9.5
Free T3 pg/dL	3.4	6.3
Free T4 ng/dL	1.1	3.8
Serum creatinine mg/dL	4.6	6.8
Blood Urea mg/dL	99.8	120.5
S Uric acid mg/dL	5.0	10.3
eGFR ml/Min	44.2	30.9

Table 13: Pearson correlation coefficient: Serum creatinine correlation with TFT

	Free T3	Free T4	TSH
Pearson correlation coefficient (r)	0.53	0.66	0.78

DISCUSSION

Thyroid dysfunction in chronic kidney disease (CKD) patients represents a complex and multifaceted clinical challenge, intertwining the intricate interplay between two vital systems in the human body. The thyroid, a key regulator of metabolism and energy balance, is intricately linked with renal function. CKD, a progressive deterioration of kidney function, significantly impacts the thyroid axis, leading to a myriad of alterations in thyroid hormone synthesis, metabolism, and action. Altered synthesis and metabolism of thyroid hormones is one of the key manifestations of thyroid dysfunction in chronic kidney disease (CKD). In the early stages of CKD, reduced clearance of thyrotropin (TSH), the hormone that stimulates the thyroid gland, can lead to elevated TSH levels, indicating hypothyroidism. Simultaneously, impaired conversion of thyroxine (T4) to its active form, triiodothyronine (T3), within the kidney exacerbates the hypothyroid state. These changes contribute to the classical features of hypothyroidism, such as fatigue, weight gain, and cold intolerance. As CKD progresses, however, a shift may occur towards a hyperthyroid state, partly due to decreased binding of thyroid hormones to proteins, leading to an increase in free thyroid hormones. The complex interplay between the thyroid and kidneys is further influenced by disruptions in the hypothalamic-pituitary-thyroid

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(HPT) axis. The impaired renal clearance of TSH and altered production of thyroid hormones create a feedback loop that disrupts the delicate balance of the HPT axis. This dysregulation is especially pronounced in advanced stages of CKD, where the prevalence of thyroid dysfunction is higher.

Additionally, the presence of uremic toxins, characteristic of CKD, further complicates the scenario by interfering with thyroid hormone synthesis and action, creating a hostile environment for the thyroid gland. The impact of thyroid dysfunction on CKD outcomes cannot be overstated. Hypothyroidism in CKD is associated with an increased risk of cardiovascular events, an already prevalent concern in this patient population. The proatherogenic effects of hypothyroidism, including dyslipidemia and endothelial dysfunction, synergize with the cardiovascular complications inherent in CKD, leading to a higher incidence of adverse cardiovascular events. On the contrary, hyperthyroidism has been linked to an increased risk of atrial fibrillation and accelerated cardiovascular disease progression, further emphasizing the intricate relationship between thyroid function and cardiovascular outcomes in CKD patients. Management of thyroid dysfunction in CKD requires a nuanced approach. Traditional treatment modalities such as levothyroxine replacement for hypothyroidism must be carefully tailored to the unique challenges posed by renal impairment. CKD patients often require lower doses of levothyroxine due to reduced renal clearance, preventing the inadvertent induction of iatrogenic hyperthyroidism. Monitoring thyroid function becomes a critical aspect of CKD management, necessitating regular assessment of TSH, free T4, and free T3 levels to guide appropriate adjustments in thyroid hormone replacement therapy.

Furthermore, addressing the underlying causes of thyroid dysfunction in CKD is important. Attention to factors such as inflammation, malnutrition, and alterations in the gut-kidney-thyroid axis is essential for comprehensive management. Emerging research also suggests a potential role for novel therapeutic agents, such as thyromimetics, in the management of thyroid dysfunction in CKD, providing a promising avenue for future interventions. In 2016, Chandra et colleagues did a study to determine the prevalence of hypothyroidism in people who have chronic renal disease. Out of a total of 1,863 individuals with chronic kidney disease (CKD), 358 patients were subjected to biochemical examination to determine the presence of hypothyroidism. Among them, 143 individuals showed biochemical evidence of subclinical hypothyroidism, while 59 were diagnosed with overt hypothyroidism. Patients in the overt hypothyroid group exhibited markedly elevated TSH levels and a diminished free T4 level compared to those in the non-hypothyroid group. Individuals diagnosed with hypothyroidism, including both clinical and subclinical cases, had notably reduced levels of blood albumin and serum calcium in comparison to the non-hypothyroid group. The levels of intact parathyroid hormone were significantly elevated in the hypothyroid groups. Patients with reduced glomerular filtration rate (GFR) demonstrated a higher prevalence of hypothyroidism. There is mounting evidence indicating a higher occurrence of hypothyroidism in people with chronic kidney disease (CKD) who do not require dialysis. This group exhibits several abnormalities, including decreased levels of serum albumin, serum calcium, and hemoglobin, as well as elevated levels of intact parathyroid hormone. Targeted therapy can improve the condition of these patients. Therefore, it is necessary to develop specific criteria for evaluating this group for hypothyroidism.[12]

In 2023, Naguib et al. conducted a study on the relationship between Thyroid Dysfunction and Renal Function. The study demonstrated a significant reduction in mean serum creatinine levels in hypothyroid patients after treatment compared to pre-treatment levels. Additionally, the mean estimated glomerular filtration rate (eGFR) showed a significant improvement after treatment, as compared to before treatment. Additionally, individuals with hyperthyroidism showed significantly lower mean serum creatinine levels before treatment compared to after treatment. Furthermore, the mean estimated glomerular filtration rate (eGFR) experienced a significant decrease following treatment. The study found a strong positive relationship between TSH levels and serum creatinine levels, as well as a strong negative relationship between TSH levels and eGFR (estimated glomerular filtration rate) in all individuals with thyroid dysfunction. Thyroid dysfunction is associated with impaired kidney function.

The clinician must be cognizant of the association between thyroid problems and abnormal renal function in order to contemplate a thyroid function test when managing a patient with only slightly increased biochemical indicators of renal function. Monitoring creatinine levels is necessary in people with thyroid disease.[13] In 2023, Ansari et al conducted a study on the occurrence of Thyroid Dysfunction at various stages of chronic kidney disease. Among the 200 patients who participated, 181 individuals (91.5%) exhibited thyroid problems. Among this group of patients, 57% had low T3 syndrome, 23% had low T4 syndrome, and 10.5% had primary hypothyroidism. According to the findings, there was a statistically significant increase in TSH levels as the stages of CKD progressed ($p=0.04$). The likelihood of developing hypothyroidism increases as kidney function declines, particularly in stage five.[14]

CONCLUSION

In conclusion, thyroid dysfunction is a common issue in individuals with chronic kidney disease (CKD), with a higher prevalence of hypothyroidism and

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subclinical hypothyroidism compared to general population. Among the patients with CKD, thyroid function tests i.e., FT3, FT4, TSH were more deranged. Serum creatinine level effects the fluctuation of FT3, FT4 and TSH. Moving forward, further research is needed to elucidate the underlying mechanisms

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