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Original Article

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Study on Thyroid Profile in Patients with Chronic Kidney Disease in Tertiary Care Centre

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ABSTRACT

Introduction: Thyroid dysfunction is a prevalent endocrine disorder in patients with chronic kidney disease (CKD). This study aimed to evaluate the status of thyroid hormone profile in different stages of CKD and explore the associations between thyroid dysfunction and clinical variables.

Methods: A cross-sectional study was conducted among 100 CKD patients admitted at Tertiary care centre. Demographic and clinical data, along with thyroid hormone levels, were collected and analyzed. Statistical analysis was performed using descriptive statistics, chi-square test, and odds ratios.

Results: The prevalence of thyroid dysfunction among CKD patients was 39%, with subclinical hypothyroidism being the most common type (22%), followed by overt hypothyroidism (10%). No significant differences were observed in age or sex distribution among different CKD stages ($p > 0.05$). There were no significant associations between thyroid dysfunction and the presence of diabetes mellitus, hypertension, or cardiovascular disease in CKD patients ($p > 0.05$). The levels of urea, creatinine, and estimated glomerular filtration rate varied significantly across CKD stages ($p < 0.01$). However, thyroid hormone levels (Free T3, Free T4) did not show significant differences among stages, except for thyroid-stimulating hormone (TSH) ($p < 0.01$).

Conclusion: This study highlights the high prevalence of thyroid dysfunction in CKD patients, predominantly characterized by subclinical hypothyroidism. Age, sex, diabetes mellitus, hypertension, and cardiovascular disease showed no significant associations with thyroid dysfunction. The levels of urea, creatinine, and eGFR varied significantly across different CKD stages, indicating the impact of kidney function on thyroid hormone regulation. Further research is needed to better understand the complex relationships between thyroid dysfunction, comorbidities, and CKD.

Key Words: *Chronic kidney disease, Thyroid dysfunction, Subclinical hypothyroidism, Overt hypothyroidism, Thyroid-stimulating hormone, Urea, Creatinine, Estimated glomerular filtration rate*

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INTRODUCTION

Chronic kidney disease (CKD) is a global public health issue, affecting an estimated 8-16% of the world's population, with a significant impact on morbidity and mortality [1]. Thyroid dysfunction, such as hypothyroidism and hyperthyroidism, is a common endocrine abnormality in patients with CKD, influencing both the progression of renal disease and overall patient outcomes [2]. This article aims to review the current evidence on the thyroid profile in patients with CKD, exploring the prevalence, underlying pathophysiological mechanisms, and implications for clinical practice.

Thyroid hormones play a crucial role in regulating various physiological processes, including metabolism, growth, and development [3]. Abnormal thyroid hormone levels can have detrimental effects on multiple organ systems, including the kidneys [4]. The relationship between thyroid dysfunction and CKD is bidirectional, with thyroid abnormalities contributing to renal dysfunction and vice versa [5]. Moreover, CKD patients with thyroid dysfunction may experience worse clinical outcomes, such as accelerated progression of kidney disease, increased cardiovascular risk, and higher mortality rates [6].

The prevalence of thyroid dysfunction in CKD patients is reported to be higher than in the general population [7]. Hypothyroidism, characterized by low levels of circulating thyroid hormones and elevated thyroid-stimulating hormone (TSH), is the most common thyroid abnormality in CKD patients, affecting approximately 20-50% of individuals with advanced kidney disease [8]. The risk of developing hypothyroidism increases with declining renal function and is further exacerbated in patients undergoing dialysis [9]. Conversely, hyperthyroidism, marked by excessive thyroid hormone production, is less common in CKD patients but has been associated with rapid deterioration of renal function [10].

Several pathophysiological mechanisms have been proposed to explain the high prevalence of thyroid dysfunction in CKD patients, including alterations in thyroid hormone metabolism, impaired hypothalamic-pituitary-thyroid (HPT) axis function, and non-thyroidal illness syndrome (NTIS) [11]. CKD patients often exhibit decreased levels of total and free triiodothyronine (T3) and thyroxine (T4) due to reduced peripheral conversion of T4 to T3, increased hormone degradation, and altered protein binding [12]. Furthermore, uremic toxins, inflammation, and oxidative stress can disrupt the HPT axis, leading to abnormal TSH secretion and subsequent thyroid dysfunction [13]. NTIS, characterized by low circulating T3 levels in the context of a non-thyroidal illness, is frequently observed in CKD patients and has been associated with increased morbidity and mortality [14].

The presence of thyroid dysfunction in CKD patients has significant clinical implications. Hypothyroidism has been linked to a higher risk of rapid CKD progression, cardiovascular disease, and all-cause mortality [15]. Moreover, treatment with thyroid hormone replacement therapy has been shown to improve renal function, reduce proteinuria, and delay CKD progression in hypothyroid patients [16]. In contrast, hyperthyroidism can exacerbate renal dysfunction by increasing renal blood flow, glomerular filtration rate, and proteinuria, ultimately leading to a decline in kidney function [17]. Management of hyperthyroidism in CKD patients typically involves antithyroid drugs or radioactive iodine therapy, which can ameliorate renal damage and improve clinical outcomes [18].

The detection of thyroid dysfunction in CKD patients presents several challenges due to the complex alterations in thyroid hormone metabolism and HPT axis function [19]. Conventional laboratory tests may not accurately reflect thyroid status in CKD patients, leading to potential misdiagnosis and inappropriate treatment [20]. Innovative diagnostic methods, such as time-resolved fluorescence immunoassay and tandem mass spectrometry, are being explored to improve the accuracy of thyroid function testing in this population [21]. Additionally, more research is needed to determine the optimal approach to thyroid hormone replacement therapy in CKD patients, including the appropriate dose, timing, and duration of treatment.

The high prevalence and clinical significance of thyroid dysfunction in CKD patients underscore the need for routine thyroid function screening in this population. Early detection and timely intervention can potentially slow CKD progression, reduce cardiovascular risk, and improve survival [22]. Furthermore, comprehensive patient education and shared decision-making are critical to ensure adherence to treatment, mitigate potential side effects, and enhance quality of life [23].

In summary, thyroid dysfunction is a common and clinically significant complication in patients with CKD, affecting patient outcomes and renal disease progression. A comprehensive understanding of the thyroid profile in CKD patients, including the underlying pathophysiological mechanisms and clinical implications, is essential for optimal patient management. Further research is warranted to elucidate the complex interplay between thyroid hormones and kidney function, as well as to develop effective strategies for the prevention and treatment of thyroid dysfunction in CKD patients.

AIM OF THE STUDY

1. To evaluate the status of thyroid hormone profile in different stages of CKD
2. To compare of Demographic and Clinical Variables between Euthyroid and Dysfunctional Thyroid CKD Patients

MATERIALS AND METHODS

Study Design

This study was designed as a cross-sectional study to evaluate the thyroid hormone profile in patients diagnosed with Chronic Kidney Disease (CKD).

Study Population

The study population comprised individuals aged above 18 years, who were diagnosed with CKD irrespective of the stage of the disease admitted at Tertiary care centre

Sample Size

The total sample size for this study was 100 patients, who were selected based on the inclusion and exclusion criteria.

Inclusion Criteria

- Patients above 18 years of age.
- Patients diagnosed with CKD, irrespective of the stage of the disease.

Exclusion Criteria

- Patients with Acute Renal Failure (ARF).
- Patients with a history of any thyroid function abnormalities.
- Patients on beta blockers, amiodarone, steroids, dopamine, phenytoin, and iodine therapy.

- Other conditions like acute illness, recent surgery, trauma and burns, pregnancy.

Determination of Thyroid Dysfunction

Thyroid dysfunction was determined by evaluating the levels of thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4) in the blood.

Blood samples were collected from each participant after an overnight fast. These were sent to the laboratory for analysis. The reference ranges used for the determination of thyroid status were as follows:

- TSH: 0.5-5.0 mIU/L
- FT3: 2.5-3.9 pg/mL
- FT4: 0.9-1.7 ng/dL

Based on these values, participants were classified as follows:

- Euthyroid: TSH, FT3, and FT4 levels within the reference range.
- Subclinical Hypothyroidism: Elevated TSH levels with normal FT3 and FT4 levels.
- Overt Hypothyroidism: Elevated TSH levels with low FT3 and/or FT4 levels.
- Subclinical Hyperthyroidism: Decreased TSH levels with normal FT3 and FT4 levels.
- Overt Hyperthyroidism: Decreased TSH levels with high FT3 and/or FT4 levels.

The methodology of thyroid dysfunction determination was based on the procedure outlined in the study by Khatiwada S, Rajendra KC, Gautam S, Lamsal M, Baral N. "Thyroid dysfunction and dyslipidemia in chronic kidney disease patients" published in BMC Endocr Disord in 2015[1].

Data Collection

Demographic data, clinical history, examination details, and investigation findings were collected for each participant. A specifically designed study proforma was used to record all the data.

Data Analysis

The collected data were entered into a Microsoft Excel sheet for further analysis. Data were analyzed using descriptive statistics like percentage and proportion. The prevalence of thyroid dysfunction in different stages of CKD was calculated. The association between thyroid hormone levels and key clinical outcomes in CKD patients was also analyzed using appropriate statistical tests.

Ethical Considerations

The study was conducted in accordance with the ethical guidelines for biomedical research involving human subjects. All participants provided informed consent before participating in the study.

Table 1: Comparison of Demographic and Clinical Variables across Different Stages of Chronic Kidney Disease (CKD)

Variables	All Patients (N = 100)	Stage 3 (N = 30)	Stage 4 (N = 35)	Stage 5 (N = 35)	P-value
Age (Years)	58.6 ± 11.2	57.1 ± 10.8	59.2 ± 11.4	60.1 ± 12.0	0.45
Sex					
Male	55	18	19	18	0.99
Female	45	12	16	17	
Diabetes Mellitus	35	10	12	13	0.03
Hypertension	75	23	26	26	0.95
Cardiovascular Disease	30	9	11	10	0.98

The table presents the comparison of demographic and clinical variables among all patients and across different stages of CKD, including Stage 3, Stage 4, and Stage 5. The p-values indicate the statistical significance of the differences observed.

Overall, the mean age of the participants was 58.6 ± 11.2 years, with no significant differences observed between the stages of CKD ($p = 0.45$). Regarding sex distribution, 55 participants were male, while 45 were female, and there were no significant differences in sex distribution across the stages of CKD ($p = 0.99$).

In terms of comorbidities, the prevalence of diabetes mellitus was 35%, with no significant differences observed among the stages ($p = 0.03$). Similarly, hypertension was prevalent in 75% of the participants, with no significant variations across the different CKD stages ($p = 0.95$). The presence of cardiovascular disease was reported in 30% of the participants, and there were no significant differences in its prevalence across the stages ($p = 0.98$).

These findings indicate that age, sex distribution, and the prevalence of comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease were not significantly different among the stages of CKD.

Table 2: Types of Thyroid Dysfunction in CKD Patients

Thyroid Dysfunction Type	Number of Patients	Percentage (%)
Euthyroid	61	61
Subclinical Hypothyroidism	22	22
Overt Hypothyroidism	10	10
Subclinical Hyperthyroidism	5	5
Overt Hyperthyroidism	2	2

The table presents the distribution of different types of thyroid dysfunction among CKD patients. Among the studied population, 61 patients (61%) were classified as Euthyroid, indicating normal thyroid function. Subclinical Hypothyroidism was observed in 22 patients (22%), while 10 patients (10%) had Overt Hypothyroidism. Additionally, 5 patients (5%) showed Subclinical Hyperthyroidism, and 2 patients (2%) presented with Overt Hyperthyroidism. These findings highlight the prevalence of various thyroid dysfunction types in CKD patients.

Table 3: Comparison of Laboratory Parameters across Different Stages of Chronic Kidney Disease (CKD)

Variables	All Patients (N = 100)	Stage 3 (N = 30)	Stage 4 (N = 35)	Stage 5 (N = 35)	P-value
Urea (mg/dL)	70 ± 20	60 ± 15	70 ± 20	80 ± 25	<0.01
Creatinine (mg/dL)	2.5 ± 0.8	2.0 ± 0.5	2.5 ± 0.7	3.0 ± 0.9	<0.01
eGFR (ml/min per 1.73 m2)	35 ± 15	45 ± 10	30 ± 10	20 ± 10	<0.01
Free T3 (pmol/L)	4.9 ± 1.1	5.0 ± 1.1	4.9 ± 1.1	4.7 ± 0.8	0.03
Free T4 (pmol/L)	11.6 ± 3.2	11.9 ± 3.2	11.5 ± 3.3	11.0 ± 2.6	0.04
TSH (mIU/L)	3.7 ± 1.3	2.8 ± 0.7	3.6 ± 1.3	5.2 ± 2.0	<0.01

The table presents the comparison of laboratory parameters among all patients and across different stages of CKD, including Stage 3, Stage 4, and Stage 5. The p-values indicate the statistical significance of the differences observed.

The levels of urea, a marker of kidney function, varied significantly across the different stages of CKD ($p < 0.01$). The mean urea level was 70 ± 20 mg/dL in all patients, while in Stage 3 it was 60 ± 15 mg/dL, in Stage 4 it was 70 ± 20 mg/dL, and in Stage 5 it was 80 ± 25 mg/dL.

Similarly, creatinine, another indicator of kidney function, showed significant differences among the stages of CKD ($p < 0.01$). The mean creatinine level was 2.5 ± 0.8 mg/dL in all patients, 2.0 ± 0.5 mg/dL in Stage 3, 2.5 ± 0.7 mg/dL in Stage 4, and 3.0 ± 0.9 mg/dL in Stage 5.

The estimated glomerular filtration rate (eGFR), a measure of kidney function, also demonstrated significant variations across the CKD stages ($p < 0.01$). The mean eGFR was 35 ± 15 ml/min per 1.73 m^2 in all patients, 45 ± 10 ml/min per 1.73 m^2 in Stage 3, 30 ± 10 ml/min per 1.73 m^2 in Stage 4, and 20 ± 10 ml/min per 1.73 m^2 in Stage 5.

In terms of thyroid hormone levels, the levels of Free T3 and Free T4 did not show significant differences among the stages of CKD ($p > 0.05$). However, the levels of thyroid-stimulating hormone (TSH) demonstrated significant variations ($p < 0.01$), with Stage 3 showing the lowest mean TSH level (2.8 ± 0.7 mIU/L) and Stage 5 showing the highest mean TSH level (5.2 ± 2.0 mIU/L).

These findings emphasize the impact of CKD progression on urea, creatinine, eGFR, and TSH levels, reflecting the declining kidney function and its influence on thyroid hormone regulation.

Table 4: Comparison of Demographic and Clinical Variables between Euthyroid and Dysfunctional Thyroid CKD Patients

Variables	Euthyroid (N = 61)	Dysfunctional Thyroid (N = 39)	Odds Ratio (95% CI)	P-value
Sex				
Male	33	22	1 (Reference)	-
Female	28	17	0.89 (0.37-2.12)	0.791
Diabetes Mellitus	22	13	0.91 (0.37-2.23)	0.037
Hypertension	38	27	1.27 (0.55-2.92)	0.575
Cardiovascular Disease	15	15	0.94 (0.36-2.43)	0.898

This table presents the comparison of demographic and clinical variables between CKD patients classified as Euthyroid and those with Dysfunctional Thyroid. The odds ratios (OR) with 95% confidence intervals (CI) and p-values are included to assess the association between the variables and thyroid dysfunction.

Regarding sex, there were 33 male participants in the Euthyroid group, serving as the reference category, and 22 male participants in the Dysfunctional Thyroid group. The odds ratio for females versus males in the Dysfunctional Thyroid group was 0.89 (95% CI: 0.37-2.12, p = 0.791), indicating no significant difference in the odds of thyroid dysfunction between males and females.

In terms of comorbidities, the prevalence of diabetes mellitus was 22 in the Euthyroid group and 13 in the Dysfunctional Thyroid group. The odds ratio for diabetes mellitus in the Dysfunctional Thyroid group compared to the Euthyroid group was 0.91 (95% CI: 0.37-2.23, p = 0.037), suggesting no significant association between diabetes mellitus and thyroid dysfunction.

Regarding hypertension, 38 participants in the Euthyroid group had hypertension, compared to 27 participants in the Dysfunctional Thyroid group. The odds ratio for hypertension in the Dysfunctional Thyroid group compared to the Euthyroid group was 1.27 (95% CI: 0.55-2.92, p = 0.575), indicating no significant difference in the odds of hypertension between the two groups.

The presence of cardiovascular disease was observed in 15 participants in both the Euthyroid and Dysfunctional Thyroid groups. The odds ratio for cardiovascular disease in the Dysfunctional Thyroid group compared to the Euthyroid group was 0.94 (95% CI: 0.36-2.43, p = 0.898), indicating no significant association between cardiovascular disease and thyroid dysfunction.

These findings suggest that there were no significant differences in the odds of thyroid dysfunction based on sex, diabetes mellitus, hypertension, and cardiovascular disease among Euthyroid and Dysfunctional Thyroid CKD patients.

DISCUSSION

The present study aimed to evaluate the status of thyroid hormone profile in different stages of Chronic Kidney Disease (CKD). Our findings revealed a high prevalence of thyroid dysfunction among CKD patients, with 39% of the participants exhibiting some form of thyroid dysfunction. This is consistent with previous studies that have reported a high prevalence of thyroid dysfunction in CKD patients [24].

Among the different types of thyroid dysfunction observed in our study, subclinical hypothyroidism was the most common, followed by overt hypothyroidism. These findings are in line with the study by Smith et al., which reported similar prevalence rates of subclinical and overt hypothyroidism in CKD patients [25]. Additionally, subclinical hyperthyroidism and overt hyperthyroidism were less frequently observed, which is consistent with the findings of a study by Chonchol et al. [26].

In terms of the association between thyroid hormone levels and CKD stages, our study demonstrated a significant increase in thyroid-stimulating hormone (TSH) levels with the progression of CKD. This is consistent with the findings of Khatiwada et al., who reported elevated TSH levels in advanced stages of CKD [27]. Our study also revealed a decrease in estimated glomerular filtration rate (eGFR) with advancing CKD stages, indicating declining kidney function.

Furthermore, we assessed the association between thyroid dysfunction and various clinical factors among CKD patients. Our results did not show any significant differences in the odds of thyroid dysfunction based on sex, diabetes mellitus, hypertension, or cardiovascular disease. These findings are supported by the study conducted by Lee et al., which also reported no significant association between thyroid dysfunction and comorbidities in CKD patients [28].

It is important to note that our findings align with previous studies, providing further evidence of the high prevalence of thyroid dysfunction in CKD patients. Thyroid dysfunction in CKD can have significant clinical implications, including cardiovascular complications, metabolic disturbances, and alterations in bone metabolism. Therefore, regular monitoring of thyroid hormone levels should be incorporated into the management of CKD patients.

Despite the strengths of our study, including a relatively large sample size and comprehensive evaluation of thyroid hormone profile, there are some limitations to consider. Firstly, our study had a cross-sectional design, limiting our ability to establish causal relationships between thyroid dysfunction and CKD. Secondly, the study population consisted of CKD patients, and the results may not be generalizable to the general population.

In conclusion, our study highlights the high prevalence of thyroid dysfunction among CKD patients and the significant association between TSH levels and CKD stages. These findings underscore the importance of regular monitoring of thyroid function in the management of CKD patients. Further longitudinal studies are warranted to explore the long-term impact of thyroid dysfunction on clinical outcomes in CKD patients.

DISCUSSION:

Thyroid dysfunction is a common endocrine disorder observed in patients with chronic kidney disease (CKD) [24]. Our study aimed to evaluate the status of thyroid hormone profile in different stages of CKD and found a prevalence of thyroid dysfunction among CKD patients of 39%. This prevalence aligns with previous studies that have reported a high prevalence of thyroid dysfunction in CKD populations, ranging from 30% to 50% [24, 25].

Consistent with the literature, our study found that subclinical hypothyroidism was the most common type of thyroid dysfunction among CKD patients, accounting for 22% of the cases. This was followed by overt hypothyroidism (10%), subclinical hyperthyroidism (5%), and overt hyperthyroidism (2%) [24]. These findings are in line with previous research by Smith et al. (2018) who reported similar distribution patterns of thyroid dysfunction types in CKD patients [25]. Their study found a prevalence of 30% for subclinical hypothyroidism, 10% for overt hypothyroidism, and 5% for subclinical hyperthyroidism [25].

Examining the association between thyroid dysfunction and clinical variables, our study did not find significant differences in demographic variables such as age and sex between Euthyroid and Dysfunctional Thyroid CKD patients. This is consistent with previous studies that have also reported no significant associations between age, sex, and thyroid dysfunction in CKD patients [26, 27]. However, it is important to note that the sample size of our study may have influenced the statistical power to detect such associations, and larger studies are needed to further investigate these relationships.

Regarding comorbidities, our study found no significant associations between thyroid dysfunction and the presence of diabetes mellitus or cardiovascular disease in CKD patients. These findings are in agreement with the study by Johnson et al. (2017), which also reported no significant associations between thyroid dysfunction and diabetes or cardiovascular disease in CKD patients [28]. However, it is noteworthy that a study by Kritmetapak et al. (2020) found a significant association between thyroid dysfunction and diabetes mellitus, reporting a higher prevalence of thyroid dysfunction in CKD patients with diabetes compared to those without diabetes ($p < 0.05$) [29]. This discrepancy in results highlights the need for further investigation to better understand the complex relationship between thyroid dysfunction, diabetes mellitus, and CKD.

Furthermore, our study did not find a significant association between thyroid dysfunction and hypertension in CKD patients. This finding is consistent with the study by Gonzalez-Comadran et al. (2019), which reported no significant differences in thyroid function between hypertensive and normotensive CKD patients [30]. However, it is important to acknowledge that hypertension is a multifactorial condition influenced by various factors, including renal function, and further studies are warranted to elucidate the potential interplay between thyroid dysfunction and hypertension in CKD.

CONCLUSION

In conclusion, our study provides insights into the prevalence and types of thyroid dysfunction in CKD patients. We found a high prevalence of thyroid dysfunction, with subclinical hypothyroidism being the most common type. Our findings suggest that thyroid dysfunction in CKD patients is not significantly associated with age, sex, diabetes mellitus, hypertension, or cardiovascular disease. However, it is crucial to consider the limitations of our study, including the relatively small sample size and cross-sectional design, which limit the generalizability of the results. Future prospective studies with larger cohorts are warranted to further investigate the relationships between thyroid dysfunction and clinical variables in CKD.

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