DOI: https://doi.org/10.54393/pjhs.v7i4.3944

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 7, Issue 04 (April 2026)

Original Article

OPEN ACCESS

Frequency of Hypothyroidism among Patients with Chronic Kidney Disease at a Tertiary Care Hospital in Pakistan

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ARTICLE INFO

Keywords:
Hypothyroidism, Chronic Kidney Disease, Thyroid Dysfunction, Subclinical Hypothyroidism Dialysis, Endocrine Disorders

How to Cite:
Ullah, H., Ahmed, A., Hussain, M., Ali, A., Ali, M., Shehzad, S., Israr, H., Amin, A., & Ali, A. (2026). Frequency of Hypothyroidism among Patients with Chronic Kidney Disease at a Tertiary Care Hospital in Pakistan: Frequency of Hypothyroidism among Patients with Chronic Kidney Disease . Pakistan Journal of Health Sciences, 7(4), 138-143. https://doi.org/10.54393/pjhs.v7i4.3944

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Received Date: 4th February, 2026
Revised Date: 14th April, 2026
Acceptance Date: 20th April, 2026
Published Date: 30th April, 2026

ABSTRACT

Patients with Chronic kidney disease (CKD) suffer from endocrine axis disruption as a part of the complications involving several other organ systems. Hypothyroidism is one of the imbalances seen in patients with CKD, both in clinical practice and research. Thyroid dysfunction remains undiagnosed due to its non-specific symptoms and lack of routine screening, especially in resource-limited settings. **Objectives:** To determine the frequency of hypothyroidism among patients with CKD and to differentiate its clinical and subclinical forms. **Methods:** This cross-sectional (descriptive) study was conducted over a period of six months in the Department of Medicine, Mardan Medical Complex, Khyber Pakhtunkhwa. 131 CKD patients (18-70 years) were recruited by non-probability consecutive sampling. Serum levels of thyroid-stimulating hormone (TSH), free T3, and free T4 were used to evaluate the patient's thyroid status. Based on serum hormone levels, the patients were categorized into hypothyroidism, subclinical hypothyroidism, or euthyroid states. The data were analysed through SPSS (version 26.0). **Results:** Out of 131 CKD patients, clinical hypothyroidism was found in 24 (18.3%), while 27 (20.6%) of the patients had subclinical hypothyroidism. Thyroid dysfunction was more common in patients above 60 (p=0.003) and females (p=0.041). A significant association was also found with dialysis status (p=0.006). **Conclusions:** Hypothyroidism is a prevalent complication in CKD, especially among older and female patients. The study emphasizes the value of routine thyroid screening in all stages of CKD to facilitate early diagnosis and treatment, especially in dialysis-dependent people.

INTRODUCTION

Chronic Kidney Disease (CKD) is a chronic and progressive disease characterized by a progressive decline in renal function. Among the top ten causes of death globally in developed countries, CKD affects approximately 10–16% of the adult population worldwide and has become a major public health concern. In Pakistan, the prevalence of CKD is continuously increasing; however, many healthcare settings fail to recognize it. Alongside its widely recognized cardiovascular, hematologic, and metabolic complications, CKD is also associated with many endocrine abnormalities, including disturbances in thyroid function [1, 2]. The kidneys and thyroid glands are linked in a complicated and interdependent relationship. The kidneys play an essential role in the metabolism, clearance, and excretion of thyroid hormones, while thyroid hormones have a major impact on the renal blood flow, glomerular filtration rate (GFR), and electrolyte homeostasis. As the kidney functions decline gradually, changes in thyroid hormone levels become more prominent, often resulting in either clinical or subclinical hypothyroidism. However, the

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symptoms of hypothyroidism, such as fatigue, cold intolerance, and weight gain, can resemble the general symptoms of uraemia, making early diagnosis challenging in patients with CKD [3, 4]. Several international studies have documented the high prevalence of thyroid dysfunction in patients with CKD; however, there is a dearth of regional data, especially from clinical settings in Pakistan [5, 6]. Moreover, subclinical hypothyroidism remains overlooked most of the time due to the absence of its common clinical signs, despite its potential influence on disease progression and cardiovascular risk in CK.

Therefore, this study aimed to find out the frequency of clinical and subclinical hypothyroidism in CKD patients who were admitted to a tertiary care hospital in Mardan. The results will help in early detection and customized therapeutic interventions by raising clinical awareness and highlighting the importance of routine thyroid function screening in clinical practice. Moreover, finding out how common it is among CKD patients at a Pakistani tertiary care hospital offers crucial information for early screening, prompt intervention, and better patient management, all of which improve the quality of treatment for this high-risk group.

METHODS

This cross-sectional study (descriptive) was conducted in the Medical Unit of Mardan Medical Complex (MMC), Mardan, Khyber Pakhtunkhwa, from August 2024 to January 2025. The study aimed to determine the frequency and pattern of hypothyroidism, including both clinical and subclinical forms, in patients diagnosed with chronic kidney disease (CKD). The study was conducted after receiving ethical clearance from two official bodies. Approval was obtained from the Ethical Committee of Bacha Khan Medical College, Mardan, under approval number 229/BKMC, dated May 30, 2022. Additionally, the study was reviewed and approved by the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan (CPSP) with reference number CPSP/REU/MED-2020-028-16933, dated August 10, 2024. Informed written consent was taken from all participants or their legal guardians. Confidentiality and privacy of patient data were strictly maintained. One hundred and thirty-one patients were recruited using a non-probability consecutive sampling technique. The sample size was calculated using the WHO sample size calculator based on an anticipated prevalence of hypothyroidism in CKD of 14.2%, with a 95% confidence interval and a 6% margin of error [7]. Inclusion criteria consisted of patients aged 18 to 70 years, admitted with a confirmed diagnosis of CKD. CKD was diagnosed based on any two or more of the following [8]: Urinary albumin-to-creatinine ratio (ACR) > 30 mg/g [9].––– Abnormal findings on renal ultrasound (e.g., increased cortical echogenicity, loss of corticomedullary differentiation, renal length < 8 cm, or cortical thickness < 6 mm), estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 [10]. Exclusion criteria included patients with a prior diagnosis of hyperthyroidism, those already on thyroid hormone replacement therapy, and individuals with comorbid conditions that could affect thyroid function, such as infections, malignancies, or autoimmune diseases. After taking informed consent, demographic details like age, gender, address, educational status, and socioeconomic class were recorded. Blood samples were taken from the cubital vein aseptically and sent to the hospital laboratory for the analysis of free serum triiodothyronine (FT3), free serum thyroxine (FT4), and thyroid-stimulating hormone (TSH). Based on these test results, the patients were categorized into: Clinical hypothyroidism, defined as elevated serum TSH (>4.0 mIU/L) with low levels of serum Free T3 and Free T4 hormones [9]. Subclinical hypothyroidism is defined as elevated serum TSH (between 4.0 and 10.0 mIU/L) with normal levels of serum Free T3 and Free T4 hormones. Euthyroide state, patients having all three hormone values within the normal range.

Data were entered and analysed using SPSS version 26.0. The Shapiro-Wilk test was used for checking the normal distribution of numerical variables like age and hormone levels, and the data were presented in the form of mean ± standard deviation or median with interquartile range as appropriate. Frequencies and percentages were used to describe the categorical variables such as gender, thyroid status, and comorbidities. For categorical variables, Chi-square or Fisher's exact tests were used to find the associations between thyroid dysfunction and demographic or clinical factors. A p-value of <0.005 was considered statistically significant. To identify potential effect modifiers, stratification of data was performed for age group, gender, educational status, and dialysis status of the patients.

RESULTS

The mean age of the study participants was 55.6 years, indicating that most patients with chronic kidney disease were in the middle to older adult age group. Male patients slightly outnumbered female patients; however, this difference was not statistically significant. Nearly 60% of the participants belonged to urban areas. The majority of patients were from a lower socioeconomic background. Educational status varied among participants, with a considerable proportion being illiterate or having education limited to primary schooling. The Demographic characteristics of CKD patients are represented (Table 1).

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Table 1: Demographic Characteristics of CKD Patients(n=131)

Variables	Category	n (%)	p-value
Age (years)	Mean ± SD	55.6 ± 10.4	–
Gender	Male	72 (54.9%)	0.341
	Female	59 (45.1%)	
Residence	Urban	78 (59.5%)	0.228
	Rural	53 (40.5%)	
Socioeconomic Status	Low	64 (48.9%)	0.172
	Middle	51 (38.9%)	
	High	16 (12.2%)	
Education Level	Illiterate	42 (32.1%)	0.087
	Primary/Secondary	58 (44.3%)	
	Higher	31 (23.6%)	

Abnormal thyroid function tests were observed in a substantial number of patients with chronic kidney disease. Subclinical hypothyroidism was more frequently identified than overt hypothyroidism. Overall, more than one-third of the study population had some form of hypothyroidism. The thyroid status of the CKD patients is shown(Table 2).

Table 2: Thyroid Status Among CKD Patients

Thyroid Status	n (%)	95% Confidence Interval
Clinical Hypothyroidism	24 (18.3%)	11.7% – 25.0%
Subclinical Hypothyroidism	27 (20.6%)	13.7% – 27.5%
Euthyroid (Normal)	80 (61.1%)	52.7% – 69.4%

Biochemically, higher levels of serum TSH were observed in patients with chronic kidney disease upon testing for thyroid functions, along with comparatively lower levels of free serum T3 and free T4. This hormonal pattern was demonstrated by a larger proportion of the study population, pointing towards a higher prevalence of subclinical hypothyroidism than clinical hypothyroidism. The mean biochemical parameters of thyroid functions are reported(Table 3).

Table 3: Mean Biochemical Parameters of Thyroid Function

Parameters	Normal range	Mean ± SD
TSH (mIU/L)	0.4-4.5 mIU/L	5.98 ± 3.21
Free T3 (pg/mL)	2.3-5.0 pg/mL	2.31 ± 0.76
Free T4 (ng/dL)	0.93-1.7 ng/dL	0.84 ± 0.22

The study represents the stratification of hypothyroidism by demographic factors. Hypothyroidism was more prevalent among patients over 60 years of age. Moreover, thyroid dysfunction was also more frequently observed in female patients compared with male patients. Likewise, patients with lower literacy levels and those residing in rural areas exhibited a higher occurrence of thyroid dysfunctions, although these associations were not statistically significant. The data were analysed row-wise (Table 4).

Table 4: Stratification of Hypothyroidism by Demographic Factors

Variables	Hypothyroidism Present, n (%)	Hypothyroidism Absent, n (%)	p-value
Age >60 Years	28 (50.9%)	19 (23.7%)	0.003
Female	31 (54.4%)	28 (35.0%)	0.041
Rural Residence	25 (43.9%)	28 (35.0%)	0.291
Low Socioeconomic	29 (50.9%)	35 (43.8%)	0.432
Illiterate	22 (38.6%)	20 (25.0%)	0.089

The association of hypothyroidism with clinical comorbidities is shown. There was a significant association of the dialysis status with the presence of hypothyroidism among patients with chronic kidney disease, with a highly significant p-value. Moreover, although a higher proportion of comorbidities such as cardiovascular disease and diabetes mellitus were observed among patients with hypothyroidism; however, these associations were not statistically significant (Table 5).

Table 5: Association of Hypothyroidism with Clinical Comorbidities

Comorbidity	Hypothyroidism Present, n (%)	Hypothyroidism Absent, n (%)	p-value
Diabetes Mellitus	26 (45.6%)	30 (37.5%)	0.314
Cardiovascular Disease	21 (36.8%)	19 (23.8%)	0.081
On Dialysis	18 (31.6%)	10 (12.5%)	0.006

DISCUSSION

Thyroid hormones have a direct and indirect effect on both tubular function and glomerular filtration rate, which are important components of renal hemodynamics. Multiple studies have demonstrated that thyroid dysfunction and chronic renal disease have a direct interaction; a Nepalese study found a significantly increased frequency of thyroid dysfunction in CKD patients. There is strong evidence of the reciprocal association between thyroid and kidney function, as thyroid hormones are directly involved in renal development, kidney structure, and hemodynamic performance [11, 12]. There is a widely acknowledged recognition of the clinical importance of thyroid dysfunction in individuals with renal disease, as data show a significant correlation with cardiovascular morbidity and mortality [13]. The implications of our study for healthcare are particularly relevant in the Pakistani context, where access to specialized endocrine treatment is varied, and healthcare resources may be limited. The current findings are supported by a recent Pakistani study that also demonstrated a larger frequency of hypothyroidism among patients with chronic kidney disease in tertiary care settings, highlighting the local relevance of this clinical issue [14]. The current findings are also supported by new international research that has shed further light on the thyroid-kidney relationship. The impact of thyroid status

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on initial renal failure and CKD progression in a nationally representative population was shown in large US cohort research [6]. Subclinical thyroid dysfunction is clearly linked to chronic renal disease, according to population-based studies conducted in South Korea [4]. This study found a high prevalence of both subclinical and clinical hypothyroidism in patients with chronic renal disease. Among the 131 patients studied, roughly 39% had some form of thyroid abnormality. This finding is consistent with the previous global and local research, supporting a clear association between progressive kidney damage and impaired thyroid hormone metabolism [15, 16]. The most notable aspect of this study was the slightly higher frequency of subclinical hypothyroidism (20.6%) than clinical hypothyroidism (18.3%). This result is in line with a comparable study from a tertiary care hospital in Saudi Arabia, in which the prevalence of clinical hypothyroidism in CKD patients was 34.9%, while subclinical hypothyroidism accounted for a larger fraction of the total. Similarly, the pattern of biochemical abnormalities, such as increased serum TSH with either normal or low levels of serum free T3 and T4, further supports the slight but common nature of thyroid dysfunction in patients with CKD [17-19]. Thyroid disturbance has also been linked to chronic renal disease in a variety of demographic groups, according to research from northeastern Indian communities [20]. Most encouragingly, new research from Pakistan indicates that patients with end-stage renal illness may benefit from therapeutic intervention for thyroid dysfunction, underscoring the potential advantages of early identification and therapy. This reversibility concept offers hope for better patient outcomes through targeted therapy and supports the clinical significance of routine thyroid hormone screening in CKD patients [21]. Another significant aspect of this study was that hypothyroidism was more common in the older adults and female patients with CKD, which is also supported by the existing literature. The higher prevalence of hypothyroidism in older adults is explained by the age-related decline in thyroid function, which is frequently made worse in CKD due to impaired hormone clearance and altered peripheral conversion of T4 to T3, a fact supported by a study in a tertiary care hospital with similar demographics. The higher incidence of hypothyroidism in females as compared to males is consistent with broader endocrine trends, because females are usually at a greater risk for thyroid dysfunctions, including autoimmune-associated causes [22, 23]. Serum albumin is an important factor in the significant frequency of subclinical hypothyroidism in patients with end-stage renal illness, according to earlier studies from South India [24]. One of the notable deductions from this study was the statistically significant association between hypothyroidism and dialysis status (p=0.006). Patients undergoing dialysis were about three times more likely to have thyroid dysfunction than those not on dialysis. This relationship may be explained by the effect of haemodialysis on the thyroid hormone physiology, including altered protein binding, metabolic changes, and increased hormone clearance. In addition, the hypothalamic-pituitary-thyroid axis is also disrupted by the uremic environment in patients on dialysis, leading to dysregulation without obvious symptoms [25, 26]. Although comorbid conditions such as diabetes and cardiovascular diseases were frequently observed in hypothyroid patients, the differences were not statistically significant. Nevertheless, their clinical importance cannot be overlooked. As shown by the studies, hypothyroidism significantly exacerbates cardiovascular risk, promotes fluid retention, and worsens anaemia, all of which are the well-known risk factors for the progression of CKD. Further longitudinal studies are needed to clarify these causal relationships and the potential benefits of early screening and replacement of thyroid hormones in this population [27, 28]. The strength of this study is that it provides important local data on the Pakistani population, helping to address a significant lack of regional evidence available on thyroid dysfunction in patients with chronic kidney disease. The existing literature heavily depends upon the Western or Gulf studies, which may not accurately reflect the Pakistani healthcare setting because of differences in iodine levels, healthcare access, socioeconomic factors, and awareness regarding thyroid disorders. Consequently, this study offers essential, context-specific evidence to improve diagnostic and treatment protocols in local nephrology and internal medicine practice. Our results are in favour of routinely screening CKD patients for thyroid function in Pakistani healthcare facilities. Early thyroid dysfunction identification may enable prompt care, thereby lowering cardiovascular consequences and slowing the progression of chronic kidney disease. Healthcare professionals who treat patients with chronic kidney disease (CKD) should be aware of the high incidence of thyroid dysfunction and consider comprehensive screening procedures. The creation of regional clinical guidelines that include thyroid monitoring could enhance patient outcomes and care in general.

This study has several limitations; despite the important insights it provides. Because of its cross-sectional study design, it cannot assess changes in thyroid status over time and cannot establish causality between hypothyroidism and CKD. In addition, due to financial limitations, autoimmune markers such as anti-thyroid peroxidase (anti-TPO) antibodies were not evaluated, which could be helpful in differentiating the underlying cause of hypothyroidism. Future studies should consider

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longitudinal study designs to monitor changes in thyroid function over time and clarify causal associations. Studies involving larger and more diverse populations would improve the generalizability of findings. Furthermore, the inclusion of autoimmune markers such as anti-TPO antibodies and other relevant investigations may provide a deeper understanding of the pathophysiology and causes of hypothyroidism in patients with CKD. Multicentre collaboration and the use of advanced diagnostic approaches may further strengthen the quality and scope of future studies.

CONCLUSIONS

Patients with CKD have a high prevalence of thyroid dysfunction, particularly subclinical hypothyroidism. The findings of this study provide an evidence-based need to screen all patients with CKD for the presence of thyroid abnormalities regularly, especially among females, older adults, and those receiving dialysis. The overall health of these patients can be improved, and the complications can be prevented through early detection and timely management of thyroid dysfunction. We highly recommend incorporating endocrine evaluation in routine nephrology practices for providing a comprehensive patient-centred approach to care.

Authors' Contribution

Conceptualization: AA[1]
Methodology: AA[1], MH, MA, SS, HI, AA[3], AA[4]
Formal analysis: AA[2]
Writing and Drafting: AA[1], HU, MH, AA[2], MA, AA[3], AA[4]
Review and Editing: AA[1], HU, MH, AA[2], MA, SS, HI, AA[3], AA[4]

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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