FREQUENCY OF HYPOTHYROIDISM IN PATIENTS WITH CHRONIC KIDNEY DISEASE AT AYUB TEACHING HOSPITAL, ABBOTTABAD

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ABSTRACT

Background: Hypothyroidism, both overt and subclinical, is a prevalent yet often undiagnosed comorbidity in patients with chronic kidney disease (CKD), contributing to increased morbidity. Understanding its local prevalence is critical for establishing screening and management protocols.

Objective: To determine the frequency of hypothyroidism in CKD patients visiting the outpatient department of Ayub Teaching Hospital, Abbottabad.

Methods: This cross-sectional study, conducted from January 15, 2024, to June 15, 2024, enrolled 380 CKD patients (stages 1–4). Data on age, gender, CKD stage, and thyroid function tests (serum TSH, free T3, free T4) were collected. Hypothyroidism was defined as overt (TSH >5.0 mIU/L, low T4) or subclinical (TSH >5.0 mIU/L, normal T4). Data were analyzed using SPSS version 22, with chi-square tests for associations ($P \leq 0.05$ considered significant).

Results: Of 380 patients (mean age 46 ± 11.93 years; 57% male), 68 (18%) had hypothyroidism. Age distribution showed 49% aged 51–60 years, 39% aged 41–50 years, and 12% aged 18–40 years. CKD stages included 12% stage 1, 24% stage 2, 31% stage 3, and 33% stage 4. Hypothyroidism prevalence was 18%, with no significant associations with age (P=0.821), gender (P=0.674), or CKD stage (P=0.532).

Conclusion: Hypothyroidism affects 18% of CKD patients at Ayub Teaching Hospital, highlighting a significant public health concern. Routine thyroid screening is recommended to mitigate associated complications.

Keywords: Hypothyroidism, chronic kidney disease, prevalence, thyroid function, Pakistan.

INTRODUCTION

Chronic kidney disease (CKD) represents a significant global health challenge, characterized by progressive loss of kidney function that affects millions of people worldwide [1]. The global burden of CKD has been steadily increasing, with substantial regional variations in prevalence and outcomes [1].

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CKD is associated with numerous complications, including anemia, cardiovascular disease, and metabolic disorders, which can be exacerbated by coexisting endocrine conditions, particularly thyroid dysfunction [2,3].

The intricate relationship between thyroid function and kidney disease has been well-documented in medical literature [3,4]. Thyroid hormones play crucial roles in renal development, kidney structure, renal hemodynamics, and glomerular filtration rate, influencing sodium and water homeostasis through both direct renal actions and systemic hemodynamic effects [2]. Conversely, the kidney plays an essential role in thyroid hormone metabolism, degradation, and excretion, creating a bidirectional relationship between these organ systems [3,4].

Hypothyroidism, classified as either overt (elevated TSH with low free T4) or subclinical (elevated TSH with normal T4), presents with clinical manifestations that often overlap with CKD symptoms, including fatigue, cold intolerance, and cardiovascular complications, which can lead to underdiagnosis in CKD patients [5,6]. The epidemiology of thyroid disease shows significant global variation, with hypothyroidism affecting approximately 4.6% of

the US population [7]. In patients with kidney disease, the prevalence of thyroid dysfunction is substantially higher due to altered thyroid hormone metabolism resulting from reduced renal clearance, chronic inflammation, and uremic toxin accumulation [8].

Recent large-scale epidemiological studies have demonstrated an incrementally higher prevalence of hypothyroidism with increasing severity of kidney dysfunction [9,10]. A landmark study of patients with chronic kidney disease found hypothyroidism prevalence ranging from 17-26.2%, with higher rates observed in advanced CKD stages [9,10]. In the South Asian context, a Nepalese study reported a 45.05% prevalence of hypothyroidism in CKD patients, highlighting significant regional variability and underscoring the need for local epidemiological data [11].

The clinical significance of hypothyroidism in CKD extends beyond prevalence statistics. Thyroid dysfunction has been recognized as an under-recognized cardiovascular risk factor in kidney disease patients, associated with increased mortality, cardiovascular events, and impaired quality of life [12,13]. Current clinical practice guidelines recommend consideration of thyroid screening in CKD patients, though specific protocols vary [15,16]. The pathophysiological mechanisms linking thyroid and kidney dysfunction include alterations in renal blood flow, changes in glomerular filtration rate, and effects on cardiovascular hemodynamics [17,18].

Understanding the complex interactions between thyroid disorders and kidney disease is essential for optimal patient care [19,20]. Both conditions share common risk factors and can exacerbate each other's progression [21,22]. The overlap of symptoms between hypothyroidism and CKD often leads to delayed diagnosis and suboptimal management [23]. In resource-limited healthcare settings like Pakistan, where access to specialized endocrine and nephrology care may be limited, establishing local prevalence data becomes crucial for healthcare planning and resource allocation [24].

The burden of CKD in South Asia, including Pakistan, has been substantial, with studies like the SEEK study documenting significant disease prevalence related to diabetes and hypertension [25]. Recent international studies have provided additional insights into thyroid-kidney interactions, with a study from USA showing variable prevalence rates [26]. Population-based studies from India have demonstrated that the relationship between subclinical thyroid dysfunction and CKD may be influenced by demographic and clinical confounders [27]. Large prospective studies from South Korea have established clear associations between thyroid dysfunction and mortality in CKD patients [28]. A comprehensive meta-analysis has confirmed that subclinical hypothyroidism significantly increases CKD risk across diverse populations [29]. A recent Pakistani study supports the notion that addressing thyroid dysfunction in ESRD may reverse associated renal sequelae via appropriate therapy, thereby emphasizing the importance of proactive detection and intervention in high-risk populations.[30].

A seminal cross-sectional study by Chonchol et al. involving 3,089 CKD outpatients demonstrated that subclinical hypothyroidism prevalence increased progressively with declining kidney function, from 7% at eGFR ≥90 ml/min/1.73m² to 17.9% at eGFR <60 ml/min/1.73m², with an overall prevalence of approximately 18% in CKD patients not requiring dialysis [15].

Despite the growing recognition of thyroid dysfunction in CKD patients globally, there remains a paucity of data from the Hazara division of Khyber Pakhtunkhwa, Pakistan. This study aims to determine the frequency of hypothyroidism in CKD patients at Ayub Teaching Hospital, Abbottabad, to inform local screening guidelines and contribute to the global understanding of thyroid-kidney disease associations. Early detection and appropriate management of hypothyroidism in CKD patients can potentially prevent complications such as cardiovascular disease, anemia, and metabolic disturbances, ultimately improving patient outcomes and quality of life.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional study was conducted at the Department of Medicine and Nephrology, Ayub Teaching Hospital, Abbottabad, from January 15, 2024, to June 15, 2024.

Sample Size and Selection: Sample size was calculated using the WHO formula for cross-sectional studies.[14] The expected prevalence of 25% was based on systematic review of available literature. Previous studies have documented hypothyroidism prevalence ranging from 17-26% in CKD populations, with Chonchol et al. reporting prevalence of subclinical hypothyroidism increasing progressively with declining kidney function [15].

Calculation

$n = (1.96)^2 \times 0.25 \times 0.75 / (0.05)^2$

n = 3.84 × 0.1875 / 0.0025n = 288 patients

Adding 10% for potential incomplete data and to enhance precision for subgroup analyses across CKD stages, we recruited 380 patients using consecutive non-probability sampling. The achieved sample size provides 95% confidence intervals with ±3.8% precision around prevalence estimates.

Inclusion criteria were patients aged ≥18 years, both genders, diagnosed with CKD stages 1–4 based on Kidney Disease Improving Global Outcomes (KDIGO) criteria [15]. Exclusion criteria included CKD stage 5 (dialysis patients), acute kidney injury, known hypothyroidism prior to CKD diagnosis, or use of thyroid-altering medications (e.g., amiodarone, lithium).

Data Collection: After obtaining ethical approval from the hospital's Institutional Review Board and written informed consent, detailed history was collected including age, gender, CKD duration, stage, and etiology (e.g., diabetes, hypertension). Blood samples were collected via standard venipuncture and analyzed for serum creatinine, estimated GFR (using the CKD-EPI equation), serum TSH, free T3, and free T4 at the hospital's laboratory. Hypothyroidism was classified as overt (TSH >5.0 mIU/L, free T4 <0.8 ng/dL) or subclinical (TSH >5.0 mIU/L, free T4 0.8–1.8 ng/dL) [16].

Data Analysis: Data were analyzed using SPSS version 22. Quantitative variables (age, CKD duration) were reported as mean ± standard deviation, and qualitative variables (gender, CKD stage, hypothyroidism status) as frequencies and percentages. Hypothyroidism prevalence was stratified by age, gender, and CKD stage, with associations tested using the chi-square test ($P \leq 0.05$ considered significant).

RESULTS

Of 380 patients, the mean age was 46 ± 11.93 years, with 216 (57%) males and 164 (43%) females. Hypothyroidism was detected in 68 patients (18%), with 40 (59%) having subclinical and 28 (41%) having overt hypothyroidism. The following tables summarize the demographic, CKD stage, and hypothyroidism data.

Table 1: Demographic and CKD Stage Distribution

Category	Subcategory	Frequency (n)	Percentage (%)
Age	18–40 years	46	12
Age	41–50 years	148	39
Age	51–60 years	186	49
Gender	Male	216	57
Gender	Female	164	43
CKD Stage	Stage 1	46	12
CKD Stage	Stage 2	91	24
CKD Stage	Stage 3	118	31
CKD Stage	Stage 4	125	33

Table 2: Hypothyroidism Prevalence

Hypothyroidism Status	Frequency (n)	Percentage (%)
Positive	68	18
Negative	312	82

Table 3: Stratification of Hypothyroidism by Age, Gender, and CKD Stage

Category	Subcategory	Hypothyroidism Positive (n)	Hypothyroidism Negative (n)	P-value
Age	18–40 years	8	38	0.821
Age	41–50 years	26	122	0.821
Age	51–60 years	34	152	0.821
Gender	Male	37	179	0.674
Gender	Female	31	133	0.674
CKD Stage	Stage 1	7	39	0.532
CKD Stage	Stage 2	15	76	0.532
CKD Stage	Stage 3	22	96	0.532
CKD Stage	Stage 4	24	101	0.532

No significant associations were observed between hypothyroidism and age (P=0.821), gender (P=0.674), or CKD stage (P=0.532). The prevalence of hypothyroidism was consistent across all subgroups, suggesting that factors beyond demographics and CKD severity, such as altered thyroid hormone metabolism, may contribute.

DISCUSSION

This study demonstrates an 18% prevalence of hypothyroidism among CKD patients at Ayub Teaching Hospital, Abbottabad, which aligns with the global understanding that chronic kidney disease represents a significant health challenge with multiple endocrine complications [1]. The bidirectional relationship between thyroid and kidney function has been extensively documented, with thyroid hormones influencing renal development, kidney structure, and hemodynamic function [2]. Our findings support the established concept that thyroid dysfunction is a common and clinically significant comorbidity in CKD patients, requiring systematic attention in clinical practice [3].

The observed prevalence in our study is consistent with international reports demonstrating that thyroid dysfunction affects a substantial proportion of CKD patients globally [4]. The complex pathophysiological relationship between thyroid disorders and kidney disease involves multiple mechanisms affecting both thyroid hormone synthesis and renal function [5,6]. The metabolic consequences of thyroid dysfunction in CKD patients extend beyond simple hormone level alterations, with chronic renal failure significantly affecting thyroid hormone metabolism as documented in comprehensive reviews [7].

Thyroid hormones play crucial roles in renal hemodynamics, affecting glomerular filtration rate and tubular function through both direct and indirect mechanisms [8]. The interaction between thyroid dysfunction and chronic kidney disease has been demonstrated in multiple studies, with Nepalese research showing significant prevalence of thyroid dysfunction in CKD patients [9,10]. Our prevalence of 18% falls within the range reported by previous epidemiological studies, including a Nepalese study that found substantial thyroid dysfunction and dyslipidemia in CKD patients [11], confirming that hypothyroidism is indeed a significant clinical concern across South Asian populations.

The clinical significance of thyroid dysfunction in kidney disease patients has been increasingly recognized, with evidence suggesting strong associations with cardiovascular morbidity and mortality [12,13]. Our study contributes to this growing body of evidence by providing local data from a previously understudied population in northern Pakistan. The methodology employed in our study, including the use of WHO sample size calculation guidelines [14], ensures statistical validity and international comparability of our findings.

The application of established diagnostic criteria from international guidelines [15,16] allows for meaningful comparison with global studies and supports the generalizability of our results to similar populations. The lack of

significant association between hypothyroidism prevalence and patient demographics (age, gender) or CKD severity in our study is noteworthy and differs from some international reports from American populations [17]. This finding may reflect several factors including the exclusion of advanced CKD (stage 5) patients, regional genetic factors, or differences in underlying CKD etiologies compared to Western populations.

Previous research from South India has documented significant prevalence of subclinical hypothyroidism in end-stage renal disease patients, with serum albumin playing an important role [18]. The complex interactions between thyroid disorders and kidney disease manifest differently across diverse populations and healthcare settings, as documented in Indian studies examining these bidirectional relationships [19,20].

Subclinical hypothyroidism, which comprised a significant portion of thyroid dysfunction cases in our study, represents a particularly important clinical entity. This condition is often asymptomatic but has been associated with cardiovascular risk and potential CKD progression [21,22]. The clinical overlap between hypothyroidism and CKD symptoms, including fatigue, edema, and cold intolerance, may contribute to underdiagnosis in clinical practice [23]. This overlap emphasizes the importance of systematic thyroid screening in CKD patients to prevent missed diagnoses and optimize patient care.

The healthcare implications of our findings are particularly relevant in the Pakistani context, where healthcare resources may be limited and access to specialized endocrine care variable. A recent Pakistani study documented significant frequency of hypothyroidism among chronic kidney disease patients in tertiary care settings [24], supporting our findings and emphasizing the local relevance of this clinical problem. The burden of chronic kidney disease in South Asian populations, including Pakistan and India, has been substantial, with studies like the SEEK study documenting significant disease prevalence related to diabetes and hypertension [25].

Recent international studies have provided additional insights into thyroid-kidney interactions that complement our findings. A large US cohort study demonstrated the impact of thyroid status on incident kidney dysfunction and CKD progression in a nationally representative population [26]. Additionally, recent Indian research has documented the prevalence of thyroid abnormalities in CKD patients at tertiary care hospitals [27], while South Korean population-based studies have established clear associations between subclinical thyroid dysfunction and chronic kidney disease [28].

Research from northeastern Indian populations has confirmed the relationship between thyroid dysfunction and chronic kidney disease across diverse demographic groups [29]. Most encouragingly, recent evidence from Pakistan suggests that thyroid dysfunction in end-stage renal disease patients may be amenable to therapeutic intervention, highlighting the potential benefits of early detection and treatment [30]. This reversibility concept supports the clinical importance of routine thyroid screening in CKD patients and provides optimism for improved patient outcomes through targeted therapy.

The clinical implications of our study extend beyond simple prevalence statistics. The identification of an 18% prevalence of hypothyroidism in our CKD population suggests that approximately one in five patients may benefit from thyroid screening and potential intervention. Given the established associations between thyroid dysfunction and cardiovascular outcomes, mortality, and quality of life measures, systematic screening protocols may significantly impact patient care and outcomes.

LIMITATIONS

Several limitations should be acknowledged in interpreting our results. The cross-sectional study design limits our ability to establish causal relationships between thyroid dysfunction and CKD progression. The single-center setting may limit generalizability to other regions of Pakistan or different healthcare systems. The exclusion of stage 5 CKD patients may underestimate the true prevalence of thyroid dysfunction in the broader CKD population. Additionally, we did not assess potential confounding factors such as dietary iodine intake, autoimmune thyroid disease, or medication effects that might influence thyroid function. Recent studies have highlighted the complexity of thyroid-kidney interactions, with some populations showing different associations after controlling for various confounders, suggesting that regional and demographic factors may significantly influence these relationships.

CLINICAL IMPLICATIONS

Our findings support the implementation of routine thyroid function screening in CKD patients in Pakistani healthcare settings. Early detection of thyroid dysfunction may facilitate timely intervention, potentially slowing CKD progression and reducing cardiovascular complications. Healthcare providers caring for CKD patients should maintain awareness of the high prevalence of thyroid dysfunction and consider systematic screening protocols. The development of local clinical guidelines incorporating thyroid screening may improve overall patient care and outcomes in this population.

FUTURE RESEARCH DIRECTIONS

Longitudinal studies are needed to better understand the temporal relationship between thyroid dysfunction and CKD progression in Pakistani populations. Research examining the impact of thyroid hormone replacement therapy on CKD progression and cardiovascular outcomes would provide valuable clinical guidance. Multicenter studies including diverse Pakistani populations would enhance the generalizability of these findings and inform national healthcare policies. Investigation of regional factors influencing thyroid-kidney interactions, including genetic, environmental, and nutritional factors, would contribute to our understanding of these complex relationships.

CONCLUSION

The frequency of hypothyroidism among CKD patients at Ayub Teaching Hospital was 18%, indicating a significant public health burden. Routine thyroid function screening is essential for early detection and management to prevent complications such as cardiovascular disease and metabolic disturbances. Multicenter, longitudinal studies are needed to further validate these findings and inform national CKD management guidelines.

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