ORIGINAL ARTICLE

Frequency of Hypothyroidism among Chronic Kidney Disease in a Tertiary Care Hospital

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Abstract

Objective: To assess the prevalence of hypothyroidism and its association with socio-demographic factors, serum creatinine, and thyroid profile in chronic renal disease patients who visit a tertiary care facility in Karachi, Pakistan.

Methodology: At the Nephrology ward of the Liaquat National Hospital and Medical College in Karachi, this cross-sectional study was conducted from Jan 2022 to Jul 2022. All patients with chronic renal failure who were older than 18 years and of either gender were enrolled in the study. The patient's complete medical history was gathered, which included details on their age, co-morbidities, baseline renal function, and thyroid profile. The data were analyzed using SPSS version 25.

Results: The median age of included patients was 60 years with an interquartile range of 52 to 65 years. Of 127 patients with chronic kidney disease, 14.2% had hypothyroidism. Patients with hypothyroidism had marginally higher serum creatinine levels than patients without the condition. The difference in serum creatinine between patients with and without hypothyroidism was statistically insignificant (p=0.655). Significantly elevated TSH was observed in hypothyroidism patients (p=0.001), while significantly lower FT3 (p=0.001) and FT4 (p=0.001) were observed in hypothyroidism patients as compared to non-hypothyroid patients. The duration of chronic kidney disease was higher in hypothyroid patients as compared to non-hypothyroid patients (p=0.048). The proportion of diabetes (p=0.050) and cardiovascular disease (p=0.050) was significantly different among patients with and without hypothyroid.

Conclusion: Hypothyroidism is common in patients with chronic kidney disease and is significantly associated with serum creatinine, thyroid profile, duration of disease, diabetes, and cardiovascular disease. Thus, it is crucial to keep an eye on thyroid function in people with chronic kidney disease.

Keywords: *Hypothyroid, chronic kidney disease, Thyroid stimulating hormone, glomerular filtration rate.*

INTRODUCTION

A chronic inflammatory condition called chronic kidney disease raises the risk of infection, cardiovascular disease, morbidity, and mortality [1]. It is one of the main global causes of death and disability. People in developing nations are more vulnerable to chronic kidney disease, accounting for almost 387.5 million cases [2]. Moreover, according to a recent systematic review, in Nepal, the burden of chronic kidney disease was 10.6%, in India 10.2%, and in Pakistan 23.3% [2]. There are multiple risk factors for chronic kidney disease such as older age, obesity, hypertension, diabetes, and certain autoimmune illnesses, however, there are also other potential risk factors that should be considered [2, 3].

Multiple studies have highlighted the association between chronic kidney disease and thyroid dysfunction [4-7]. Changes in cardiac output, alterations in the renin-angiotensin-aldosterone system, changes in intra-renal hemodynamics, changes in the structure of the glomerulus, and adaptive changes in the kidney (decrease kidney-to-body weight ratio) are all possible causes of renal dysfunction caused by thyroid function [8]. Hypothyroidism-induced hyperlipidemia causes atherosclerotic alterations in the vascular bed and endothelial dysfunction [9].

Common thyroid anomaly in patients with chronic kidney disease who do not exhibit any clinical symptoms (subclinical) and laboratory parameters usually shows low FT3 and T3 (T3 decreases greater than FT3) [10]. Changes in different parameters found in chronic kidney diseases patients, such as haemoglobin, C-reactive protein, albumin, and beta 2 microglobulin, have an independent impact over the sick euthyroid state, interplay between multiple hemodynamic factors in the hypothyroid population leads to 40% reduction in eGFR, which is reversible with treatment [11, 12].

To the best of our knowledge, there are not many recent kinds of research in South Asia looking at how common hypothyroidism is among people with chronic renal disease and its association with socio-demographic and thyroid profile and serum creatinine. Therefore, the purpose of this study was to determine the frequency of hypothyroidism and its association with socio-demographic factors, serum creatinine, and thyroid profile in individuals with chronic renal disease. This study would help in identifying the magnitude of disease and high-risk groups for specific interventions.

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METHODOLOGY

It was a cross-sectional study conducted in the nephrology ward, at Liaquat National Hospital and Medical College, Karachi, Pakistan. Using the WHO sample size calculator, a sample size of 127 was determined based on the prevalence of hypothyroidism in chronic renal disease as 30.8% [13], a confidence level of 95%, and an absolute precision of 8%. The inclusion criteria for the study were all patients with chronic renal disease (eGFR less than 60 ml/min/1.73 m2 for more than 3 months) who were older than 18 years old and of either gender. The study excluded patients with infection, malignancy, autoimmune disease, hyperthyroidism, and those who were already receiving treatment for hypothyroidism. Consecutive non-probability sampling was used.

The Liaquat National Hospital's research board and ethics committee gave its ethical clearance before the study could be carried out. Patients gave their informed consent to be a part of the study and have their data used for research after explaining the details and the researcher assured about the confidentiality of the data. A thorough history was collected, including information on age, co-morbidities, baseline renal function, and thyroid profile. The TSH level greater than 5.5 mIU/L and the FT4 level less than 12 pmol/L were labelled as hypothyroidism. The lead investigator in a pre-proforma recorded all data. Exclusion criteria were closely adhered to prevent bias and confounding factors.

SPSS version 25 was used to analyze the data. Age, TSH, FT3, FT4, body mass index, serum creatinine, and the length of time from CKD diagnosis were summarized as a median and interquartile range because the distribution of data was non-parametric. The distribution of data was checked using Shapiro-Wilk's test. Gender, and comorbid conditions like diabetes, hypertension, and cardiovascular diseases were assessed on history with at least one year, and hypothyroidism was summarized as frequency and percentage. Effect modifiers were stratified and a chi-square test was applied. A p-value ≤ 0.05 was considered significant.

RESULTS

The median age of included patients was 60 years with the interquartile range as 52 to 65 years. Of 127 patients, most of the patients were males (59.8%). The median duration of chronic kidney disease was 4 years. The majority of the patients with chronic kidney disease have hypertension (31.5%). Other baseline information regarding study samples is displayed in Table **1**.

Of 127 patients with chronic kidney disease, 14.2% had hypothyroidism. Serum creatinine was marginally higher in patients with hypothyroidism as compared to patients without hypothyroidism, however, the difference was statistically insignificant (p=0.655). TSH was significantly higher in patients with hypothyroidism (p=0.001), whereas FT3 (p=0.001) and FT4 (p=0.001) were significantly higher in non-hypothyroid patients (**Table 2**).

Table 1: Baseline information of study sample (n=127).

Variables	
Age (years)	60 (52-65)
BMI (kg/m2)	42.22 (38.71-44.56)
Duration of chronic kidney disease (years)	4 (2-5)
Gender	
Male	76 (59.8)
Female	51 (40.2)
Comorbid	
Hypertension	40 (31.5)
Diabetes mellitus	76 (59.8)
Cardiovascular disease	11 (8.7)

Data presented as median (IQR) or n(%)

Table 2: Comparison of hypothyroidism with serum creatinine and thyroid profile.

Variables	**Hypothyroidism**		**p-value**
	Yes	**No**	
Serum creatinine	3.15 (2.60-3.40)	2.80 (2.20-4.20)	0.65
TSH mIU/L	20.15 (12.20-33)	2.70 (2-3.30)	0.001*
FT3 pmol/L	0.80 (0.50-1.30)	2.60 (2.20-3.10)	0.001*
FT4 pmol/L	0.40 (0.32-0.64)	1.30 (1.10-1.40)	0.001*

Data presented as median (IQR)
*Significant at 0.05 level of significance

Table 3: Comparison of socio-demographic and risk factors with hypothyroidism.

Variables	**Hypothyroidism**		**p-value**
	Yes (n=18)	**No (n=109)**	
Age (years)	62 (55-69)	59 (51-65)	0.148
BMI (kg/m^2)	42.47 (38.10-49.99)	42.22 (38.72-44.45)	0.062
Duration of chronic kidney disease (years)	4.5 (3-6)	4 (2-5)	0.64
Gender			
Male	10 (13.2)	66 (86.8)	0.680
Female	8 (15.7)	43 (84.3)	
Hypertension			
Yes	7 (17.5)	33 (82.5)	0.460
No	11 (12.6)	76 (87.4)	
Diabetes			
Yes	7 (9.2)	69 (90.8)	0.050
No	11 (21.6)	40 (78.4)	
Cardiovascular disease			
Yes	4 (36.4)	7 (63.6)	0.050
No	14 (12.1)	102 (87.9)	

Data presented as Median (IQR) or n (%)
*Significant at 0.05 level of significance

The duration of chronic kidney disease was higher in hypothyroid patients as compared to non-hypothyroid patients (p=0.048). The proportion of diabetes (p=0.050) and cardiovascular disease (p=0.050) was significantly different among patients with and without hypothyroidism (**Table 3**).

DISCUSSION

Subclinical hypothyroidism and thyroid autoimmunity are highly frequent in chronic kidney disease patients not needing long-term treatment of dialysis [14]. Thus,

in the current study, we have evaluated the frequency of hypothyroidism in patients with chronic kidney disease.

Numerous studies have revealed that people with chronic renal illness frequently experience thyroid issues [15-18]. In the current investigation, we found hypothyroidism in 14.2% of the patients with the chronic renal illness. While in Lo *et al.* study the prevalence of hypothyroidism in patients with the chronic renal disease was 23% [7]. According to Alshammari *et al.* 35% of those receiving hemodialysis had hypothyroidism [16]. In the Ahmad *et al.* research, 17% of hemodialysis patients had hypothyroidism. Additionally, 9% of individuals had overt hypothyroidism, and 8% had subclinical hypothyroidism [19, 20]. Amro *et al.* revealed that 5.3% of the patients had hypothyroidism [17].

In the present study, patients with hypothyroidism had higher serum creatinine as compared to patients without hypothyroidism, but the difference was statistically insignificant (3.15 mg/dL *vs.* 2.80 mg/dL, p=0.64). Whereas, in the study by Alshammari *et al.* the mean serum creatinine in individuals with and without hypothyroidism was similar (383.60 vs. 385.40) [16]. In another study by Saha *et al.* individuals with drug-naive primary hypothyroidism had higher serum creatinine than the control group (1.18 ± 0.13 mg/dL vs. 0.79 ± 0.09 mg/dl, p=0.001) [21]. In another hospital-based study by Arora *et al.* individuals with hypothyroidism were shown to have substantially higher blood creatinine levels than euthyroid controls (p=0.001) [22]. We also found that TSH was elevated in hypothyroid patients as compared to patients without hypothyroidism (p=0.001). Furthermore, FT3 (p=0.001) and FT4 (p=0.001) were significantly higher in hypothyroid patients than in normal patients. Vanani *et al.* in their research found most frequent thyroid hormone derangement was high TSH and low fT3 in chronic kidney disease patients as compared to controls [23]. Alshammari *et al.* revealed that TSH and T4 were higher in patients with hypothyroidism, whereas lower in patients without hypothyroidism [16]. Saha *et al.* found that TSH level was higher and FT4 was lower in patients with hypothyroidism as compared to controls.21 Hence, patients with chronic kidney disease have altered function of kidney and thyroid hormones. Therefore, early monitoring of thyroid function should be done, to benefit chronic kidney disease patients.

We found that patients with hypothyroidism had a long duration of chronic kidney disease as compared to non-hypothyroid patients (p=0.048). However, we observed a significantly lower proportion of diabetes (p=0.05) and cardiovascular disease (p=0.05) in chronic kidney disease patients having hypothyroidism [24]. Bajaj *et al.* revealed that diabetes can increase the risk of developing hypothyroidism as it affects how well your body uses insulin to control blood sugar levels, which may lead to an imbalance in hormone production by the thyroid gland resulting in symptoms such as fatigue, weight gain and depression [25]. Another study by Inoue *et al.* showed cardiovascular disease mediated 14.3% and 5.9% of the associations between subclinical hypothyroidism and high-normal TSH respectively, with CVD mediation being most pronounced in women (7.5%-13.7%) or participants aged 60 years old or older (6%-14%) [26].

In our study, we were unable to assess the causality because it was a cross-sectional study. In the future, a prospective study with a larger sample size should be done, to see the effect of thyroid dysfunction on chronic kidney disease or the relationship of frequency of hypothyroidism with the stage of CKD.

CONCLUSION

The prevalence of hypothyroidism was high in patients with chronic kidney disease. Thus, it is necessary to monitor thyroid function in chronic kidney disease patients.

ETHICS APPROVAL

The Liaquat National Hospital's research board and ethics committee gave its ethical clearance before the study could be carried out (Ref# 0741-2022 LNH-ERC). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all the eligible participants.

AVAILABILITY OF DATA

Data is available from the corresponding author on a reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

All authors contributed equally.

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