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ORIGINAL ARTICLE

Thyroid dysfunction in patients with chronic kidney disease.

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ABSTRACT… Objective: To determine the frequency of thyroid dysfunction among patients with chronic kidney disease (CKD). **Study Design:** Cross-sectional study. **Setting:** Department of Medicine, Ayub Teaching Hospital's. **Period:** September 2019 to August 2020. **Methods:** The study included adult patients with CKD who were at least 18 years old, regardless of gender. Patients with acute kidney injury, pregnant and lactating females, patients with history of goiter, thyroid surgery or radioactive iodine treatment, familial diseases of thyroid disorders, history of medication for thyroid disorders, and known cases of thyroid disorders were not included. Likewise, patients who were on concurrent medications which could affect thyroid function like amiodarone, lithium, iodine, glucocorticoids and interferon were also excluded. **Results:** A total of 165 patients of CKD were enrolled. The mean age of the patients was 38 ± 14 years, there were 71 (43%) males and 94 (57%) females. The mean TSH, T3 and free T4 were 3.73257 ± 16.52632 mIU/L, 1.5869 ± 0.76796nmol/L, and 1.4480 ± 0.57540 ng/L respectively. Thirty-nine (23.6%) patients had thyroid dysfunction while 126 (76.4%) were euthyroid. Regarding thyroid status of the patients, twenty-two (13.3%) patients of CKD had subclinical hypothyroidism, eight (4.8%) had hypothyroidism, six (3.6%) had subclinical hyperthyroidism, three (1.8%) had hyperthyroidism 126 (76.4%) were euthyroid. **Conclusion:** Thyroid dysfunction is common among patients with CKD. Subclinical hypothyroidism is the most prevalent anomaly, followed by hypothyroidism. In view of the increased CVD and mortality in these patients, it is imperative to regularly screen CKD patients for thyroid dysfunction and to appropriately treat them.

Key words: Chronic Kidney Disease, Thyroid Dysfunction.

INTRODUCTION

Globally, chronic kidney disease (CKD) is a public health concern, which causes renal derangement and development of end-stage kidney disease. CKD is one of the conditions that increases the risk of cardiovascular disease (CVD) leading to increased morbidity and mortality and thus it has substantial impact on global health.[1] Due to the increase in the burden of diabetes mellitus (DM), hypertension, obesity, and aging population, an increase in the prevalence of CKD is also observed.[2] This rise is alarming since CKD development is linked to higher rates of morbidity and death.[1]

The metabolism and excretion of thyroid hormones are significantly influenced by the kidneys.[2] On the other hand, disorders od thyroid function have an effect on glomerular filtration, renal blood flow, electrolytes homeostasis, and electrolyte pump functions.[3] These effects further increase the risk of CVD.[2] Thyroid hormone replacement therapy can lower the clinically significant decline in the estimated glomerular filtration rate (eGFR) caused by hypothyroidism.[4] Additionally, hyperlipidemia and atherosclerosis in the peripheral and coronary vasculature are known to be caused by hypothyroidism, which raises the risk of CVD and all-cause death.[5] Euthyroid sick syndrome(ESS) has also been shown to have association with endothelial dysfunction in CKD stage 3 and 4, cardiomyopathy and an increased risk of mortality.[6] According to a study done in Oman, patients with CKD had an 11.7% prevalence of thyroid dysfunction.[7] The frequency of subclinical primary hypothyroidism increased from 5.4% (stage 1 CKD) to more than 20% (stage 3 CKD), according to another study.[8]

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According to a Pakistani study, 31.94% of CKD patients had thyroid dysfunction.[9]

This study sought to ascertain the prevalence of thyroid dysfunction in individuals with chronic kidney disease (CKD) in medical units of Ayub Teaching Hospital Abbottabad and to assess its association with age, gender, eGFR and other factors.

METHODS

This cross-sectional study was carried out at the Ayub Teaching Hospital's Department of Medicine after getting approval from the ethical committee of the institution (CPSP/REU/MED-2017-010-13397) from September 2019 to August 2020. Patients gave their informed written consent before being chosen using a nonprobability consecutive sampling procedure. Based on an estimated 14% proportion of thyroid abnormality[10], 95% confidence interval, 5% margin of error, 165 was the sample size. The openEpi program was used to calculate the sample size.[11] The study comprised adult patients with CKD who presented to the inpatient and outpatient departments of medicine and were at least 18 years of age, regardless of gender. Patients with acute kidney injury, pregnant and lactating females, patients with history of goiter, thyroid surgery or radioactive iodine treatment, familial diseases of thyroid disorders, history of medication for thyroid disorders, and known cases of thyroid abnormalities were not included. Likewise, patients who were on concurrent medications which could affect thyroid function like amiodarone, lithium, iodine, glucocorticoids, and interferon were also excluded. History, physical examination, and laboratory investigations were performed for confirmation of CKD.

Taking all antiseptic precautionary measures, venous blood sample was obtained for the estimation of blood urea, serum creatinine, total T3 (TT3), total T4 (TT4), FT4, and thyroid stimulating hormone (TSH). Patients were diagnosed to have subclinical hyperthyroidism when they had suppressed TSH with a normal T4 level. When a person had elevated TSH together with low FT4, TT4, and/or TT3 values, it was considered clinical hypothyroidism, while clinical hyperthyroidism was defined when the patients had suppressed TSH with elevated FT4, TT4 and/or TT3 levels. Patients were labeled to have subclinical hypothyroidism when they had elevated TSH with normal T4 levels. When FT3, TT3, and/or lower FT4, TT4 were present together with normal or lowered TSH, the patient was diagnosed as euthyroid sick syndrome (ESS).[6] Regardless of the underlying etiology, chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR) of less than 60 ml/min per 1.73 m^2 of body surface area sustained for more than three months, while end-stage renal disease (ESRD) was defined as an eGFR of less than 15 ml/min per 1.73 m^2.[12]

Data Analysis

The statistical software SPSS version 20.0 was utilized to enter and evaluate the data. The mean ± standard deviation is used to characterize quantitative data including age, thyroid function tests, and the length of chronic kidney disease. Frequencies and percentages were used to define categorical factors like gender, the presence or absence of thyroid disease, and the kind of thyroid dysfunction. Age, gender, and type of thyroid malfunction were used to stratify the condition, and the post-stratification Chi-square test was used at the 5% significance level.

RESULTS

A total of 165 patients of CKD were enrolled. The mean age of the patients was 38 ± 14 years, there were 71 (43%) males and 94 (57%) females. Eighteen (10.9%) patients were in the age range of 16 -30 years, forty-eight (29.1%) were of 31-45 years while 99 (60%) were in the age range of 46-60 years. Regarding duration of CKD, sixty-five (39.4%) patients had a duration of 1-5 years, sixty-five (39.4%) had 6-10 years duration while 35 (21.2%) had a duration of CKD of more than 10 years.

The mean TSH was 3.73257 ± 16.52632 mIU/L with a range of 0.003 to 176.213 mIU/L. The mean serum T3 was 1.5869 ± 0.76796nmol/L with a range of 0.05 to 4.97 nmol/L. The mean serum FT4 was 1.4480 ± 0.57540 ng/L with a range of

0.21 to 4.65 ng/L. Out of 165 patients of CKD, thirty-nine (23.6%) had thyroid dysfunction while 126 (76.4%) were euthyroid.

Regarding thyroid status of the patients, twenty-two (13.3%) patients of CKD had subclinical hypothyroidism, eight (4.8%) had hypothyroidism, six (3.6%) had subclinical hyperthyroidism, three (1.8%) had hyperthyroidism 126 (76.4%) were euthyroid. The frequency distribution of thyroid dysfunction in patients of CKD with regard to age and gender is presented in Table-I and II, respectively. The frequency distribution of thyroid dysfunction with regard to CKD duration is presented in Table-III and IV.

DISCUSSION

The results of this study demonstrated that 23.6% of patients with CKD had thyroid dysfunction with subclinical hypothyroidism being the most common abnormality. A study conducted in Bahawalpur, Pakistan demonstrated that 23 (31.94%) patients of CKD had thyroid dysfunction.[9]

Age Groups	Status of Thyroid Function of the Patients					Total
	Hypothyroidism	Subclinical Hypothyroidism	Euthyroid	Subclinical Hyperthyroidism	Hyper-thyroidism	
1(18-30 years)	0	4 (22%)	14 (78%)	0	0	18 ()10.9%
2(31-45 years)	4 (8.4%)	7 (14.5%)	37 (77.1%)	0	0	48 (29.1%)
3(46-60 years)	4 (4%)	11 (11.1%)	75 (75.75%)	6 (6.06%)	3 (3%)	99 (60%)
Total	8 (4.8%)	22 (13.3%)	126 (76.4%)	6 (3.6%)	3 (1.8%)	165 (100%)
P-Value	0.359	0.577	0.286	0.138	0.069	

Table-I. Frequency distribution of age with thyroid status

Thyroid Status	Gender of Patients		Total	P-Value
	Male	Female		
Subclinical hypothyroid	13 (18.30%)	9 (9.57%)	22 (13.3%)	0.089
Hypothyroid	4 (5.63%)	4 (4.25%)	8 (4.8%)	0.196
Euthyroid	50 (70.42%)	76 (80.85%)	126 (76.4%)	0.154
Subclinical hyperthyroid	4 (5.63%)	2 (2.12%)	6 (3.6%)	0.189
Hyperthyroid	0	3 (3.2%)	3 (1.8%)	0.163
Total	71 (43%)	94 (57%)	165 (100%)	

Table-II. Frequency distribution of gender with thyroid status

Thyroid Status	Duration of CKD			Total	P-Value
	1-5 Years	6-10 Years	>10 Years		
Subclinical hypothyroid	13 (20%)	7 (10.76%)	2 (5.71%)	22 (13.3%)	0.136
Hypothyroid	4 (6.15%)	3 (4.61%)	1 (2.85%)	8 (4.8%)	0.067
Euthyroid	48 (73.84%)	49 (75.38%)	29 (82.85%)	126 (76.4%)	0.075
Subclinical hyperthyroid	0	3 (4.61%)	3 (8.51%)	6 (3.6%)	0.123
Hyperthyroid	0	3 (4.61%)	0	3 (1.8%)	0.103
Total	65 (39.4%)	65 (39.4%)	35 (21.2%)	165 (100%)	

Table-III. Thyroid status and CKD duration frequency distribution

		Duration of CKD			Total	P-Value
		1 to 5 years	6 to 10years	More than 10 years		
Thyroid Dysfunction	Yes	17 (26.15%)	16 (24.61%)	6 (17.14%)	39 (23.6%)	0.583
	No	48 (73.84%)	49 (75.38%)	29 (82.855)	126 (76.4%)	
Total		65 (39.4%)	65 (39.4%)	35 (21.2%)	165 (100%)	

Table-IV. Stratification of duration of CKD with respect to thyroid dysfunction

Our study revealed that subclinical hypothyroidism was the most prevalent thyroid abnormality found among patients with CKD followed by overt hypothyroidism while hyperthyroidism and subclinical hyperthyroidism were the least common abnormalities found. These outcomes concur with the research by Pan et al., which also showed that subclinical hypothyroidism and hypothyroidism were most common abnormal thyroid function in CKD patients.[6] Likewise, these patients were also more likely to develop overt and subclinical hypothyroidism asper findings of a study by Kamal et al.[13]

The relation of thyroid dysfunction with the gender was also analyzed and there was no significant association detected between them. However, it was found that majority of patients who had subclinical hypothyroidism were males, whereas an equal number of male and females had overt hypothyroidism. These outcomes resemble those of research conducted by Sinjari et al., who also demonstrated that subclinical hypothyroidism was mostly seen in males.[14] Moreover they also revealed a significant a significant association between hypothyroidism and gender. Despite these findings, some studies have not demonstrated an association of thyroid abnormality in CKD patients with gender.[15,16] This indicates that hypothyroidism and subclinical hypothyroidism in these patients might be due to the underlying CKD and not just because of gender. Research indicates that when the GFR declines, the prevalence of both overt and subclinical hypothyroidism rises.[17,18]

Regarding age, our study reported that Individuals who suffer from subclinical hypothyroidism tend to be older. This finding is like the results of study by Sinjari et al who demonstrated that CKD patients who exhibited hypothyroidism and subclinical hypothyroidism were mostly of older age group.[14] A study by Rhee et al also reported similar findings.[19] However, such an association of age with thyroid abnormality in CKD patients was not demonstrated in other studies.[15,20] Regarding relation of thyroid status with the duration of CKD, no statistically significant association was observed in the current study. This finding is similar to the results of study by Gupta A et al.[21] The relationship between CKD and thyroid dysfunction has been explained by a number of processes, including reduced hormone sensitivity, autoimmune thyroiditis, and altered metabolism of iodine.[22]

In summary, the current study revealed a higher frequency of overt and subclinical hypothyroidism in CKD patients. These findings are of great clinical significance. This suggests that in order to lower the risk of CVD, patients with CKD should undergo routine thyroid dysfunction screening and treatment.

LIMITATIONS

This study had few limitations. Firstly, thyroid autoimmunity of the study population was not assessed. Secondly, the iodine status of the participants was not evaluated. It is important to note that iodine deficiency or excess in this part of the world may lead to thyroid disorders.

CONCLUSION

Thyroid dysfunction is common among patients with CKD. Subclinical hypothyroidism is the most prevalent anomaly, followed by hypothyroidism. Subclinical hypothyroidism is the most prevalent anomaly, followed by hypothyroidism. In view of the increased CVD and mortality in these patients, it is imperative to regularly screen CKD patients for thyroid dysfunction and to appropriately treat them. This early identification and treatment will help in better management of these patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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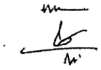
3	Muhammad Salman Aamir	Introduction Writing.	
4	Azmat Ali	Discussion writing.	
5	Jalal Ahmad	Data collection & Tabulation.	
6	Arif Mumtaz	Critical review & methodology.	
7	Shafiullah Khan	Statistical analysis.