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Original Research Article

Thyroid dysfunction in patients of chronic kidney disease

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ABSTRACT

Background: Thyroid hormones play a very important role in regulating metabolism, development, protein synthesis, and influencing other hormone functions. CKD has been known to affect the pituitary-thyroid axis and the peripheral metabolism of thyroid hormones. We aimed to study the thyroid dysfunction in patients of chronic kidney disease for the prevalence of subclinical hypothyroidism.
Methods: This cross-sectional study was conducted at Chhatrapati Shivaji Subharti Hospital and Medical College, Meerut, Uttar Pradesh, India, over a 2 year period. The study group comprised 100 patients with Chronic kidney disease. Free thyroxine (fT3, fT4) and thyroid-stimulating hormone (TSH) were measured. Patients with family history of thyroid disorder or past history of any medication for thyroid disease or history of any surgery or any radiological intervention to thyroid gland were excluded from the study.
Results: Of 100 CKD patients, 25 were found to have subclinical hypothyroidism (SCH) and 75 were euthyroid. The mean age in patients with SCH was 47.72±10.09 and in euthyroid patients was 46.11±14.332. 12 males (48%) and 13 females (52%) patients were found to have subclinical hypothyroidism and 49 male (65%), 26 female (35%) patients were euthyroid. Prevalence of SCH was 25% with a mean TSH level of 8.68± 1.84.
Conclusions: We observed a high prevalence of SCH in our CKD patients. SCH is an additional risk factor in CKD patients and the present study finds thyroid dysfunction being SCH to be very common in CKD patients and reveals significant association between CKD progression and thyroid dysfunction.

Keywords: Chronic kidney disease, Subclinical hypothyroidism, Thyroid dysfunction, TSH

INTRODUCTION

CKD is a long-term form of kidney disease; thus, it is differentiated from acute kidney disease (acute kidney injury) in that the reduction in kidney function must be present for over 3 months. CKD is an internationally recognized public health problem affecting 5-10% of the world population.[1]

According to the 2010 Global Burden of Disease study, chronic kidney disease was ranked 27th in the list of causes of total number of deaths worldwide in 1990, but rose to 18th in 2010. This degree of movement up the list was second only to that for HIV and AIDs.[2]

Over 2 million people worldwide currently receive treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need treatment to live.[3]

The prevalence of these stages of CKD in the US population is as follows: 1.8% for stage 1, 3.2% for stage 2, 7.7% for stage 3 and 0.35 % for stages 4 and 5. Patients with stage 3 or 4 disease progress to end stage renal disease or stage 5 at a rate of 1.5% per year. Stage 1

or 2 CKD patients progress to more advanced stages at approximately 0.5% per year.[4]

Thyroid hormones play a very important role regulating metabolism, development, protein synthesis, and influencing other hormone functions. The two main hormones produced by the thyroid are triiodothyronine (T3) and thyroxine (T4). These hormones can also have significant impact on kidney disease so it is important to consider the physiological association of thyroid dysfunction in relation to chronic kidney disease (CKD). CKD has been known to affect the pituitary-thyroid axis and the peripheral metabolism of thyroid hormones. Low T3 levels are the most common laboratory finding followed by subclinical hypothyroidism in CKD patients. Hyperthyroidism is usually not associated with CKD but has been known to accelerate it. One of the most important links between thyroid disorders and CKD is uremia. Patients who are appropriately treated for thyroid disease have a less chance of developing renal dysfunction.

One of the most important conditions that has been less studied is thyroid hormone levels and how they affect the progression of CKD. Disorders in renal function have been seen to coexist with specific levels of thyroid hormone. This study is done to simplify the importance of interactions between thyroid function and kidney disease.[5]

The objective of this study was to study the thyroid dysfunction in patients of chronic kidney disease for the prevalence of subclinical hypothyroidism.

METHODS

We carried out a prospective cross-sectional study over 2 years-time period on patients attending outpatient department of General Medicine and admitted in medicine ward of Chhatrapati Shivaji Subharti Hospital and Medical College, Meerut, Uttar Pradesh, India.

A total number of 100 patients were included in this study after fulfilling the inclusion criteria. An informed consent was taken from all the cases before their inclusion into the study.

Inclusion criteria

All the patients of Chronic Kidney Disease above 18 years of age. The CKD was diagnosed on the basis of history, examination and on NKF (National Kidney Foundation) criteria.

- Kidney disease of 3 or more than 3 months duration.
- Structural abnormality, functional abnormality (GFR), urea, creatinine, urine examination and imaging test.

Exclusion criteria

- Family history of thyroid disorder
- Past history of any medication for thyroid disease
- History of any surgery or any radiological intervention to thyroid gland.

The study did not focus on the cause of CKD but its presentation. The study consists of a survey estimation of thyroid hormones in patients of CKD. The data was analysed and observations were discussed.

Patient's work up

- History regarding diabetes mellitus, hypertension and any associated chronic illness
- General physical examination and systemic examination
- Complete blood count
- Urine routine and microscopic examination
- Renal function test
- S. electrolytes (Na+, K+)
- Thyroid profile (fasting) (fT3, fT4, TSH)
- Fasting lipid profile
- Liver function test
- USG abdomen
- 24 Hour urine protein.

Statistical analysis

Descriptive analysis of the collected data was done and association of various parameters with the presence or absence of Subclinical or overt Hypothyroidism was studied using Chi Square test and correlation with taking 5% as level of significance (p value = <0.001). The statistical analysis was performed using SPSS software version 20.

RESULTS

Study group comprised of 100 cases of chronic kidney disease. Various demographic data, clinical characteristics, thyroid profile were collected and subjected to statistical analysis.

The patients were further classified into two groups:

- Patients with SCH - n = 25 (25%)
- Patients with normal TSH - n = 75 (75%).

Out of 100 patients, maximum was in the age group of 40-50 years (Figure 1).

There were 61 males and 39 females patients. There was no significant difference among patients with TSH levels with respect to sex (Figure 2).

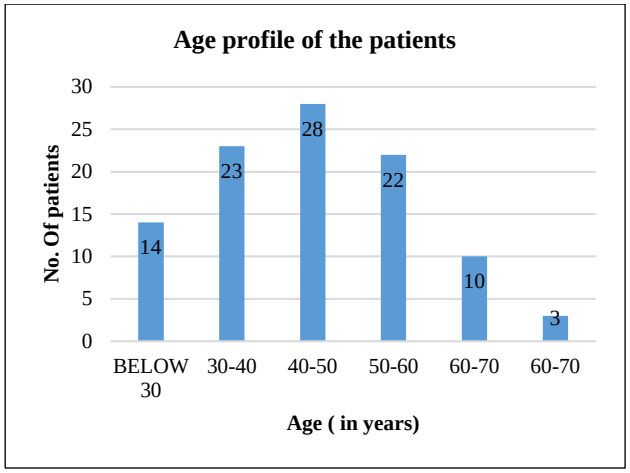

Figure 1: Distribution of patients according to age.

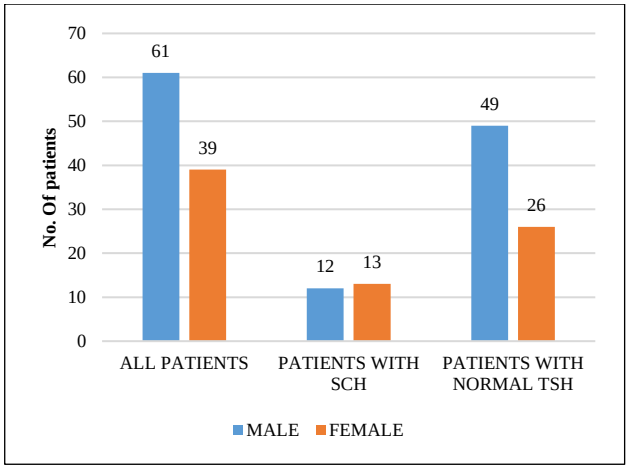

Figure 2: Gender distribution of patients.

Table 1: Distribution of patients based on serum creatinine with correlation with TSH levels.

		TSH					Total
		Less than 4	4-6	6-8	8-10	Above 10	
Serum creatinine (mg%)	Less than 5	0	0	1	0	0	1
	5-7	10	0	1	0	0	11
	7-9	18	3	1	1	1	24
	9-11	16	1	1	4	1	23
	11-13	10	1	0	3	3	17
	13-15	9	1	2	2	0	14
	15-17	4	0	0	0	0	4
	More than 17	5	0	0	1	0	6

Table 2: Distribution of patients based on serum albumin and TSH levels.

		TSH					Total
		Less than 4	4-6	6-8	8-10	Above 10	
Serum albumin (gm%)	1	6	2	1	4	4	17
	2	46	2	5	7	1	61
	3	20	2	0	0	0	22

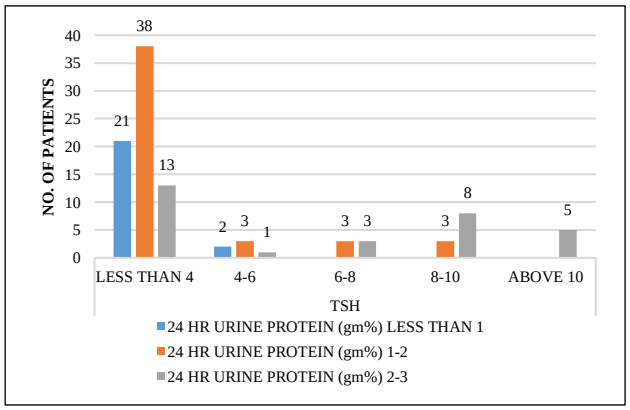

Figure 3: Distribution of patients based on 24 hour urine protein levels.

The correlation between serum creatinine levels and serum TSH levels was not statistically significant (p value ≤ 0.147) (Table 1).

The correlation between serum albumin levels and serum TSH levels was found to be statistically significant (p value ≤ 0.001) (Table 2).

The correlation between 24 hours urine protein levels and serum TSH levels was found to be highly statistically significant (p value ≤ 0.0001) (Figure 3).

DISCUSSION

In this study, 100 patients of Chronic Kidney Disease were divided into two groups i.e. patients with SCH

group n= 25 (25%) and patients with normal TSH n= 75 (75%).

The present study showed that the prevalence of SCH was highest in age group of 40-50 years. A similar study was conducted by Shantha et al, where they found the prevalence of SCH was 24.8%.[6]

The present study showed that the prevalence of SCH was 25%, which was more in females (52%) as compared to males (48%). This is in contrast to the study of Shantha et al, which showed prevalence of disease was higher in males (73.5%) as compared to females (26.5%) out of 137 ESRD patients.[6]

This study has shown a decreased level of serum albumin to be a risk factor for SCH in ESRD patients. Our patients with SCH had significantly lower serum albumin levels compared to patients with normal TSH. Contrary to our observation, Kang et al, reported that in their study cohort comprising 51 ESRD patients on continuous ambulatory peritoneal dialysis, patients with SCH had significantly higher serum albumin levels compared to patients with normal serum TSH levels.[7] The reason for this difference is not clear. However, the important differences between our study and their study are that they included patients on continuous ambulatory peritoneal dialysis while our study involved hemodialysis patients; further, their study cohort was relatively small compared to ours. Details about urinary albumin loss in their study cohort are not known. These differences render it difficult to arrive at a conclusion.

Gilles et al, made the interesting observation that patients with proteinuria had higher TSH levels, which can be explained by the possible loss of thyroid hormones in the urine.[8] Evidence has not favored the association between hypoalbuminemia and other endocrine abnormalities in CKD.[9] However, hypoalbuminemia in patients with CKD is an independent risk factor for cardiovascular mortality.[10] There have been controversies as to whether SCH in ESRD warrants thyroxine supplementation. Depressed thyroid function can be considered as an adaptation to minimize protein catabolism in ESRD patients. Hence, attempts to correct this might be detrimental to the patient. Proof to this statement comes from the observation that ESRD patients who received thyroxine replacement were observed to have a negative nitrogen balance and an increased leucine flux.[11] However, the cardiovascular risk among patients with a combination of ESRD, SCH, and hypoalbuminemia is yet to be determined.

Study found subclinical hypothyroidism (25%) to be very common in CKD patients as also depicted in study done by Khatiwada S et al, where prevalence of subclinical hypothyroidism was (27.2%).[12] It has been estimated that the prevalence of subclinical hypothyroidism ranges between 4 and 10% in the general population and it has been well observed that hypothyroidism (overt or clinical) increases the risk for CVD.

Although numerous hypothesis for contributing factors, like altered iodine metabolism, decreased peripheral sensitivity to hormones, and autoimmune thyroiditis, the exact underlying mechanisms linking advanced CKD and primary thyroid dysfunction remain unclear.[13]

In summary, our study showed a higher prevalence of Subclinical Hypothyroidism (SCH) in patients of CKD. Our findings of present study have a great clinical significance. It suggests that the importance of regular screening and treatment of thyroid dysfunction and dyslipidemia in patients with CKD, which may further help to prevent CVD risk.

CONCLUSION

This study was conducted among the patients with CKD to show that the SCH is an additional risk factor in CKD patients. Based on the results of the present study, SCH should be sought in patients with CKD by Thyroid profile (fasting) which is a simply employed technique. Further studies are needed with more patients to understand the possible link of SCH to CKD. The present study finds thyroid dysfunction being SCH to be very common in CKD patients and reveals significant association between CKD progression and thyroid dysfunction. Subclinical hypothyroidism is more common in patients with CKD. As subclinical hypothyroidism has been associated with increased cardiovascular risk in CKD patients, adult patients with CKD should be routinely screened for subclinical hypothyroidism and further studies concentrating on improving clinical and biochemical criteria to diagnose thyroid dysfunction in CKD patients are needed.

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