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Original Research Article

Study of Thyroid Profile in Patients of Chronic Kidney Disease

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Abstract:

Background: Chronic kidney disease (CKD) encloses a range of different pathophysiological procedures. Kidney is involved in the metabolism and eradication of the thyroid hormone, consequently the decline in the kidney function is assisted by changes in the synthesis, secretion, metabolism and elimination of the thyroid hormones leading to thyroid dysfunction.

Material and Methods: In this prospective cross-sectional study all the patients admitted or attended OPD in Department of medicine SRMSIMS Bareilly between March 2021 to August 2022 and diagnosed as chronic kidney disease were included. Patients with known case of thyroid disease and those CKD patients were on dialysis excluded. Serum creatinine, Triidothyronine (T3), Thyroxine (T4) and Thyroid stimulating hormone (TSH) were measured with and aim to evaluate Thyroid profile in patients of CKD.

Results: A total of 100 patients with CKD were included. The mean age of study was 54.26±16.92 years. 54% patients were male, and 46% patients were female. 28% of patients were diabetic and 54% of patients were hypertensive. 54% of patients were smoker and 36% of patients were alcoholic Total 30% patients had low, 57% patients had normal, and 13% patients had high T3 levels. 21% patients had low while 79% patients had normal T4 levels. 1% patients had <0.25, 82% patients had 0.25-5.50, and 17% patients had >5.50 TSH levels.

Conclusion: In this study it was observed that the patients with severe renal disease had a significantly lower T3 levels (P<0.0001). Although, we could not found significant association between T4, TSH and severity of renal disease but small sample size and single centre study was our limitation.

Keywords: Chronic kidney disease (CKD), Thyroid profile, Tri-iodothyronine (T3), Thyroid stimulating hormone (TSH).

Introduction

Chronic kidney disease (CKD) encloses a range of different pathophysiological procedures connected with the abnormal kidney function and a continuous decrease in glomerular filtration rate (GFR <60 mL/min per 1.73 m2) for 3 or more months, irrespective of the etiology or by signs of kidney damage like proteinuria involving hematuria, abnormal imaging, micro-albuminuria, or biopsy findings. [1]

Kidney is involved in the metabolism and eradication of the thyroid hormone, consequently the decline in the kidney function is assisted by changes in the synthesis, secretion, metabolism and elimination of the thyroid hormones leading to thyroid dysfunction. However, thyroid hormone is required for the growth and development of the kidney and also for the maintenance of water and electrolyte homeostasis. [2]

The overall frequency of the chronic kidney disease in India is about 17.2% and the frequency of the chronic kidney disease stages 1, 2, 3, 4 and 5 is about 7%, 4.3%, 4.3%, 0.8% and 0.8%, accordingly. [3]

The kidney plays a chief part in the metabolism, degradation, and elimination of thyroid hormones. [4-6] Consequently, long-standing and a continuous decline of the renal structure and function like in chronic kidney disease (CKD) can alter the synthesis, secretion, metabolism, and degradation of the thyroid hormones which then depicts with the varying clinical syndromes of the thyroid dysfunction. [7,8]

Multiple procedures can account for these syndromes: alteration of peripheral hormone metabolism, possible reduction in tissue thyroid content, lowering circulating thyroid hormone concentration, disturbed binding to carrier proteins, and a raised iodine stores in thyroid glands. [9] Tri-iodothyronine (T3), the most metabolically active thyroid hormone, for example, can decrease in CKD patients even with a normal level of TSH. This is referred as 'Low T3 Syndrome. [10]

Thyroid dysfunction may depict in one of the following form such as: thyroid hormone deficiency or in excess (hypothyroidism or hyperthyroidism); thyroid enlargement (diffuse or nodular); asymptomatic or symptomatic (the subclinical state or overt). [11]

The glomerular filtration rate (GFR) decreases in hypothyroidism by reduced cardiac output, intrarenal vasoconstriction, raised peripheral vascular resistance, decreased renal response to vasodilators, and a decreased expression of renal vasodilators. [12,13] Furthermore, pathologic alteration in the glomerular structure in hypothyroidism, like thickening of the glomerular basement membrane and the mesangial matrix expansion, might also lead to a decline in GFR. [14] The influence of the hyperthyroidism on the kidney are generally opposite to the effects of hypothyroidism. [15] Amid the pre-renal factors, thyroid hormones raise the cardiac output by a positive chronotropic and inotropic effects also a decrease in systemic vascular resistance. It raises the endothelial production of nitric oxide (NO) and leads to vasodilation. [8]

CKD patients might have different symptoms and signs indicative of hypothyroidism such as cold intolerance, sallow complexion, alopecia, dry coarse skin, edema, hyporeflexia, reduced basal metabolic rate, lethargy, fatigue and asthenia. Therefore, it is difficult to eliminate the thyroid function abnormality in patients having chronic kidney disease solely on clinical background. Different studies conducted have noted the abnormalities such as hypothyroidism, hyperthyroidism and euthyroid states. The connection between the severity of renal failure and thyroid dysfunction is unclear. The evaluated difficulty of hypothyroidism is between 0-9 percent in the end stage renal disease. In ESRD a raised frequency of thyroid swelling (goitre) has also been reported. In regard to variability of thyroid function test in patients having CKD in earlier studies, a prospective clinical and a biochemical study on the thyroid function in CKD patients in the Department of medicine was done.

Material and Methods

In this prospective cross sectional study all the patients admitted or attended OPD in Department of medicine SRMSIMS Bareilly between March 2021 to August 2022 and diagnosed as chronic kidney disease were included.

Exclusion Criteria

1. Patients on peritoneal and hemodialysis
2. Pregnancy
3. Known cases of thyroid dysfunction
4. Drugs affecting thyroid profile like amiodarone, beta-blocker, phenytoin, dopamine, iodine containing drugs, estrogen pills and steroids
5. Acute illness
6. Burns

Definition of Chronic Kidney Disease

Chronic kidney disease is defined as abnormalities in kidney function, present for more than three months with implications for health.[16]

Chronic kidney disease stages were defined according to Kidney Disease Improving Global Outcomes (KDIGO) and classify using estimated GFR.

Stage	GFR ml/min/1.73m^2
0	>90
1	<90
2	60-89
3	30-59
4	15-29
5	<15

eGFR calculated using CKD – EPI Equation (Chronic Kidney Disease Epidemiology Collaboration).

Definition and classification of categories of thyroid dysfunction: Thyroid dysfunction was considered if a patient's thyroid hormones fall outside the reference range. The categories of thyroid dysfunction were classified based on the reference intervals for the hormones and pattern of derangement in the thyroid hormones profile

The abnormal thyroid function tests result was classified into any of the following:

Subclinical hypothyroidism: TSH elevation between >4.7 mIU/L in patients with normalserum TT3 or FT3 and TT4 or FT4.

Primary subclinical hypothyroidism: TSH >4.7 mIU/L and suppressed serum TT3 or FT3 and TT4 orFT4T4.

Primary overt hypothyroidism: TSH (>20 µIU/dl) with low serum FT4 and low FT3 Subclinical hyperthyroidism: suppressed TSH (<0.27) mIU/L and normal TT3 or FT3 andTT4or FT4 serum concentration.

Overt hyperthyroidism: Suppressed TSH (<0.27) mIU/L and elevated serum TT3 or FT3 and TT4 or FT4 concentration.

Non-thyroidal illness or low T3 syndrome: Low TT3 or FT3 in the presence of normal TSH, TT4 and FT4 levels.

Euthyroid hyperthyroxinemic: Isolated elevation of FT4 or TT4 in the presence of TSH, FT3 and TT3 within reference limits.[11]

Components of thyroid profile in this study

- Serum triiodothyronine(T3)- 0.60-1.58 ng/ml
- Serum thyroxine(T4)-4.82-15.65 µg/dl.
- Serum thyroid stimulating hormone (TSH)-0.25-5.5µI U/ml.

Results

The present study was aimed to evaluate thyroid function abnormalities in chronic kidney disease. A total of 100 patients with CKD were included in the study at Department of General Medicine.

In this study, the mean age of study was 54.26±16.92 years. 54% patients were male, and 46% patients were female. 28% of patients were diabetic and 54% of patients were hypertensive. 54% of patients were smoker and 36% of patients were alcoholic The mean of serum T3 was 2.32±7.93. Total 30% patients had low, 57% patients had normal, and 13% patients had high T3 levels.

Table 1: Serum T3

Serum T3 (ng/dl)	Frequency	Percentage
Low	30	30%
Normal	57	57%
High	13	13%
Mean	2.32±7.93	

In this study, the mean of serum T4 was 6.64±2.74. 21% patients had low while 79% patients had normal T4 levels.

Table 2: Serum T4

Serum T4 (ug/dl)	Frequency	Percentage
Low	21	21%
Normal	79	79%
Mean	6.64±2.74	

In this study, the mean of TSH was 5.27±6.67. 1% patients had <0.25, 82% patients had 0.25-5.50, and 17% patients had >5.50 TSH levels.

Table 3: TSH

TSH	Frequency	Percentage
<0.25	1	1%
0.25-5.50	82	82%
>5.50	17	17%
Mean	5.27±6.67	

Table 4: eGFR

eGFR Grade	Frequency (n=100)	Percentage (%)
Grade I	-	-
Grade II	11	11%
Grade IIIa	15	15%
Grade IIIb	18	18%
Grade IV	26	26%
Grade V	30	30%
eGFR Mean	20.36±14.38	

Table 5: eGFR with T3

eGFR	T3 Group			P Value
	<0.60	**0.60-1.58**	**>1.58**	
Grade I	-	-	-	<0.0001
Grade II	0	3	8	
Grade IIIa	1	9	5	
Grade IIIb	3	15	0	
Grade IV	17	9	0	
Grade V	9	21	0	

Our study observed that the patients with severe renal disease had a significantly lower T3 levels (P<0.0001).

Table 6: eGFR with T4

eGFR	T4 Group		P Value
	<4.82	4.82-15.65	
Grade I	0	0	0.509
Grade II	6	5	
Grade IIIa	5	10	
Grade IIIb	11	7	
Grade IV	14	12	
Grade V	13	17	

Our study found no significant association between T4 and severity of renal disease.

Table 7: eGFR with TSH

eGFR	TSH Group			P Value
	<0.25	0.25-5.50	>5.50	
Grade I	-	-	-	0.755
Grade II	3	3	5	
Grade IIIa	5	3	7	
Grade IIIb	6	4	8	
Grade IV	6	8	12	
Grade V	9	13	8	

Our study found no significant association between TSH and severity of renal disease (P=0.755).

Discussion

In our study, the mean age of study was 54.26±16.92 years. In a study by Khatiwada et al,[17] the mean age of study population was 44.1 ± 16.4 years. In a study by Sadara and Visawa,[18] the mean age of the patients was 34.30 ± 7.37 years. In a study by BR et al, [19] the mean age was 53.93±9.91 years.

In our study, 54% patients were male, and 46% patients were female. In a study by Khatiwada et al,[17]the study population comprised 360 CKD patients with 53.8% males and 46.1% females. In a study by Enia et al, [20] 12 patients were male and 2 patients were female in group I, in group II 7 patients each was male and female while group III 7 patients each was male and female. In a study by Rafeeq et al, [21] 80% were male and 20% female.

In our study, 54% of patients were hypertensive, 28% of patients had diabetic, 54% of patients had smoker, 36% of patients had alcoholic. In a study by Enia et al, [20] in I tertile <5.9 pg/ml, 64% patients were smoker, 14% patients were diabetics and 71% hypertensive, in II tertile 6.0–10.9 pg/ml, 54% were smoker, 15% were diabetics and 61% hypertensive and III tertile >10.9 pg/ml, 50% patients were smoker, 21% patients were diabetics and 71% hypertensive..

Thyroid Hormone

In our study, the mean of T3 was 2.32±7.93.30% patients had low, 57% patients normal, and >30% patients had low T3 levels. The mean of serum T4 was 6.64±2.74.21% of patients had low while 79% patients had normal T4 levels. The meaning of TSH was 5.27±6.67.1% of patients had low, 82% patients had normal, and 17% patients had high TSH levels.

In a study by Manickam, [22] the prevalence of low T4 among the males was 18.9% and among the females was 30.8%. The difference among the sexes was not statistically significant i.e., P>0.05. The prevalence of TSH in clinical hypothyroidism range among males was 2.7%. And among the females was 7.7%. The prevalence of the sexes was not statistically significant (P>0.05).

In a study by Rafeeq et al, [21] T3 level varied from 0.2 to 2 ng/ml. The mean value of T3 was 0.67ng/ml. Excluding the patients with primary hypothyroidism, the mean value is 0.71 ng/ml. This value was in low normal limit. Serum T4 level in the study varies from 0.5 to 9.5 µg/dl. Mean value of serum T4 among 50 patients 5.62 µg/dl Excluding hypothyroid patients, the mean value is 5.99 µg/dl. This value is within the low normal level of T4. Values of TSH vary from 0.6 to 27 µIU/ml with mean value in 6.53 µIU/ml. Excluding hypothyroidism mean value is 4.75 µIU/ml.

In a study by Okaka et al, [23] T3 levels had a negative correlation with age. This agrees with the findings in previous studies, for T3 levels. It is thought that age-dependent decline in T3 levels is due to the decreased deiodination of T4 to form T3 that occurs with advancing age. [24] In addition, the prevalence of anti-thyroperoxidase and anti-thyroglobulin antibodies increases with age,

especially in women above 60 years of age and this may contribute to the decrease in T3 levels with advancing age. [25]

A study by Chonchol et al, [26] showed that 9.5% of patients with CKD had subclinical hypothyroidism and 7% of patients with mild CKD had low thyroid function, compared to 18% of those with moderate CKD. In our study the patients in CRF stage 4 and 5 had subclinical hypothyroidism and hypothyroidism (22% and 15%) which is in line with this study. [26] Recently, [27] have also reported higher prevalence of up to 5% of frank hypothyroidism in patients with CKD, in comparison with hospitalized patients with normal renal function (0.6%). In an Indian study by, [28] out of 127 patients with CRF studied, 93 patients (73%) showed significant ($p<0.05$) reduction in their T3, T4, FT3 levels in serum. Similarly in our study the same results were observed there was a significant change in the thyroid hormones levels ($p<0.001$).

In a study by Kumar et al, [29] There is significant reduction of serum T3,T4 mean in comparison of controls ,this finding was similar to most of the results of investigators who have studied thyroid hormones level in clinically euthyroid patients with varying grades of chronic renal failure. [30,31]

Conclusion

The present study was aimed to evaluate thyroid function abnormalities in chronic kidney disease. A total of 100 patients with CKD were included .Total 30% patients had low, 57% patients had normal, and 13% patients had high T3 levels. 21% patients had low while 79% patients had normal T4 levels. 1% patients had <0.25, 82% patients had 0.25-5.50, and 17% patients had >5.50 TSH levels. It was observed that the patients with severe renal disease had a significantly lower T3 levels ($P<0.0001$). Although, we could not found significant association between T4, TSH and severity of renal disease but small sample size and single centre study was our limitation.

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