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THYROID FUNCTION ABNORMALITIES IN PATIENTS WITH CHRONIC KIDNEY DISEASE

General Medicine

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ABSTRACT

Introduction: Chronic Kidney Disease is a worldwide health problem with an increasing incidence and prevalence. Abnormalities in the structure and function of the thyroid gland and in the metabolism and plasma concentration of thyroid hormones are common in patients with CKD. Since kidney competes with iodine clearance, thyroid hormonal system is affected. So, it is important to evaluate thyroid function in CKD patients. **Aim:** To study thyroid function abnormalities in patients with chronic kidney disease. To correlate the thyroid function abnormalities with severity of renal failure. To differentiate primary hypothyroidism from thyroid dysfunction due to chronic kidney disease. **Materials and methods:** This is an observational, cross sectional study done at Narayana Medical College and hospital, Nellore, from July 2021- November 2022 on 50 patients with CKD on conservative management fulfilling the criteria. A detailed history, a thorough clinical and general examination, blood investigations were done. Data collected and statistically analyzed. **Results:** Out of 50 patients with CKD, 29(58%) had low T3 syndrome, 12(24%) had low T4 syndrome and 4 had primary hypothyroidism. Excluding Primary Hypothyroidism, analysis of serum T3, T4 and TSH in the study subjects shows high significance. Distribution of Thyroid dysfunction among various creatinine clearance levels showed that as glomerular filtration rate declines, number of patients with low T3 syndrome increased. In patients with low T3 syndrome, the mean values of TSH in various stages of renal disease are within normal range, values of TSH did not show any linear correlation with GFR. Number of patients with low T4 syndrome did not correlate with severity of renal disease. **Conclusion:** Thyroid dysfunction occurred in 66% of the patients with CKD, it does not indicate a state of hypothyroidism, but a reflection of the state of chronic illness/malnutrition. The low T3 state of CKD can be viewed as being protective, promoting conservation of protein. The number of patients with low T3 syndrome progressively increases with the severity of renal failure.

KEYWORDS

Thyroid dysfunction, chronic kidney disease, low T3 syndrome

INTRODUCTION:

Chronic kidney disease is a clinical syndrome which occurs due to irreversible loss of renal function leading to metabolic, endocrine, excretory and synthetic function resulting in accumulation of non-protein nitrogenous substances which leads to metabolic derangements and ends up with distinct clinical manifestations. In spite of diverse etiologies, CKD is the final common pathway of irreversible loss of nephrons finally resulting in alteration of "milieu interior" affecting every system in the body including thyroid hormonal system.

The functions of thyroid and kidney are interrelated. The thyroid hormones are essential for growth and development of the kidney and for maintaining electrolyte and water homeostasis. On the other hand, kidney has its vital role in metabolism and elimination of thyroid hormones. In CKD patients reduction of renal function leads to change in the synthesis, secretion, metabolism and elimination of thyroid hormone.

The kidney helps in the clearance of iodine mainly by glomerular filtration. So excretion of iodine is reduced in advanced renal failure. Impaired renal clearance of iodine leads to elevated serum levels of inorganic iodide that potentially blocks thyroid hormone production resulting in "Wolff Chaikoff" effect.

CKD is associated with thyroid function abnormalities leading to low levels of serum total and free T3 concentration and normal reverse T3 and free T4 levels. The TSH levels are almost normal in most patients and found to be in euthyroid state. CKD patients may have various symptoms and signs suggestive of hypothyroidism like cold intolerance, dry coarse skin, sallow complexion, lethargy, fatigue, edema, reduced basal metabolic rate, alopecia, hyporeflexia and asthenia. So it is difficult to exclude thyroid function abnormality in patients with CKD merely on clinical background.

Various studies have been conducted to study thyroid function abnormalities in CKD patients. All abnormalities like hypothyroidism, hyperthyroidism and euthyroid state have been reported in the studies done previously.

The relation between severity of renal failure and thyroid dysfunction is not clear. The estimated problem of hypothyroidism is between 0-9 percent in End Stage Renal Disease. In view of variability of thyroid profile in CKD patients in previous studies, a prospective biochemical and clinical study on thyroid function has been undertaken in the department of medicine, Narayana Medical college and Hospital, Nellore.

AIMS AND OBJECTIVES

1. To study thyroid function abnormalities in patients with chronic kidney disease.
2. To correlate the thyroid function abnormalities with severity of renal failure.
3. To differentiate primary hypothyroidism from thyroid dysfunction due to chronic kidney disease.

MATERIAL AND METHODS

An observational, cross-sectional study was done at Narayana medical college and hospital, Nellore, from July 2021 to November 2022 on 50 patients with chronic renal failure who are on conservative management were included in the study.

Inclusion criteria:

Patients who fulfill the criteria for CKD and who were on conservative management. Criteria for CKD is, Presence of uremic symptoms for 3 months or more; Raised blood urea, serum creatinine and reduced creatinine clearance; USG evidence of CKD- Bilateral contracted kidneys (size <9cm), Poor cortico-medullary differentiation, Type 2 or 3 renal parenchymal changes and Supportive laboratory evidence of CKD like anaemia, changes in serum electrolytes.

Exclusion criteria:

Patients who underwent peritoneal dialysis or hemodialysis, nephrotic range of proteinuria, hypoalbuminemia, history of long time hypothyroidism, other conditions such as acute illness, recent surgery, trauma or burns, and diabetes mellitus. Patients with liver diseases, patients taking drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, estrogen pills, and iodine containing drugs were excluded.

Thyroid profile would be done in all patients who fulfill the inclusion criteria. Informed consent was obtained from all patients. Detailed

clinical history and clinical examination were undertaken with preference to thyroid and renal diseases. The following investigations were performed urine for specific gravity and broadcast, renal parameters such as blood urea, serum creatinine, and creatinine clearance (using Cockcroft-Gault formula), 24h urine protein, and serum protein to rule out nephrotic syndrome and hypoproteinemia, respectively.

The normal values:
Total T3 →0.6–2.1ng/ml
Total T4 →5–13mg/dl
TSH →0.4–7μIU/ml

RESULTS

50 patients who are fulfilling the criteria for CKD and on conservative management were studied and following results were made.

Table 1: Age wise distribution of study patients

Age in years	No. of patients	Percentage
<30	9	18%
30–60	35	70%
>60	6	12%
Total	50	

Table 2: Gender wise Distribution of patients

Gender	No. of patients	Percentage
Male	34	68%
Female	16	32%
Total	50	

Table 3: Distribution of creatinine clearance in CKD patients

Creatinine clearance(ml/minute)	No. of patients	Percentage
<15	33	66%
15-30	15	30%
>30	2	4%

Table 4: Analysis of T3, T4, TSH excluding Hypothyroidism

Thyroid dysfunction	No. of patients		
	Normal value	Low value	High value
Serum T3	17	29	Nil
Serum T4	34	12	Nil
Serum TSH	46	Nil	Nil

Table 5: Distribution of low T3 and T4 among various levels of TSH

TSH levels	Low T3	Normal T3	Low T4	Normal T4
Normal	29	17	12	34
High	4	0	4	0
Total	33	17	16	34

Table 6: Analysis of Hypothyroid symptoms in CKD

Variants	Total No. of patients	No. of patients with symptoms	Percentage
Low T3	29	19	65.51%
Primary hypothyroidism	4	4	100%
CKD without thyroid dysfunction	17	11	64.7%
Total	50	34	

Table 7: Analysis of Thyroid dysfunction in patients with CKD

Thyroid dysfunction	Number of patients	Percentage
Low T3 syndrome	29	58%
Low T4 syndrome	12	24%
Hypothyroidism	4	8%

Table 8: Distribution of creatinine clearance in patients with low T3 and T4 syndrome

Creatinine clearance (ml/min)	Total no. of patients	Low T3 syndrome(%)	Low T4 syndrome(%)
<15	33	20(60.6%)	13(39.39%)
15–30	15	8(53.33%)	3(20%)
>30	2	1(50%)	0(0%)

Table 9: Correlation of Thyroid hormones excluding Hypothyroidism

Thyroid hormones	Normal range	Study range	Mean	SD	Mean excluding Hypothyroidism	SD
Serum T3	0.6-2.1	0.2–2.0	0.67	0.53	0.706	0.53
Serum T4	5-13	0.9–8.5	5.65	2.31	5.94	2.31
Serum TSH	0.4-7	0.6-38	6.49	6.99	4.55	6.99

Table 10: Correlation of Thyroid hormones with severity of renal failure excluding Hypothyroidism

Creatinine clearance (ml/minute)	T3		T4		TSH	
	Mean	SD	Mean	SD	Mean	SD
<15	0.67	0.52	5.78	2.30	4.47	5.50
15–30	0.72	0.47	6.04	2.28	4.60	7.97
>30	1.05	0.73	7.55	2.63	5.35	8.10

DISCUSSION

This study was aimed to assess the thyroid function abnormalities in patients with CKD, and to determine the correlation between thyroid dysfunction and severity of renal disease. Various studies were conducted about thyroid dysfunction and severity of CKD and shown different results. In this study, CKD patients only on conservative management were studied. This is because thyroid profile undergoes changes due to dialysis independent of that due to chronic kidney disease. Dialysis also changes the previous serum thyroid hormone status in patients with renal failure. Various studies have been studied by comparing CKD patients on conservative management and patients on HD by Ramirez and Kayima et al.

In this study, 50 CKD patients who were on conservative management fulfilling the criteria were studied, among these, 34(68%) were males and 16(32%) were females, their age varied from 20-68 years. Among these, 9 patients are ≤30 years old, 35 patients were between 31-60 years and 6 patients were ≥60 years of age. The duration of symptoms of CKD varied from 4 to 30 months, mean duration being 9.84 months and the creatinine clearance varied from 6ml/min-32ml/min. Of these, 33(66%) patients had GFR of <15ml/min, 15(30%) had GFR ranging from 15–30ml/min and 2(4%) had GFR ranging from >30ml/min.

In this study out of 50 patients, 33(66%) had low serum T3 levels. 4(8%) patients among low serum T3 value, they also had low T4 and high TSH suggesting primary hypothyroidism. So, excluding 4 patients of hypothyroidism, 29 patients had low T3 syndrome in this study. 16 patients had low T4 levels in this study, out of which 4 had low T3 and high TSH suggesting primary hypothyroidism. Excluding hypothyroidism 12(24%) patients had low T4 in our study. The TSH values are ranged from 0.6-38 μIU/ml, the mean value being 6.494. Among 50 patients, 46 were in the normal range and 4 had high value of more than 20μIU/ml. In patients who were in the high range 3 were males and 1 was female. These 4 patients with primary hypothyroidism had creatinine clearance of <15ml/min. It indicates the severity of renal failure in hypothyroid patients.

Excluding hypothyroidism, mean TSH level is within normal limits. The mean TSH levels are also within normal limits for the various ranges of GFR. But TSH level doesn't show any linear correlation with the severity of renal failure. In this study of CKD patients with low T3 syndrome, the mean TSH values in several stages of renal failure are found to be in normal range. TSH values did not show any linear correlation with glomerular filtration rate.

One similar study showed similar results which was conducted by Spector and Ramirez et al, Dudani et al, Karunanidhi et al. These studies depicted abnormality in hypophyseal mechanism of TSH release in uraemic patients as the TSH response to the TRH was blunted. Another study which was conducted by Joseph et al and Hardy et al revealed low T3, T4 level with high TSH level suggesting maintenance of pituitary thyroid axis. Several studies reported in CKD patients showed low T3 values. Low T3 had been reported in Ramirez et al, Hegedus et al, Beckett et al, P Iglesias and JJ Diez and many others. Ramirez and Spector et al study showed linear correlation between mean serum T3 and T4 and severity of renal failure.

Among 50 patients of CKD, 17 patients did not show any thyroid function abnormalities but out of them 11(64.7%) had symptoms suggestive of hypothyroidism.

Previous studies by Quionverde et al reported high preponderance of hypothyroidism in CKD. It was estimated to be about 5% in patients

with terminal stage of renal failure. Elaborated study by Kaptein et al, estimated the prevalence of primary hypothyroidism was about 2.5 times much frequent in chronic kidney disease and dialysis. The hypothyroidism in CKD was estimated to range between 0 and 9.5%. Kaptein study also estimated the presence of anti-thyroid antibody titer in 6.7% of CKD.

In this study, hypothyroidism is present in 8% of the patients but doesn't correlate with the severity of the renal failure. The symptoms of hypothyroidism were distributed equally in both hypothyroid and CKD patients. So, diagnosis of hypothyroidism in CKD mainly rest on TSH level which should be very high (>20μIU/dl) with low serum T4. In this study none of the patients had clinical or biochemical features of hyperthyroidism.

Age incidence of CKD patients with low T3 syndrome in our stud showed that, CKD patients having low T3 syndrome 44.44% were <30 years of age, 60% were in the age group 30–60 years of age and 66.66% were >60 years of age. It tells that as the age increases number of patients with low T3 syndrome also increases. Among the patients 58% had low T3 syndrome, 24% had low T4 syndrome and 8% had primary hypothyroidism.

Creatinine clearance were found to be <15ml/min in 20 patients of low T3 syndrome and 13 patients of low T4 syndrome, 15–30ml/min in 8 patients of low T3 syndrome and 3 patients of low T4 syndrome, and >30ml/min in 1 patient of low T3 syndrome only. As with other studies, mean T3 level in this study was reduced in GFR <15ml/min. In patients with low GFR, T3 level was found to be reduced and it shows there was direct linear relationship between T3 level and GFR, which is consistent with Avinashi et al study.

CONCLUSION

In this study population, 50 CKD patients who were on conservative management were studied. Among them 66% of the patients had low T3 values. The change in the serum levels of T3 and T4 in patients with CKD can be considered as being protective, promoting conservation of protein. There is progressive increase in the number of patients with Low T3 and T4 syndrome with the severity of renal failure. There is increase in incidence of hypothyroidism in patients with chronic kidney disease. Excluding hypothyroidism T3 level is found to be low in 58% of the patients and T4 level is low in 24% of the patients. As the age increases there is increase in incidence of Low T3 syndrome in patients with CKD. In patients with low GFR the serum T3 level was found to be decreased. This shows a direct linear relationship between GFR and T3 level.

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