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SEVERITY OF CKD AND THYROID FUNCTION - DEMYSTIFIED

General Medicine

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ABSTRACT

Kidney and thyroid are related to each other functionally and physiologically. CKD alter peripheral thyroid hormone metabolism as well as pituitary thyroid axis. Thyroid hormone plays a major role in development and growth of kidneys. **Objective:** To study the prevalence of thyroid dysfunction in patients with chronic kidney disease. To study the correlation between thyroid dysfunction and severity of renal failure. A Hospital based cross sectional study was done for a period of 1 year. The eGFR was calculated by using the Modification of Diet in Renal Disease. Components of thyroid profile in this study were Triiodothyronine (T3) Thyroxin (T4) Serum thyroid stimulating hormone (TSH). Blood Urea was significantly different between patients with different levels of TSH. Serum Creatinine also found significantly high in patients with Hyperthyroidism and Hypothyroidism. Patients with CRF often have signs & symptoms suggestive of thyroid dysfunction & hence the diagnosis of thyroid disease in these patients has obvious prognostic implications. TSH values will be useful to differentiate hypothyroidism from nonthyroidal illness due to CKD

KEYWORDS

thyroid hormones,Chronic Kidney Disease, thyroid dysfunction, eGFR, hypothyroidism, hyperthyroidism

INTRODUCTION

Chronic kidney disease is considered as a global health problem due to high morbidity, poor prognosis, high cost and reduced patient quality of life (1, 2 and 7). An irreversible impairment in renal function over a long duration of time is referred to as chronic kidney disease (CKD). It begins as a biochemical abnormality and progresses to kidney failure due to the loss of excretory, metabolic, and endocrine processes. In the last two decades, the incidence of End Stage Renal Disease (ESRD) has risen dramatically, and the relative incidence of CKD etiologies has shifted (3, 4).

The thyroid gland produces two related hormones, thyroxin (T4) and triiodothyronine (T3). TSH, secreted by the thyrotrope cells of the anterior pituitary, plays a pivotal role in control of the thyroid axis and serves as the most useful physiologic marker of thyroid hormone action. In the presence of elevated TSH, low T4 especially free T4 is necessary to confirm hypothyroidism. Laboratory investigation shows TSH below normal level. Free and total thyroid hormone levels are increased. (7)

Kidney and thyroid are related to each other functionally and physiologically. CKD alter peripheral thyroid hormone metabolism as well as pituitary thyroid axis. Thyroid hormone plays a major role in development and growth of kidneys. (7) Hypothyroidism by altering the effects of cardiac output, intra renal hemodynamics, renin angiotensin aldosterone system and structural changes like decreased kidney to body weight ratio, truncated tubular mass and altered glomerular architecture causes altered kidney function. (6) The classical clinical features of hypothyroidism in CKD is obscured some of symptoms which patient can complain are dry skin, shallow complexion, low temperature, cold intolerance, lethargy, fatigue, edema and signs noted are hyporeflexia and decreased basal metabolic rate.

Outcomes of few research documented hyperthyroidism, hypothyroidism and euthyroidism. With these inconsistent results in previous researches was planned with a clinical prospective and biochemical investigation to examine co-relation between thyroid hormone and severity of renal disease in undialysed chronic kidney disease.

OBJECTIVE:

- To study the prevalence of thyroid dysfunction in patients with chronic kidney disease.
- To study the correlation between thyroid dysfunction and severity of renal failure.

MATERIALS AND METHODS:

A Hospital based cross sectional study was done for a period of 1 year from August 2021 to July 2022 in the Department of General Medicine at Shridevi Institute of Medical Sciences and Research Hospital Tumakuru.

CKD patients attending General Medicine outpatient department were investigated for thyroid and kidney function for overt hypothyroidism, subclinical hypothyroidism (SCH), and alteration of tri-iodothyronine (T3) and thyroxine (T4). The total number of CKD patients during this period was 72.

Inclusion Criteria Were:

- All patients with chronic kidney disease >18 years.
- Patients with symptoms of uremia>3 months.
- Patients with increased blood urea and increased serum creatinine.
- Patients with decreased creatinine clearance, USG evidence of chronic kidney disease are included in this study

Exclusion Criteria Were:

- Patients having features or history of -
- acute illness, thyroid dysfunction, thyroidectomy/thyroid disorder recent surgery.
- drugs altering thyroid profile (like amiodarone, phenytoin, steroids, estrogen pills, beta-blockers, iodine-containing drugs),
- nephrotic syndrome and diabetic nephropathy
- antenatal check-ups (ANC) patients
- trauma, and burns were excluded from the study.

Laboratory Investigation

- Urine routine and microscopic examination
- Renal parameters like blood urea, serum Creatinine and creatinine clearance (using Cockcroft — Gault formula) USG abdomen for evidence of chronic kidney disease
- Components of thyroid profile in this study
- Triiodothyronine (T3) Thyroxin (T4) Serum thyroid stimulating hormone (TSH)

Assessment of thyroid and kidney functions

The eGFR was calculated by using the Modification of Diet in Renal Disease (MDRD) formula: (eGFR in mL/min/1.73 m2) = 186 x (creatinine/88.4) - 1.154 x (age) - 0.203 x (0.742 if female) x (1.210 if black). CKD staging was done by using Kidney Disease Improving Global Outcome (KDIGO) criteria.

Statistical Analysis:
The Kolmogorov-Smirnov test was used to verify the normality of all research variables among the study population prior to data analysis. Normalcy was assumed and parametric tests were employed when the P-values were greater than 0.05. When variables did not follow normality, non-parametric tests were applied. The data will be entered in excel spread sheet. All statistical calculation were performed with SPSS (Version-16). Chi-square test was applied to check for association between categorical variables. All quantitative variables were expressed as Mean and standard deviation. Qualitative variables were expressed as frequencies and percentages. The level of statistical significance was set at P-value of <0.05.

RESULTS:
A total of 72 patients were included in the study. The mean age of the participants was 55.72 ± 14.80 years. esults: Out of the total 72 patients in the study, 44 were males and 28 were females.

Among all the patients, low blood urea level was seen in 1patient, whereas normal blood urea level was seen in 18 patients and high blood urea level in 53 patients. Majority of cases was seen in Stage 4 CKD category (44.4%) and stage 5 CKD category (30.6%). Stage 3 CKD category accounted for 25.0%. None of the patients were noted in stage 1 and stage 2.

The thyroid (T3) dysfunction among the study population was noted in only 15 cases with Low T3 syndrome was found in (16.7%) 12 cases and high in (4.2%) 3 cases. Whereas normal T3 level was seen in 79.2% of cases (57 cases). The thyroid dysfunction among the study population with the Low T4 value was found in 12 cases (13.9 %) and high T4 levels in (5.6%)4 cases, whereas normal T4 level was seen in 58 patients (80.6%). Low TSH level (Hyperthyroidism) was found in 5 patients (6.9%) and hypothyroidism in 25 patients (34.7%). Normal TSH value was found in 42 patients (58.3%).

Comparison of RFT with TFT [TSH]

Parameter	TSH	N	Mean	Std. Deviation	Kruskal-Wallis H	P-value
Blood UREA (mg/dl)	Hyperthyroidism	5	165.2	50.62	7.441	0.024
	Hypothyroidism	25	100.36	64.39		
Serum Creatinine (mg/dl)	Hyperthyroidism	5	5.76	1.8	7.847	0.02
	Hypothyroidism	25	4.09	2.44		
G.F.R(ml/min/1.73 m2)	Hyperthyroidism	5	11.2	3.83	6.727	0.035
	Hypothyroidism	25	19.52	10.48		

Blood Urea was significantly contrasting between patients with different levels of TSH. It was significantly high in patients with Hyperthyroidism (165.20±50.62) and Hypothyroidism (100.36±64.39) while it was low in normal patients (83.68±49.34) [P=0.024]. Serum Creatinine also found significantly high in patients with Hyperthyroidism and Hypothyroidism while it was less in normal patients [P=0.020]. However G.F.R was high in normal patients while it was less in patients with Hyperthyroidism and Hypothyroidism [P0.035].

There was no statistical significant difference observed between stage of Chronic Kidney disease and Level of T3 and T4. There was no statistical significant difference observed between stage of Chronic Kidney disease and Level of T4. In both Hyperthyroidism and hypothyroidism, Majority of cases was seen in stage 4 which accounts for 62.5% and 34.4% respectively. There was statistical significant difference observed between stage of Chronic Kidney disease and Level of TSH.

DISCUSSION :
A large number of hormonal systems are affected by CRF, yet it remains unclear to what extent these changes are responsible for manifestations of uremic syndrome. Patients with CRF often have signs & symptoms suggestive of thyroid dysfunction & hence the diagnosis of thyroid disease in these patients has obvious prognostic implications. The data reported deals primarily with the biochemical parameters.

The means and standard deviations of serum T3 level, serum T4 level and TSH levels were 105.89 ± 52.47 ng/dl, 6.98 ± 2.64 ng/dl and 6.58 ± 7.93 uIU/L, respectively. Low serum T3 levels were observed in 16.7% of cases (12 patients), whereas normal T3 levels were reported in 79.2% of cases (57 patients). Very low serum T3 concentration which can be explained by the normal feedback regulation of the pituitary thyroid axis. We found that incidence of abnormal low Serum T3 was more in females than in males which accounts for 21.4% and 13.6% respectively. Similarly we found that incidence of low Serum T4 was more in female (17.9%) than males (11.4%). Incidence of Abnormal TSH levels i.e. clinical hypothyroidism range were seen in 31.8 percent of males.

The majority of cases in this study were in the Stage 4 CKD, accounting for 44.4 percent of all cases.

Abnormal serum T3 and T4 level both low value and low value shows less in the present study. There was no statistical significant difference observed between stage of Chronic Kidney disease and Level of T3 and T4. We observed that the occurrence of high TSH values, i.e. hypothyroidism (34.7 percent), was higher than hyperthyroidism (6.9 percent) in association to CKD. It can be presumed that free T4 values would fall if these patients develop hypothyroidism and TSH values would rise simultaneously. Thus Free T4 and TSH levels combined can be used for the diagnosis of hypothyroidism in presence of CKD.The majority of cases were seen in stage 4 in both hyperthyroidism and hypothyroidism, accounting for 62.5 percent and 34.4 percent of cases, respectively. There was a statistically significant correlation between the stage of Chronic Kidney Disease and the TSH level. The possible explanation is due to accumulation of iodides in thyroid gland due to decreased renal clearance in CRF patients.

Number of patients with low T3 and T4 syndrome progressively increases with severity of renal failure. Serum level of total T3 and free T4 is directly proportional to creatinine clearance level. Total T3 and free T4 had correlation with the severity of renal failure. TSH values will be useful to differentiate hypothyroidism from nonthyroidal illness due to CKD. There was a significant decrease in serum T3, T4 level and elevation TSH level. A higher level of clinical and subclinical primary hypothyroidism in patients with decreased estimated eGFR was seen which was independent of age and sex. A number of hypothesis explain the various contributing factors for thyroid dysfunction in CKD patients such as low circulating thyroid hormones level, insuffient binding to carrier protiens, decreased tissue thyroid hormone content, alteration in iodine metabolism.(7)

CONCLUSION:
In relation to CKD, we discovered that high TSH readings, i.e. hypothyroidism, was more common than hyperthyroidism. At both hyperthyroidism and hypothyroidism, the majority of cases were seen in stage 4. The stage of Chronic Kidney Disease and the TSH level had a statistically significant relationship.

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