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Original Research Article

To study thyroid profile in CKD patients in Eastern Uttar Pradesh

Anupam Srivastava[1]*, Mahim Mittal[1], Minakshi Awasthi[1], Priyanka Rai[2], Mahima Goel[3]

[1]*Dept. of Medicine, BRD Medical College, Gorakhpur, Uttar Pradesh, India*
[2]*Dept. of Pathology, Autonomous State Medical College, Basti, Uttar Pradesh, India*
[3]*Dept. of Pathology, BRD Medical College, Gorakhpur, Uttar Pradesh, India*

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ABSTRACT

Background: Chronic kidney disease (CKD) remains a universal pandemic that has evolved into a serious public health problem that imposes a significant socioeconomic burden. Thyroid profile is disrupted in CKD patients due to aberrant thyroid hormone metabolism. The purpose of our study was to assess thyroid function in people who had chronic renal disease (CKD).
Materials and Methods: According to the inclusion-exclusion criteria, this cross-sectional observational research enrolled 150 chronic renal disease patients.All patients who met the above criteria underwent a detailed history as well as a general and systemic examination. Thyroid function tests, USG entire abdomen, chest X-ray, ECG, and 2D Echocardiogram, were performed.
Results: There were 84 men and 66 women among the 150 CKD patients. Thyroid hormone abnormalities were found in 93.3 % of the individuals. 14.7 % of the participants had hypothyroidism, 14.7 % had low T3 and T4 readings, 10% had low T4 values alone, 38 % had low T3 only, and 17% had subclinical hypothyroidism. Low T3 levels (58 %) were the most prevalent thyroid anomaly, with or without low T4 or elevated TSH levels. Low T3 levels were more common in patients with advanced CKD.
Conclusion: Thyroid hormone abnormalities are linked to different stages of chronic renal disease.

1. Introduction

Chronic kidney disease (CKD) is still a major public health concern, as defined by the National Kidney Foundation's Kidney Disease Outcome Quality Initiative (K/DOQI) as kidney damage lasting more than three months with structural or functional abnormalities, with or without decreased glomerular filtration rate (GFR), manifested by pathological abnormalities or markers of kidney damage, or GFR of 60 mL/min/1.73 m^2 or less.[1]

Chronic kidney disease impacts the endocrine and metabolic systems in a number of ways, according to the National Institutes of Health. When it comes to those with chronic renal disease, thyroid dysfunction is one of the most common endocrine disorders they encounter. In embryogenesis, thyroid hormone has a role in the formation and growth of many components of the kidney,[2] and chronic kidney disease causes disruptions in the hypothalamus-pituitary–thyroid axis as well as thyroid hormone peripheral metabolism. The presence of hyperuricemia is one of the most significant linkages between thyroid problems and chronic kidney disease. Glomerulotubular function, electrolyte balance, and water homeostasis are all compromised in patients with thyroid insufficiency. Hypothyroidism is associated with a reduction in glomerular filtration rate,[3] hyponatremia, and a change

* *Corresponding author*.
E-mail address: anupamsrivastava3089@gmail.com (A. Srivastava).

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in water excretion capacity, among other things. Despite the fact that hyperthyroidism is not commonly associated with chronic kidney disease, it has been demonstrated to accelerate the course of the illness.

Thyroid hormones (T3 and T4) in the peripheral circulation may be low owing to hormonal clearance during dialysis, reduced T3-binding capacity, altered hormonal catabolism, increased iodine storage in the thyroid gland, thyroid autoantibodies in the serum, and poor peripheral conversion. In individuals with chronic kidney disease (CKD), low T3 levels are the most prevalent laboratory result, followed by subclinical hypothyroidism. High levels of inflammatory markers (hsCRP, IL-6, and others) in chronic kidney disease patients have been linked to malnutrition (low prealbumin and IGF-1 levels), greater endothelial dysfunction, worse cardiac function, shorter overall survival, and higher all-cause and cardiovascular mortality in some studies.[4] The levels of free T4 in patients with chronic kidney disease, on the other hand, range from low to normal. This is mostly due to reduced T4 protein binding in patients with chronic kidney disease. Haemodialysis (HD) patients are dominantly composed of people who do not have thyroid disease. 20% of people with HD have high TSH levels in the range of 5–20 mU/L, which is considered to be normal. HD has an effect on TSH cellular transit, which may serve as a compensating mechanism to keep the thyroid in a healthy state.[5]

Thyroid hormone levels in CKD patients are one of the most important yet understudied disorders. Renal impairment has been connected to thyroid hormone levels. The goal of this study was to determine how common thyroid dysfunction is among CKD patients in Eastern Uttar Pradesh.

2. Materials and Methods

During the research period from January 2020 to January 2021, all consenting patients with CKD of any aetiology admitted to the Medicine department with the agreement of the Institutional ethics committee were included. Considering the inclusion criteria, 150 patients participated in this study.

2.1. Inclusion criteria

1. Age 18 years and above.
2. Documented CKD patients with or without haemodialysis (as defined by the National Kidney Foundation's [Kidney Dialysis Outcomes Quality Initiative (KDOQI)] current criteria).

2.2. Exclusion criteria

1. Patients previously diagnosed with any Thyroid Disorders.
2. Patients on drug therapy like amiodarone, lithium.
3. History of any surgery or any radiological intervention on the thyroid gland.

The study includes a survey to determine thyroid hormone levels in CKD patients. The data was examined, and the results were reviewed. For data input and analysis, SPSS software for Windows (SPSS Inc., Chicago, IL, USA) was used (15.0 version). The mean and standard deviation were used to present quantitative data, whereas proportions and percent ages were used to report qualitative data. To calculate the Standard Normal Deviate (Z), a test of proportion was used to compare the different proportions, and a Chi-square test was utilized to find the links. To compare more than two means at once, a one-way analysis of variance (ANOVA) was used, followed by Tukey's post hoc test. With a 95 percent confidence interval, a p-value of <0.05 was declared significant.

3. Results

A total of 150 people with CKD were enrolled in the research. Statistical analysis was performed on various demographic data, clinical features, and thyroid profiles. In our study, we evaluated 150 patients with CKD who were on conservative therapy and fulfilled the CKD criteria, of whom 84 (56%) were males, and 66 (44%) were females [Figure 1]. Males had 13 cases of SCH, 15 cases of hypothyroidism, and 31 cases of low T3 syndrome, whereas females had 11, 7 and 26 cases of SCH, hypothyroidism, and low T3 syndrome, respectively [Table 1, Figure 2].

The participants ranged in age from 14 to 79 years old. Patients aged 14 to 29 years old numbered 15, those aged 30 to 44 years numbered 37, those aged 45 to 59 years numbered 58, and those aged 60 and over numbered 40 [Figure 3]. Patients in Stage III accounted for 4.7 % of all cases, 24.7 % of Stage IV cases, and 70.7 % of Stage V cases. Most of the individuals evaluated were in Stage V [Figure 4].

The majority of the patients (93.3 %, n = 140) had abnormal serum thyroid function test results. 16 % (n=24) of the subjects had SCH (i.e., TSH >5 mIU/L with normal FT4 levels), 14.7 % (n = 22) had clinical hypothyroidism (i.e., TSH >5 mIU/L with low FT4), 38 % (n=57) had Low T3 syndrome, 14.7 % (n=22) had both low T3 and low T4 values, and 10% (n=15) only had low T4.Mean TSH levels were 4.78 ± 9.66 (U/mL) in stage III patients, 5.37 ± 7.06 (U/mL) in stage IV patients, and 11.81 ± 12.84 (U/mL) in stage V patients. T3 levels were 0.69 ± 0.71 (ng/dl) for stage III patients, 0.66 ± 0.54 (ng/dl) for stage IV patients, and 0.6 ± 0.44 (ng/dl) for stage V patients. Mean T4 levels were 5.67 ± 2.34 (g/dL) for stage III patients, 4.90 ± 2.71 (g/dL) for stage IV patients, and 2.82 ± 2.39 (g/dL) for stage V patients [Table 2]. Turkey Post hoc test showed that the mean levels of TSH were significantly higher with the increasing stages of CKD ($p<0.001$). However, the mean

levels of T3 and T4 were also significantly lower with the increasing stages of CKD (p<0.001).

There were 24 CKD patients with SCH, with 6 (5%) in Stage IV CKD and 18 (75%) in Stage V CKD. Twenty two individuals with CKD had overt hypothyroidism, with two (9.09 %) having Stage III CKD, one patient(4.5%) having Stage IIIA, one patient (4.5%) having Stage IIIB; 5 patients (22.7 %) having Stage IV, and 15 patients (68.2%) having CKD Stage V. [Table 3]

Table 1: Distribution of the patients based on Gender and status of thyroid function

Status of Thyroid	Male	Female	Total
Euthyroid	8	2	10
Hypothyroidism	15	7	22
Low T3 and T4 Syndrome	11	11	22
Low T3 Syndrome	31	26	57
Low T4 Syndrome	6	9	15
Subclinical Hypothyroidism	13	11	24
Total	84	66	150

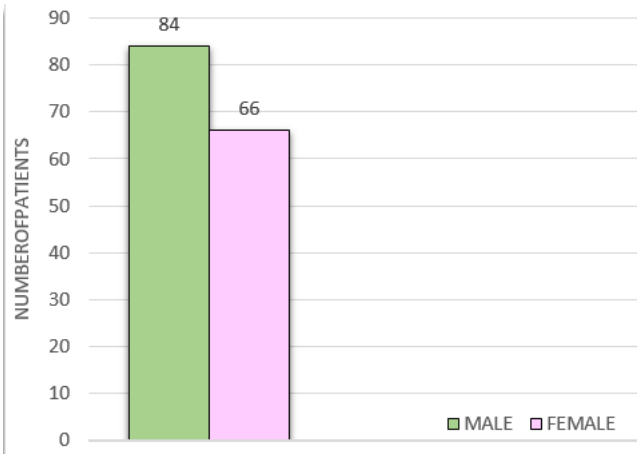

Figure 1: Graphical representation of no. of ckd patients according to gender

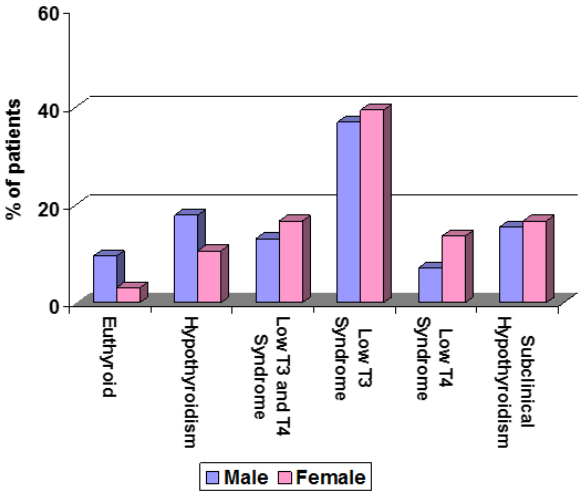

Figure 2: Graphical representation of distribution of CKD patients according to gender and thyroid dysfunctions

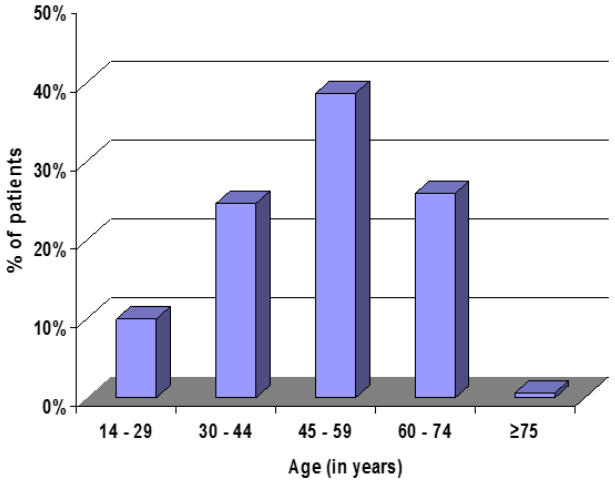

Figure 3: Graphical representation of % age of CKD patients according to age

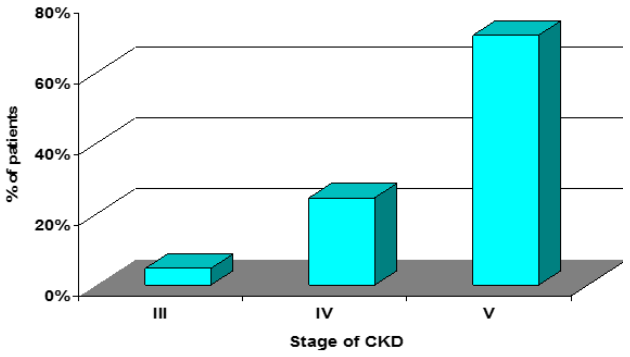

Figure 4: Graphical representation showing % age of patients in different stages of CKD

4. Discussion

Although CKD impacts a number of hormonal systems, it's unclear how much these changes contribute to uremic syndrome symptoms. Thyroid function testing has obvious prognostic implications in patients with chronic renal disease, since they commonly present with signs and symptoms suggestive of thyroid dysfunction.

Thyroid dysfunction was found in 93.3 % of the 150 participants in our research. People with chronic renal illness had low T3 and T4 mean levels which is similar to the findings of Srivastava et al.,[6] who found that the mean FT3 in cases (1.4727 ± 0.3577) was lower than in controls (2.6613 ± 0.6155), a statistically significant difference. The

Table 2: Comparison of the level of TSH, T3 and T4 according to the stages of CKD of the patients

T3, T4 and TSH	Stage of CKD	Mean	Std. Deviation	F-value	p-value
	III (n=7)	4.78	9.66		
TSH	IV (n=37)	5.37	7.06	11.09	<0.001*
	V(n=106)	11.81	12.84		
	III (n=7)	0.69	0.71		
T3	IV (n=37)	0.66	0.54	5.29	<0.001*
	V(n=106)	0.60	0.44		
	III (n=7)	5.67	2.34		
T4	IV (n=37)	4.90	2.71	3.74	0.026*
	V(n=106)	2.82	2.39		

Table 3: Distribution of patients based on Different types of thyroid disorders and stages of CKD

Status of Thyroid	Stage of CKD			Total
	III	IV	V	
Euthyroid	1	3	6	10
Hypothyroidism	2	5	15	22
Low T3 and T4 Syndrome	2	8	12	22
Low T3 Syndrome	1	13	43	57
Low T4 Syndrome	1	2	12	15
Subclinical Hypothyroidism	0	6	18	24
Total	7	37	106	150

mean FT4 in patients was 0.9013 ± 0.1916 and in controls was 1.4263 ± 0.2594, suggesting that cases had lower mean serum FT4 than controls and that the difference was statistically significant. In our study, 79 people (52.7%) had low T3 syndrome, while 22 people had both low T3 and T4 levels. With a p<0.001 and a Z=5.67, low T3 syndrome was statistically significant.

According to another study by Victoria et al.,[7] chronic renal failure impairs thyroid function in a variety of ways, including decreased circulating thyroid hormone concentrations, altered peripheral hormone metabolism, disturbed carrier protein binding, possible decrease in tissue thyroid hormone content, and increased iodine storage in thyroid glands.

Triiodothyronine (T3) and thyroxine (T4) levels in the blood are both lowered. Serum T3 deficiency is caused by insufficient extrathyroidal T4 to T3 conversion, not increased T3 breakdown or reduced thyroidal T3 production. Because circulating inhibitors prevent T4 from binding to thyroxine-binding globulin, T4 levels are reduced. Thyroid-stimulating hormone (TSH) is not elevated despite lower T4 and T3 levels in the blood.

In our study, low T3 was found in 3.8% of stage 3, 26.6 % of stage 4, and 69.6 % of stage 5. Sang et al findings' are in accordance with our study.[8] They observed that the frequency of low T3 increased as CKD progressed and there was statistically significant positive relationship between total T3 and creatinine clearance (p<0.001). This shows that even when TSH levels were normal, blood T3 levels were linked to CKD severity. It was non-significant (p value>0.27) in terms of low T3 distribution by gender, with men and females having 42 and 37 %, respectively. According to Zhang et al.[9] there is a connection between elevated TSH levels and an increased risk of developing CKD. His study concluded that in a large cohort of euthyroid men and women, high TSH and low FT3 levels, even when within the normal range, were connected to a slight increase in the risk of incident CKD. According to Rhee et al.[10] in a review publication, low T3 levels are the most often detected thyroid function test abnormalities in people with chronic renal disease. The prevalence of low T3 increased incrementally as kidney function deteriorated in a study of 2284 CKD patients with normal TSH levels, to the point where more than three-quarters of patients with Stage 5 CKD had low levels: 8, 11, 21, 60, and 79 percent, respectively, with eGFRs of 90, 60–89, 30–59, 15–29, and 15 ml/min/1.73m^2.

In our study of 150 chronic kidney disease patients, 37 (24.7%) had low T4 levels, which is similar to Mohamedali et al. (2014)[11] and Avasthi et al. (2001).[12] Males and females in the group of 37 were 17 and 20 years old, respectively. In stage 3, the low T4 is 8.1%, 27% in stage 4, and 64.9 % in stage 5. In our investigation, 22 individuals (14.7%), 11 men and 11 females, exhibited subclinical hypothyroidism, which is comparable with Michel et al. 2008 study.[13] In this study, 293 (9.5%) of the 3089 adult participants had subclinical primary hypothyroidism, while 277 (9%) had a GFR of 60 ml/min per 1.73 m^2.

9.1 percent of patients with stage 3 CKD, 22.7 percent in stage 4, and 68.2 percent in stage 5 had hypothyroidism in our study. Similar findings were found in a 2005 study by Lo et al.,[14] who discovered that the prevalence of

hypothyroidism increased with decreasing GFR (measured in mL/min/1.73 m^2, occurring in 5.4 percent of subjects with GFR 90, 10.9 percent with GFR 60-89, 20.4 percent with GFR 45-59, and 23.0 percent with GFR 30-44, respectively) among 14,623 adult participants with serum creatinine and thyroid function tests. Lower GFR was connected to a greater incidence of hypothyroidism when compared to GFR of 90 mL/min/1.73m^2.

In a cross-sectional research, Chandra et al.[15] tested 358 CKD patients for hypothyroidism using biochemical tests. Among the participants, 143 had subclinical biochemical hypothyroidism and 59 had overt hypothyroidism. TSH levels in the overt hypothyroid group were considerably higher, whereas free T4 levels were significantly lower than in the nonhypothyroid group.

According to Quvionverde et al., hypothyroidism was observed in roughly 5% of ESRD patients. Two investigations, Lim et al.[7] and Singh et al.,[16] looked at the effect of haemodialysis on the thyroid profile in persons with chronic kidney disease.[16]

5. Conclusion

Hypothyroidism is linked with a considerable rise in the severity of chronic kidney disease. Low T3 syndrome was seen in most patients (52.7%) who had a disturbed thyroid profile. The eGFR and T3 levels have a direct linear relationship. The incidence of low T3 and low T4 syndrome grows in conjunction with the severity of renal failure (with decrease in eGFR).

6. Conflicts of Interest

There were no conflicts of interest declared by the authors.

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None.

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Author biography

Anupam Srivastava, Resident https://orcid.org/0000-0002-3636-109X

Mahim Mittal, Professor & HOD

Minakshi Awasthi, Assistant Professor https://orcid.org/0009-0000-3651-5944

Priyanka Rai, Assistant Professor https://orcid.org/0000-0002-1458-9579

Mahima Goel, Junior Resident 3rd Year https://orcid.org/0009-0001-4976-2853

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