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Original Research Article

# Assessment of Thyroid Function in Ckd Patients

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**Conflict of interest: Nil**

**Abstract**

**Aim:** The aim of the present study was to assess the prevalence of thyroid dysfunction and the correlation between thyroid dysfunction and severity of renal diseases in patients with chronic kidney disease.

**Material & Methods:** A prospective study was conducted on 100 patients of whom were diagnosed to have chronic kidney disease in the Department of Physiology, Netaji Subhas medical College and Hospital, Bihta, Patna, Bihar, India in between the duration of 1 year. Informed consent was obtained from all the patients.

**Results:** In the present study majority of study subjects were from 36 to 45 years of age group. The Mean ± SD of age in study group was 46.64 ±7.63 years as compared to 45.35 ± 6.34 in control group. Maximum patients belonged to the age group 36-45 years. In this study, there were higher numbers of male as compared to female in both these groups. The Case group (N=100) shows serum urea, serum creatinine and serum TSH are significantly higher ($p<0.0001$) in the cases compared to the controls. While serum fT3 was significantly low ($p=0.01$) and serum fT4 value was not significant in study group as compared to control group. Serum fT3 was significantly decreased with decrease in GFR which was positively correlated with eGFR in study group. Serum creatinine, urea and fT4 were negatively correlated with calculated glomerular filtration rate.

**Conclusion:** CKD is a progressive disease and these patients are more prone to develop thyroid dysfunction, therefore monitoring of thyroid function should be regularly advised to such patients in order to prevent adverse events in relation to kidney and thyroid function.

**Keywords:** Thyroid Function, T3, T4, TSH Chronic Kidney Disease.



## Introduction

The function of the thyroid gland is one of the most important in the human body as it regulates majority of the body's physiological actions. The thyroid produces hormones (T3 and T4) that have many actions including metabolism, development, protein synthesis, and the regulation of many other important hormones. Any dysfunction in the thyroid can affect the production of thyroid hormones (T3 and T4) which can be linked to various pathologies throughout the body. Disorders in renal function have been seen to coexist with specific levels of thyroid hormone. Chronic kidney disease (CKD) is becoming a serious health problem; the number of people with impaired renal function is rapidly rising, especially in industrialized countries. [1] The overall prevalence of chronic kidney disease in India is 17.2% and prevalence of chronic kidney disease stages 1, 2, 3, 4 and 5 are 7%, 4.3%, 4.3%, 0.8% and 0.8%, respectively. [2] Kidney is involved in the metabolism and elimination of thyroid hormone; therefore, the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism and elimination of thyroid hormones causing thyroid dysfunction. Whereas thyroid hormone is necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. [2,3,4] Thyroid functional disorders are commonly observed in chronic kidney disease (CKD) patients. Thyroid function can also affect kidney function, CKD progression, and increase cardiovascular disease (CVD) disease risk.

CKD patients have a high risk for CVD and impaired thyroid function may increase their CVD risk as well as mortality, as has been shown for ESKD patients. [5,6,7] On the other hand, kidney is engaged in the metabolism and elimination of TH. The decrease of kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of TH. Thyroid dysfunction gains unique characteristics in those individuals with advanced kidney disease. [8] Chronic kidney disease is connected with thyroid function abnormalities leading to low levels of serum total and free T3 concentration and distinctive reverse T3 and free T4 levels. Besides, thyroid diseases, including goiter, hypothyroidism, thyroid nodules and thyroid cancer, may happen more frequently in ESRD individuals than in the all-inclusive community and may be under diagnosed due to limited clinical awareness. [9,10]

Hence, the aim of the study is to find out the prevalence of thyroid dysfunction and the correlation between thyroid dysfunction and severity of renal diseases in patients with chronic kidney disease.

**Materials & Methods**

A prospective study was conducted on 100 patients of whom were diagnosed to have chronic kidney disease in the Department of Physiology, Netaji Subhas medical College and Hospital, Bihta, Patna, Bihar, India in between the duration of 1 year. Informed consent was obtained from all the patients.

**Inclusion criteria:**

- Patients with chronic kidney disease fulfilling the criteria for CKD and who are on conservative management.

Criteria for Chronic Kidney Disease were symptoms of uremia for 3 months or more. Elevated blood urea, serum creatinine and decreased creatinine clearance. Ultra sound evidence of chronic kidney disease are Bilateral contracted kidneys — size less than 8 cm in male and size less than 7 cm in female. Poor corticomedullary differentiation. Type 2 or 3 renal parenchymal changes. Supportive laboratory evidence of CKD like anemia, low specific gravity, changes in serum electrolytes, etc., radiological evidence of renal osteodystrophy.

**Exclusion criteria:**

- Patients on peritoneal dialysis or hemodialysis.
- Nephrogenic range of proteinuria.
- Low serum protein especially albumin.
- Other conditions like acute illness, recent surgery, trauma or burns, diabetes mellitus, liver diseases, drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, beta-blocker, estrogen pills, iodine-containing drugs.

All participants were divided into two groups, Group-I and Group II. Group I was comprised of 100 normal healthy controls and Group-II was comprised of 100 chronic kidney disease patients as study group. They were primarily diagnosed by clinical examination & ultrasonographic findings and further evaluated by biochemical investigations. Patients with H/O anti-thyroid drugs, on use of chronic medicine like steroids & anticancer drugs, pregnancy and patient with systemic diseases like connective tissue disorders, liver diseases and psychiatric disorders are excluded from the study. The healthy controls were selected from the working staff and people coming for their physical fitness and all patients were admitted to the Medicine ward.

They were instructed for sample collection. After ensuring 12 hours fasting venous blood sample was collected in plain vacutainer and assessed for serum urea, creatinine by UV kinetic on fully auto-analyzer I-Lab 650 and thyroid hormones (Serum fT3, fT4 and TSH) by Elisa immunoassay on I-Mark Micro plate Absorbance Reader (Elisa Reader).[11-15] The GFR was calculated by using Modification of diet in renal disease (MDRD) formula in order to understand the status of thyroid hormones in chronic kidney disease patients.

**Statistical Parameters**

The results of the present study were analysed by using Graphpad instat version 3.0. In data analysis, comparison of all parameters between control and study group applying unpaired t-test. Values of serum urea, creatinine, fT3, fT4 and TSH were compared by using Mann Whitney U test (or Kruskal-Wallis) followed by Dunn's post hoc multiple comparisons. Interpretation of the test result was done according to p value ($p < 0.05$ – significant, $p < 0.001$ – highly significant and $p \geq 0.05$ – not significant).

**Results**

**Table 1: Age and gender distribution in CKD patients and healthy controls**

| Age groups | Cases n (%) | Controls n (%) |
|---|---|---|
| 36-45 years | 46 (46) | 54 (54) |
| 45-55 years | 30 (30) | 40 (40) |
| 56-65 years | 24 (24) | 6 (6) |
| **Gender** | | |
| Male | 64 (64) | 60 (60) |
| Female | 36 (36) | 40 (40) |

In the present study majority of study subjects were from 36 to 45 years of age group. The Mean ± SD of age in study group was 46.64 ±7.63 years as compared to 45.35 ± 6.34 in control group. Maximum patients belonged to the age group 36-45 years. In this study, there were higher numbers of male as compared to female in both these groups.

**Table 2: Comparison of Biochemical Parameters between Group I and Group II**

| Parameter | Biological Reference Interval | Control Group (N=100) | | | Study Group (N=100) | | | P value |
|---|---|---|---|---|---|---|---|---|
| | | Min. | Max. | Mean ± SD | Min. | Max. | Mean ± SD | |
| Creatinine (mg/dl) | 0.7-1.2 | 0.72 | 0.82 | 0.7±0.16 | 4.80 | 5.55 | 5±1.45 | p=0.0001 |
| Urea (mg/dl) | 15-40 | 18.80 | 23.27 | 22.18±6.04 | 120.10 | 137.23 | 131.19±40.52 | p=0.0001 |
| TSH (µIU/ml) | 0.4-4.2 | 2.45 | 2.84 | 2.78±0.84 | 4.40 | 7.14 | 6.03±5.45 | p=0.0001 |
| fT3 (pg/ml) | 2.5-5.8 | 3.14 | 3.84 | 3.66±0.80 | 2.20 | 3.42 | 3.12±2.045 | p=0.01 |
| fT4 (pg/ml) | 10-21 | 13.37 | 16.34 | 15.85±2.70 | 13.87 | 16.14 | 12.78±6.06 | p=0.12 |

The Case group (N=100) shows serum urea, serum creatinine and serum TSH was significantly higher (p<0.0001) in the cases compared to the controls. While serum fT3 was significantly low (p=0.01) and serum fT4 value was not significant in study group as compared to control group.

**Table 3: Comparison between different stages of CKD with Biochemical parameter**

| Stages of CKD | eGFR (ml/min/1.73m$^2$) | Creatinine (0.7-1.2mg/dl) | Urea (15-40mg/dl) | TSH(0.4-4.2µIU/ml) | fT3 (2.5-5.8pg/ml) | fT4(10-21pg/ml) |
|---|---|---|---|---|---|---|
| Stage- III (N=5) | 33.7±1.70 | 2.16±0.05 | 109.5±28.57 | 6.36±6.30 | 3.20±3.05 | 12.08±8.40 |
| Stage- IV (N=25) | 18.32±3.10 | 3.32±0.55 | 120.20±32.68 | 7.01±5.80 | 2.6±1.32 | 12.48±5.56 |
| Stage-V (N=70) | 10.70±2.40 | 6.74±1.26 | 133.52±41.70 | 5.60±5.40 | 1.55±1.20 | 15.12±6.24 |
| Statistical Significance | p<0.0001 | p<0.0001 | p<0.2050 | p<0.3846 | p<0.0001 | p<0.9299 |

Serum fT3 was significantly decreased with decrease in GFR which was positively correlated with eGFR in study group. Serum creatinine, urea and fT4 were negatively correlated with calculated glomerular filtration rate.

## Discussion

Chronic kidney disease (CKD) is recognized as a global health problem due to its high cost, reduced patient quality of life [16], high comorbidities and poorer prognosis of other diseases such as metabolic diseases. [17] The thyroid gland influences metabolic processes in the body and clinical/translational research supports a connection between thyroid and kidney function. Patients with CKD and end-stage kidney disease (ESKD) are prone to hypothyroidism [18-20] and low free triiodothyronine (FT3) syndrome [combined low FT3 levels with normal thyroid stimulating hormone (TSH) levels]. [21,22]

In the present study majority of study subjects were from 36 to 45 years of age group. The Mean ± SD of age in study group was 46.64 ±7.63 years as compared to 45.35 ± 6.34 in control group. Maximum patients belonged to the age group 36-45 years. In this study, there were higher numbers of male as compared to female in both these groups. The Case group (N=100) shows serum urea, serum creatinine and serum TSH are significantly higher (p<0.0001) in the cases compared to the controls. While serum fT3 was significantly low (p=0.01) and serum fT4 value was not significant in study group as compared to control group. Balaji Rajagopalan et al [23] study show that there were significantly decrease in the level of fT3 and fT4 in CKD patients. While Lim VS et al [24] reported that despite decreased circulatory T3 and T4 level, TSH level is not elevated.

Serum fT3 was significantly decreased with decrease in GFR which was positively correlated with eGFR in study group. Serum creatinine, urea and fT4 were negatively correlated with calculated glomerular filtration rate. Dialysis also changes the previous serum status of thyroid hormone in the patients with renal failure. Many studies have been conducted by comparing CKD patients on

conservative Management and patients on hemodialysis by Ramirez [25] and Kayima et a1. [26]

Previous studies by Quion verde et a1 [27] reported high prevalence of hypothyroidism in CKD. It was estimated to be about 5% in patients with terminal renal failure. In our study, hypothyroidism is present in 10% 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 in our study. Signs of hypothyroidism were more common in CKD without hypothyroidism than with hypothyroidism. Fan et al [28] suggested low-T3 syndrome to be a predictor of CKD progression. To clarify some of the raised issues, especially for patients with moderate CKD, we set out to analyse the association of a full panel of thyroid hormones with eGFR and adverse renal events. Thyroid disorders and CKD are independently some of the most prominent medical conditions found in patients in many countries. Clinicians, including nephrologists, must consider the dangers of thyroid disease and its appropriate treatment in conjunction to treating CKD. Thyroid dysfunction causes significant changes in kidney function and kidney diseases can be associated with thyroid disorders. Thus, both CKD and thyroid dysfunction mutually influence each other [29]. Similarly, dyslipidemia is the leading risk factor for CVD in CKD patients, and CVD remains the leading cause of death in CKD patients. Kidney Disease Outcomes Quality Initiative (K/DOQI) working group has suggested that, all adults and adolescents with CKD should be evaluated for dyslipidemias because of high risk for CVD [30].

## Conclusion

As CKD is a progressive disease and these patients are more prone to develop thyroid dysfunction, therefore monitoring of thyroid function should be regularly advised to such patients in order to prevent adverse events in relation to kidney and thyroid function.

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