

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## Study of Thyroid Profile In Chronic Kidney Disease.

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### ABSTRACT

**INTRODUCTION:** Chronic Kidney Disease (CKD) is a clinical syndrome characterized by irreversible renal dysfunction leading to excretory, metabolic and systemic failure as a result of accumulation of nitrogenous waste products & presenting with a myriad of clinical features with decreased creatinine clearance. Kidney is closely related to the thyroid gland, being the only other organ competing for iodide clearance.<sup>1</sup> Patients with CKD have many symptoms and signs suggestive of thyroid dysfunction. Prevalence of hypothyroidism in end stage renal disease has been estimated to range between 0 and 9.5 percent.<sup>2</sup> There is also increased prevalence of goiter in these patients. The incidence of goiter has also been variously reported in literature.<sup>5,6</sup> In view of the variability of thyroid profile in patients with CKD in previous studies, we decided to undertake a prospective clinical and biochemical study of thyroid function in CKD patients at Sree Balaji Medical College & Hospital, Bharath University, Chrompet, Chennai.

### AIMS AND OBJECTIVES

- To study the prevalence of thyroid dysfunction in CKD.
- To find out the types of thyroid dysfunction in CKD.
- To determine the correlation between the thyroid dysfunction and severity of renal disease.

### RESULTS AND OBSERVATIONS

- Our study had a male preponderance, 80% of the study group being men ie 60 male patients with the remainder 15 being female patients (20%). Ultrasound abdomen showed evidence of CKD in all the 75 patients. Bilaterally contracted kidneys were present in 65 (86.7%) patients. Remaining 10 patients (13.3%) had poor Cortico medullary differentiation.
- Among the 75 patients, low serum T3 level was found in 40 patients (53.3%). Eight patients among the low serum T3 level also had high TSH value of more than 4.05  $\mu$ IU/ml with low free T4 level and also symptoms suggestive of hypothyroidism. These patients as per the criteria were grouped under "Primary hypothyroidism" and excluded from further study.
- The remaining 32 patients with low T3 had normal TSH and hence they were all grouped under "Low T3 Syndrome."

### CONCLUSIONS

1. Thyroid dysfunction occurs in **53.3%** of chronic kidney disease patients. Incidence of hypothyroidism is **10.7%** in CKD patients, which is higher than that of general population.
2. Excluding patients with hypothyroidism serum T3 level is low (**Low T3 Syndrome**) in **42.7%** of patients and serum T4 is low (**Low T4 Syndrome**) in **21.3%** of patients with CKD. Serum TSH level is normal in all stages of CKD excluding primary hypothyroidism.

Number of patients with low T3 progressively increases with severity of renal failure. Mean **Serum T3** level has a **linear correlation** with the **severity of renal disease**. But number of patients having low T4 and low mean serum T4 levels does not correlate with the severity of renal failure

**Keywords:** CHRONIC KIDNEY DISEASE (CKD), THYROID PROFILE, T3, T4, TSH, THYROID DYSFUNCTION

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## INTRODUCTION

Chronic Kidney Disease (CKD) is a clinical syndrome characterized by irreversible renal dysfunction leading to excretory, metabolic and systemic failure as a result of accumulation of nitrogenous waste products & presenting with a myriad of clinical features with decreased creatinine clearance. End stage renal disease (ESRD) represents a clinical state characterized by irreversible loss of endogenous renal function, causing the patient to be permanently dependent on renal replacement therapy in order to prevent life threatening uremic complications. Kidney is closely related to the thyroid gland, being the only other organ competing for iodide clearance.<sup>1</sup> Patients with CKD have many symptoms and signs suggestive of thyroid dysfunction. Various studies of thyroid functions in uremic patients have been done having shown conflicting results. Hyperthyroidism, hypothyroidism and euthyroid states have all been reported by various studies<sup>3, 4</sup>. Prevalence of hypothyroidism in end stage renal disease has been estimated to range between 0 and 9.5 percent.<sup>2</sup>

There is also increased prevalence of goiter in these patients. The incidence of goiter has also been variously reported in literature.<sup>5, 6</sup>. In view of the variability of thyroid profile in patients with CKD in previous studies, we decided to undertake a prospective clinical and biochemical study of thyroid function in CKD patients at Sree Balaji Medical College & Hospital, Bharath University, Chrompet, Chennai

## AIMS AND OBJECTIVES

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## MATERIALS AND METHODS

### SETTING

The study was conducted among inpatients admitted at Sree Balaji Medical College & Hospital, Bharath University, Chrompet, and Chennai.

### STUDY DESIGN

Single Center  
Non-Randomized prospective study

### STUDY PERIOD

Our study was conducted between March 2014 and August 2014 for a period of 6 months.

### SAMPLE SIZE

A total of 75 patients were included in the study after they were screened using the exclusion and inclusion criteria.

Patients who fulfilled the criteria for CKD and on conservative management were taken into the study.

### Criteria for chronic kidney disease:

1. Presence of objective kidney damage for at least three months. Kidney damage being defined as pathologic abnormalities or markers of damage including abnormalities in blood or urine tests or imaging studies. Imaging study is usually an ultra sonogram abdomen showing.

- a. Bilateral contracted kidneys, or;
- b. Poor corticomedullary differentiation or;
- c. Type II or type III Renal parenchymal changes or;

2. Glomerular filtration rate (GFR) less than 60ml/min/1.73m<sup>2</sup> for at least three months with or without kidney damage.

#### **INCLUSION CRITERIA**

CKD patients who were on conservative management.

#### **EXCLUSION CRITERIA**

- i. Patients with Acute Renal failure (ARF)
- ii. CKD patients who underwent peritoneal dialysis or hemodialysis.
- iii. CKD due to diabetes mellitus
- iv. Patients with documented hypothyroidism
- v. Patients on beta-blockers, amiodarone, steroids, dopamine, phenytoin and iodine therapy.
- vi. Other conditions like acute illnesses, recent surgery, trauma and burns.

#### **DESCRIPTION OF THE STUDY**

Detailed clinical history was taken from all the patients who were included in the study. A detailed General Examination was done including Nourishment, pallor, facial puffiness, pedal edema and skin texture. Presence of thyroid swelling (Goiter) was noted. Vital signs like pulse, blood pressure, and temperature were taken. All the systems were examined carefully including fundus oculi and deep tendon reflex to find out the delayed relaxation of Ankle jerk. Routine investigations were done. After selecting the patients fulfilling the above criteria for the study, about 5 ml of blood sample was collected in a non heparinised sterile bottle and sent for thyroid profile after an overnight fasting of 8-12 hours. Components of thyroid profile in this study include serum T3, fT3, T4, fT4 & TSH

Quantitative determination of the serum T3, T4, fT3, fT4 and TSH was done by Radio Immuno Assay / Immuno Radio Metric Assay.

#### **RESULTS AND OBSERVATIONS**

Our study had a male preponderance, 80% of the study group being men ie 60 male patients with the remainder 15 being female patients (20%). Ultrasound abdomen showed evidence of CKD in all the 75 patients. Bilaterally contracted kidneys were present in 65 (86.7%) patients. Remaining 10 patients (13.3%) had poor Cortico medullary differentiation.

Among the 75 patients, low serum T3 level was found in 40 patients (53.3%). Eight patients among the low serum T3 level also had high TSH value of more than 4.05  $\mu$ IU/ml with low free T4 level and also symptoms suggestive of hypothyroidism. These patients as per the criteria were grouped under "Primary hypothyroidism" and excluded from further study.

The remaining 32 patients with low T3 had normal TSH and hence they were all grouped under "Low T3 Syndrome".

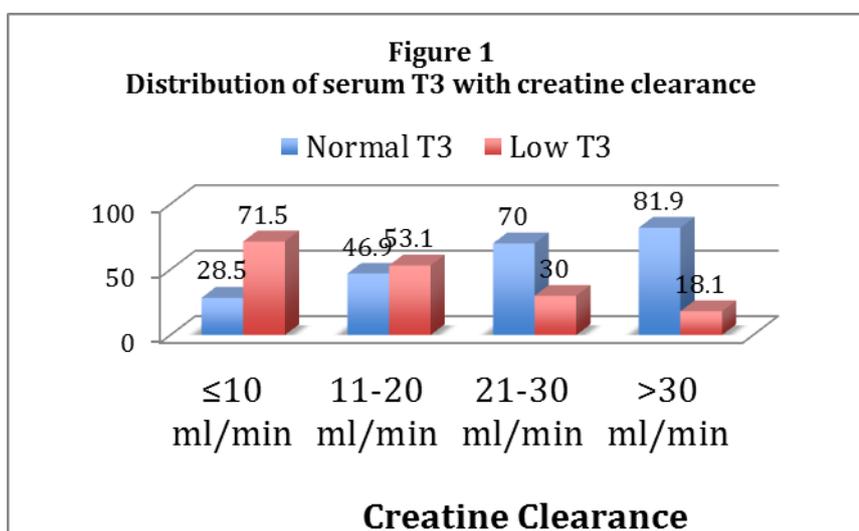
#### **Observation of T3 in the Study**

T3 level in this study varied from 0.2 to 2.0 ng/ml. The mean value of T3 is 0.68 ng/ml. Excluding the patients with primary hypothyroidism, the mean value was 0.72 ng/ml. This value is within the low normal limit. The patients with low serum T3 (low T3 syndrome) were analysed with creatinine clearance.

Excluding hypothyroidism, serum T3 levels were studied in relation to creatinine clearance (Table - 1). The mean value progressively decreases as the renal failure progresses with statistical significance, the P value being 0.002. None of the patients had serum T3 levels above the normal.

**TABLE - 1 CORRELATION OF THYROID PROFILE WITH SEVERITY OF RENAL FAILURE EXCLUDING HYPOTHYROIDISM**

Creatinine Clearance ml/min	Mean T3 ng/ml	Std. Deviation	Mean T4 µg/dl	Std. Deviation	Mean TSH µIU/ml	Std. Deviation
≤ 10 (n=14)	0.45	0.28	5.45	2.11	2.08	1.05
11-20 (n=32)	0.64	0.41	5.84	2.17	2.25	1.31
21-30 (n=10)	1.0	0.49	5.94	1.64	2.05	1.06
> 30 (n=11)	0.99	0.50	7.45	0.99	2.49	0.79
Statistical Significance	* P Value 0.002		P Value 0.079 Not Significant		P Value 0.561 Not significant	



**Observation of T4 in the Study**

Serum T4 level in the study varies from 0.8 to 9.2 µg/dl. Mean value of serum T4 among the 75 patients is 5.70 µg/ dl. Excluding hypothyroid patients the mean value is 6.12 µg/dl. This value is within low normal level of T4.

Excluding 8 hypothyroidism patients who have low T4 values, 16 (21.33%) other patients had T4 level below normal and low T3 syndrome. Number of patients with low T4 does not correlate with severity of renal disease (Table 1). The mean value of T4 excluding hypothyroidism patients was normal at all the stages of renal failure (Table - 1) except, when the creatinine clearance was below 10 mg/ml where it was below normal. The mean serum T4 was not significant with severity of renal disease, P value being 0.079. None of the patients had T4 value above normal level.

**Observation of TSH in the Study**

The value of TSH varied from 0.5 to 28.5 µIU/ml with the mean of 4.65 µIU/ml. Excluding hypothyroidism the mean TSH value is 2.11 µIU/ml. This is in normal range. In spite of low serum T3 level in 40 (53.33%) patients, serum TSH is normal in 67 (89.3%) patients. It is elevated more than 20 µIU/ml in 8 (10.67%)

patients. In our study the mean value of serum TSH is within normal limits in all groups of progressive renal disease (Table - 9). The values of TSH did not show any linear correlation with creatinine clearance.

## DISCUSSION

Various authors have studied thyroid dysfunction in chronic kidney disease. All the studies conducted thus far have shown conflicting results. Thyroid dysfunction in CKD was extensively studied by Ramirez et al.<sup>6</sup> He studied thyroid abnormalities and extensively researched about hypophyseal abnormalities in uremia. He compared CKD patients on conservative management with those on hemodialysis. His studies revealed low T3 and T4 levels but TSH being within normal limits. His study showed linear correlation between the mean T3 and T4 and severity of renal failure whilst TSH did not show any linear correlation with the severity of renal failure.

Avasthi G et al., from Ludhiana studied thyroid function in patients of chronic kidney diseases.<sup>3</sup> Mean serum T3 and T4 values were significantly decreased in his study. This study revealed high serum TSH levels suggesting maintenance of pituitary thyroid axis. This result is comparable with Joseph et al., study.<sup>7</sup> In contrast, Spector et al.<sup>8</sup> and Ramirez et al.<sup>6</sup> reported normal levels of serum TSH in patients of CKD in spite of low serum T3 levels. They demonstrated abnormality in the hypophyseal mechanism of TSH release in uremia patients as the TSH response to the administration of thyrotropin releasing hormone (TRH) was blunted.

PD Rath and PK Padhi from Cuttack did a study on thyroid function status in chronic kidney disease on conservative management. They concluded both serum T3 and T4 were decreased, TSH was not significantly increased.

Joseph LJ, Mehta HJ from Bombay conducted a study on total and free thyroid hormone levels in CKD.<sup>7</sup> They had taken thyroid profile in 127 CKD patients. Their results showed decreased T3 and T4 with no significant change in TSH value. This study's results are consistent with the results of Xess A and Gupta A from Patna's study on evaluation of thyroid hormones in CKD.<sup>9</sup> They analysed 62 patients on conservative management and 34 patients on chronic hemodialysis. They also concluded that chronic hemodialysis did not have a positive effect in alteration of serum T3, T4 and TSH levels.

Spector DA et al., studied 38 patients with CKD for thyroid function and metabolic state.<sup>8</sup> Mean values for serum T4 and T3 were within normal limits. But 43% of the patients had low serum T3. Serum TSH concentrations were normal. Kayimo JE et al., from Nairobi, Kenya conducted a study in 52 patients with CKD. This study results showed T3 and T4 were low and TSH levels were significantly higher.

Kaptien EM et al., from Los Angeles, USA studied thyroid hormone metabolism and thyroid disease in CKD.<sup>10</sup> In his study, serum T3 and T4 are reduced, with blunted TSH response to TRH. He concluded dialysis therapy minimally affects thyroid hormone metabolism and thyroid hormone metabolism normalizes with renal transplantation.

In our study patients only on conservative management were studied. This is because thyroid profile undergoes changes due to dialysis.

In our study 53.3% of the patients have thyroid profile abnormalities. Remaining 46.7% of patients had normal thyroid profile. Among the patients with thyroid dysfunction hypothyroidism is present in 10.7% of patients. Excluding the primary hypothyroidism patients 42.7% of patients had decreased serum T3 values (low T3 syndrome).

Among these low T3 syndrome patients 21.3% of patients also have decreased serum T4 value (low T4 syndrome). The percentage of patient who have low T3 syndrome increases with the decrease in creatinine clearance, which is statistically significant. The increase of low T4 percentage does not show this linear relationship with creatinine clearance.

Many studies conducted in CKD patients showed low T3 values. Low T4 had been reported in Ramirez et al., Hegedus et al., Backett et al., and studies.

In our study the mean T3 value is below normal limit. After excluding hypothyroidism patients the mean T3 value is within low normal limits. Mean T3 value progressively decreases with decline in creatinine clearance. This mean T3 value has a linear correlation with severity of renal disease, which is statistically significant. This linear correlation between mean T3 and severity of renal failure is consistent with the studies of Ramirez et al., and Spector et al.

The mean T4 level in our study is below normal in creatinine clearance less than 10 ml/min group. In all other levels of creatinine clearance the mean T4 value is in low normal level and T4 does not correlate with the severity of renal failure. This is consistent with Avasthi et al., study.

Excluding hypothyroidism mean TSH level in our study is within normal limits. The mean TSH levels are also within normal limits for the various ranges of creatinine clearance. The TSH level does not show any linear correlation with the severity of renal failure. This is consistent with the studies of Spector et al. and Ramirez et al.

In our study excluding those with hypothyroidism, no patients had elevated TSH.

In our study anemia was almost universal in CKD patients. The degree of anemia had a linear correlation with both mean T3 and mean T4 values, which were statistically significant.

Our study was consistent with the results of Ramirez et al., study showing low T3, low T4 and normal TSH. From the various studies it has been suggested that these thyroid profile derangements are part of the body adaptation mechanism.

#### **CONCLUSIONS**

- [1] Thyroid dysfunction occurs in 53.3% of chronic kidney disease patients. Incidence of hypothyroidism is 10.7% in CKD patients, which is higher than that of general population.
- [2] Excluding patients with hypothyroidism serum T3 level is low (Low T3 Syndrome) in 42.7% of patients and serum T4 is low (Low T4 Syndrome) in 21.3% of patients with CKD. Serum TSH level is normal in all stages of CKD excluding primary hypothyroidism.
- [3] Number of patients with low T3 progressively increases with severity of renal failure. Mean Serum T3 level has a linear correlation with the severity of renal disease. But number of patients having low T4 and low mean serum T4 levels does not correlate with the severity of renal failure.