

# “ Study of Thyroid Dysfunction in Patients with Chronic Kidney Disease”

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**Abstract:** *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. In view of variability of thyroid profile in CKD patients in previous studies, a prospective study of various thyroid function has been undertaken to establish a correlation if any between thyroid dysfunction and severity of renal diseases. Total number of 210 patients with Chronic Kidney Disease fulfilling the criteria for CKD who were admitted in Department of Medicine, MGM Aurangabad, tertiary care hospital, during the period of May 2014-May 2016 were selected in this study. The result showed that out of the 210 patients with CKD 60 patients had thyroid dysfunction which accounted for 28.57%. Prevalence of hypothyroidism was 28.57%. The most common thyroid derangement was low T3. The number of patients with hypothyroidism progressively increased with the severity of renal failure.*

**Keywords:** Chronic kidney disease, low T3 syndrome, Thyroid dysfunction.

## Introduction

Chronic kidney disease includes a spectrum of distinct pathophysiological processes which is associated with abnormal kidney function and a progressive reduction in glomerular filtration rate<sup>1,2</sup>. CKD 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. End stage renal disease is described as a terminal stage of chronic kidney disease that without any replacement therapy patients could not survive would result in death. 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<sup>3-6</sup>. The thyroid hormones are essential for growth and development of the kidney and for maintaining electrolyte and water homeostasis. 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. Chronic kidney disease 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. Various studies have been conducted to study thyroid function abnormalities in chronic kidney disease patients. All abnormalities like hypothyroidism, hyperthyroidism and euthyroid state have been reported in the studies done previously. Primary hypothyroidism (non-autoimmune) is commonly observed in CKD patients. Especially, the prevalence of subclinical hypothyroidism increases consistently with decline in GFR.<sup>7</sup>

## Inclusion criteria

All diagnosed patients of chronic kidney disease with no previous history of thyroid dysfunction.

### Exclusion criteria

Liver diseases (Acute and chronic liver disease), Drugs altering thyroid profile like Amiodarone, Steroids, Phenytoin, Estrogen pills, Iodine containing drugs.

### Case definition

Patients aged  $\geq 18$  years with chronic kidney disease. Chronic Kidney Disease was defined as  $eGFR \geq 90 \text{ mL/min/1.73m}^2$  with abnormal urine and blood chemistry, persistent proteinuria or abnormal imaging studies of the kidney OR  $eGFR \leq 90 \text{ mL/min/1.73m}^2$ .

### Screening

Determination of serum creatinine level was done and eGFR estimated using the Cockcroft-Gault equation<sup>15</sup> with subsequent CKD staging. The data for this study was collected by patient evaluation which was done by detailed history taking, Clinical examination, and relevant investigations .5 millilitres of blood was aseptically drawn from the participant's vein into a well labelled plain vacutainer Blood in the labelled plain vacutainer was left to clot and serum pipetted into well labelled cryovials for refrigeration at  $-20^{\circ}\text{C}$  in the laboratory. Serum Creatinine was measured by Enzymatic VITROS IFCC IDMS method. Serum TSH, T4, fT4, T3, fT3 were measured by Chemiluminescence Immunoassays (CLIA) Method.

Laboratory Reference values are fT3 :2.77 to 5.27 pg/ml; fT4 :0.78 to 2.19 ng/dl; TSH : 0.4 to 4 MIU/ml

Sr. Creatinine : 0.8 to 1.5 mg/dl

### Materials And Methods

Patients who were on conservative management fulfilling the criteria for CKD admitted in tertiary care hospital. The present study is conducted on 210 patients, who are diagnosed to have CKD and on conservative management, being admitted in Department of Medicine, MGM Hospital Aurangabad during the period of July 2014 to May 2016. Data was entered into Microsoft Excel 2007 sheet. Statistical test like percentages and chi-square test were used for analysis by Epi Info 7 version.

### Results And Analysis

Total 210 patients of CKD were included in the study. Study duration was 2 years. This was a cross sectional study. The findings of this study, presented as results and are discussed in detail with appropriate comparison with the findings of the relevant studies.

#### Relationship between thyroid dysfunction and age group.

Age	Normal	Thyroid Dysfunction	Total
18-34	45 (30%)	12 (20%)	57(27.14%)
35-51	52 (34.67%)	26 (43.3%)	78(37.14%)
52-68	40 (26.67%)	21 (35%)	61(29.05%)
69-85	13 (8.66%)	1 (1.7%)	14(6.67%)
Total	150 (100%)	60 (100%)	210(100%)

$\chi^2=6.6202, d[f]3, P=0.085$

The relationship between thyroid dysfunction and age group was not statistically significant. (P = 0.085)

**Sexwise distribution of thyroid dysfunction.**

No.of cases	Male	Female	Total
Thyroid Dysfunction	37 (28.46%)	23 (28.75%)	60 (28.57%)
Normal	93 (71.54%)	57 (71.25%)	150 (71.43%)
Total	130 (100%)	80 (100%)	210 (100%)

As shown in above table, this study had 28.75% of thyroid dysfunction in females and 28.46% thyroid dysfunction in males.

**Correlation of thyroid dysfunction with the GFR and stage of CKD.**

All the 210 cases included in study were classified into stages of CKD according to the GFR of the cases. GFR was calculated by

Cockcroft-Gault formula in all cases i.e, Estimated creatinine clearance (mL/min)=  $\{((140-\text{age}) \times \text{weight}) / (72 \text{ SCr})\} \times 0.85$  if female where CrCl is expressed in milliliters per minute, age in years, weight in kilograms, and serum creatinine (SCr) in milligrams per deciliter<sup>8</sup> Staging of CKD was done according to KDIGO guidelines.<sup>9</sup>

**Cases of hypothyroidism categorised according to GFR and stage of CKD**

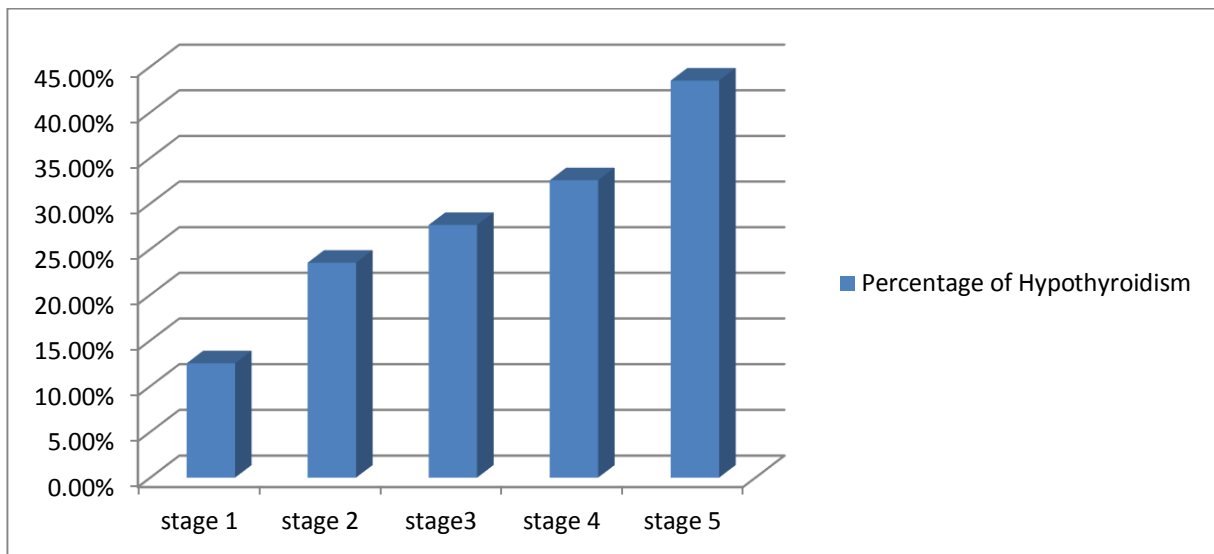
Stage of CKD	GFR(ml/min/1.73m <sup>2</sup> )	Total	Normal	Hypothyroidism cases	Percentage of hypothyroidism
1	> or = 90	40	35	5	12.50%
2	60 – 89	34	26	8	23.52%
3	30-59	47	34	13	27.65%
4	15 – 29	43	29	14	32.55%
5	< 15	46	26	20	43.47%
Total		210	150	60	

$\chi^2=10.8488, d[f]4, P=0.0283$

As shown in table no 6, out of 46 CKD cases of stage 5, 20 were found to be hypothyroid and was having maximum percentage of hypothyroidism i.e, 43.47%. While in stage 1 out of 40 cases of CKD, 5 cases were having hypothyroidism i.e, 12.50% which was least percentage among all. Study by Lo et

al.(2005) found that the prevalence of hypothyroidism increased with lower levels of GFR (in units of mL/min/1.73 m<sup>2</sup>), occurring in 5.4 % of subjects with GFR greater than or equal to 90, 10.9 % with GFR 60–89, 20.4 % with GFR 45–59, 23.0 % with GFR 30–44, and 23.1 % with GFR < 30 (p < 0.001 for trend).<sup>10</sup>

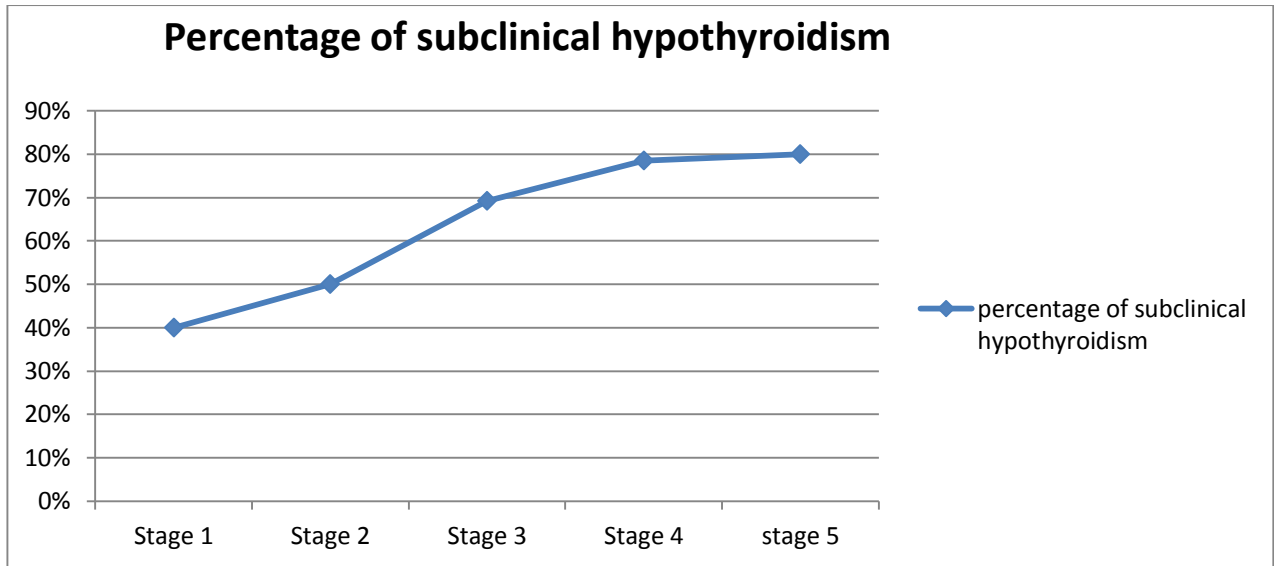
**Bar diagram showing stagewise distribution of hypothyroidism**



As shown in above bar diagram as stage of CKD increased from 1 to 5 the percentage of patients having hypothyroidism was also increased. With declining GFR there is increase in prevalence of hypothyroidism as stated above.

### Distribution of subclinical hypothyroidism

The above table shows percentage of subclinical hypothyroidism in hypothyroidism cases. It was maximum in stage 5 (80%) and it was minimum in stage 1 (40%). Out of 60 cases of hypothyroidism 42 i.e, 70% cases were found to have subclinical hypothyroidism.



Stage of CKD	GFR	No. of subclinical hypothyroidism	Total cases of hypothyroidism	percentage
1	> or = 90	2	5	40%
2	60 – 89	4	8	50%
3	30-59	9	13	69.23%
4	15 – 29	11	14	78.57%
5	< 15	16	20	80%
<b>Total</b>		<b>42</b>	<b>60</b>	<b>70%</b>

As shown in line diagram above as Stage of CKD was increased from stage 1 to stage 5 the prevalence of hypothyroidism also increased. Among 120 CKD patients which were

studied, 42 patients were found to have subclinical hypothyroidism. Overall prevalence of subclinical hypothyroidism in CKD was 35% in this study. This prevalence

was higher than most of the studies done previously. A study published in 2008 in which among 3089 adult participants, 293 (9.5%) had subclinical primary hypothyroidism and 277 (9%) had an estimated GFR < 60 ml/min per 1.73 m<sup>2</sup><sup>11</sup>.

### **Relationship between stage of chronic kidney disease and thyroid dysfunction**

The study included 210 cases of CKD out of which 60 cases were of hypothyroidism and no case of hyperthyroidism was reported. This result was similar to study done by Mohammed Shamsuddin et al (2014) which concluded that mean of T3 and T4 decreased and TSH increased significantly in cases compare to control. 10% of patients of CRF cases were hypothyroid compare to 0% in controls. There was no hyperthyroidism both in cases & controls<sup>12</sup> Khatiwada S et al (2015) performed a cross-sectional study among 360 chronic kidney disease and thyroid dysfunction was found in 38.6 % CKD patients, the most common being subclinical hypothyroidism (27.2 %), followed by overt hypothyroidism (8.1 %) and subclinical hyperthyroidism (3.3%).<sup>13</sup>

### **Prevalence of thyroid dysfunction**

The study included 210 cases of CKD out of which 60 cases were having thyroid dysfunction. So, overall prevalence of thyroid dysfunction was 28.57%. However all cases of

thyroid dysfunction were having hypothyroidism. This suggests that prevalence of hypothyroidism in this study was also 28.57%

### **Conclusion**

Most of the participants in this study were euthyroid. There were abnormalities in the thyroid hormone profiles in 28.57% of the participants. The most common thyroid hormone derangement was low T3 values (non-thyroidal illness). The prevalence of hypothyroidism in this study was 28.57% which was higher than has been reported previously. Hyperthyroidism which was found in some previous studies was not found in this study.

### **Study limitations**

Other disease processes e.g. vasculitis and medications that reduce the peripheral conversion of T4 to T3 may interfere with interpretation of the thyroid hormone profiles. However efforts were made to exclude the patients with these diseases from the medical history of the participants. The effect of Hemodialysis as well as peritoneal dialysis on thyroid profile was not studied.

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