



## STUDY OF HYPOTHYROIDISM IN CHRONIC KIDNEY DISEASE PATIENTS

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### ABSTRACT

The interactions between kidney and thyroid functions are known for years. Thyroid hormones (TH) influence kidney function both during embryonic development and in the mature functioning of the kidney. When the thyroid is either hyper- or hypo-functioning, changes in different clinical renal parameters occur. Vice versa, kidney disease influences circulating thyroid hormones. Aim of the study is to study the prevalence of hypothyroidism in CKD patients of varying stages and to study the trend of prevalence as the renal impairment increases. The study was done in Gandhi Hospital, Secunderabad and Princess Esra hospital Hyderabad over a period of one year from December 2013-December 2014. 50 patients who have CKD Stage I to V were chosen. They are advised to get thyroid profile. Prevalence of hypothyroidism in chronic kidney disease patients is about 19%. Prevalence of hypothyroidism increases as the severity of the renal impairment increases. Its prevalence in CKD Stage IV, V patients is 18%, 31% respectively. Hypothyroidism is more common in female patients with CKD compared with males. Hypothyroidism is more common in diabetic patients with CKD compared with non-diabetic patients with CKD.

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### INTRODUCTION

The interactions between kidney and thyroid functions are known for years<sup>1,2,3,4</sup>. Thyroid hormones (TH) influence kidney function both during embryonic development and in the mature functioning of the kidney, indirectly by affecting the cardiovascular system through its influence on renal blood flow (RBF), and directly by affecting glomerular function, the tubular secretory and absorptive capacities, electrolyte pumps and kidney structure (den Hollander *et al.*, 2005). When the thyroid is either hyper- or hypo-functioning, changes in different clinical renal parameters such as glomerular filtration rate (GFR), urine specific gravity (USG), urinary protein/creatinine ratio (UPC) and markers of tubular function can occur. Vice versa, kidney disease influences circulating thyroid hormones.

#### Aim of the study

1. To study the prevalence of hypothyroidism in CKD patients of varying stages.
2. To study the trend of prevalence as the renal impairment increases

### MATERIALS AND METHODS

The study was done in Gandhi Hospital, Secunderabad over a period of one year from December 2013-December 2014. 50 patients were chosen.

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The patients detected to have CKD Stage I to V.

#### Exclusion Criteria

1. Women who are pregnant
2. Subjects who are receiving drugs that could contribute to hypothyroidism (lithium, amiodarone, or iodine)
3. Subjects receiving antithyroid drugs (methimazole or propylthiouracil)

### METHODS

Diagnosed patients of chronic kidney disease from stage I to stage V are advised to get thyroid profile done to know the prevalence of clinical and subclinical hypothyroidism in the study population.

#### Parameters under the Study

Thyroid profile—Sr. TSH, Sr. T<sub>3</sub>, Sr. T<sub>4</sub>

Blood urea, Sr. creatinine

EGFR

Patients with chronic kidney disease confirmed by:

1. Ultrasonography of kidneys.
2. GFR was measured by MDRD equation :-  $EGFR (mL/min/1.73m^2) = 186 \times (\text{serum creatinine [mg/dL]})^{-1.154} \times (\text{age})^{-0.203} \times 0.742 (\text{if female}) \times 1.21 (\text{if African American})$

We also exclude women who were pregnant (given potential pregnancy-related changes in thyroid function) and subjects who were receiving concurrent treatment with drugs that could contribute to hypothyroidism (amiodarone, or iodine). The

treatment taken by patients included iron salts, vitamins, calcium and furosamide (40-160 mg/day) when indicated; and anti-hypertensive agents as required. Each patient was interviewed. Duration of CKD was reviewed carefully. Investigations (blood urea, serumcreatinine, totalT3, totalT4, TSH) were done.

The normal reference range for TSH-- 0.35to5.5μIU/ml, The normal reference range for total T4--4.5 to 10.9μg/dL, The normal reference range for total T3--0.60 to 1.81ng/ml.

Hypothyroidism was defined as a TSH level >5.5 m IU/ml or treatment with thyroid hormone (levothyroxine). Both subclinical and clinical hypothyroid cases included. Method of testing is by chemiluminescence immune assay (CLIA) in standard lab.

**Statistical analysis**

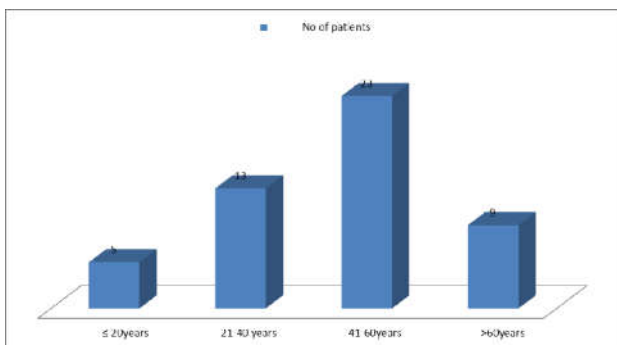
Statistical analysis was performed using the Graph PadInStat software version 3.10 for Windows. Data are expressed as mean+/- SD. The Fisher's exact test was used for comparison of categorical variables. Student's unpaired t-test was used to compare continuous variables. Statistical significance was set at P<0.05

**RESULTS**

A total of 50 patients of Chronic Kidney disease of various stages were studied. Of the 50 patients studied, 31 were males and 19 were females. Age distribution of the patients given below.

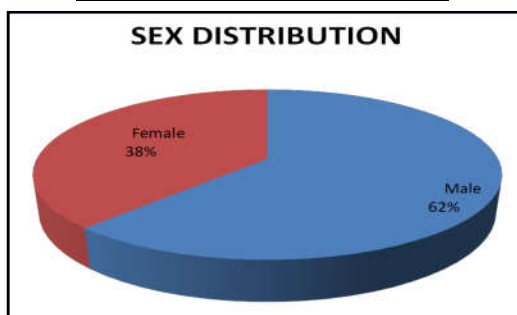
**Age distribution of the patients studied**

Age Range	No of patients	% of patients
≤ 20years	5	10%
21-40years	13	26%
41-60years	23	46%
>60years	9	18%



**Sex distribution of the patients studied**

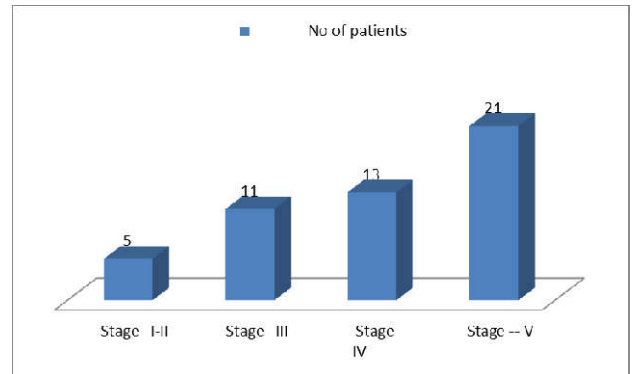
Sex	No of patients	% of patients
Male	31	62
Female	19	38
Total	50	100



Out of the 50 patients studied 19 were female (38%), 31 were male (62%).

**Distribution according to stage of CKD**

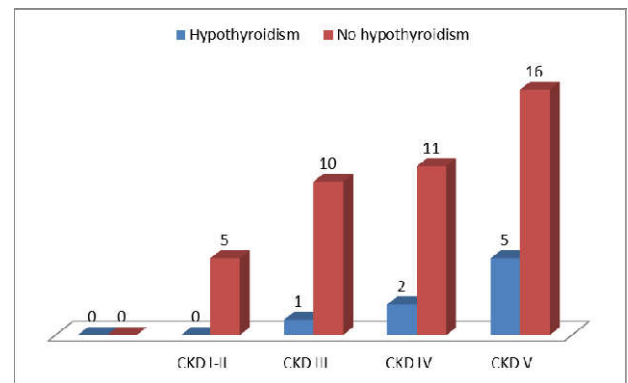
CKD Stage	No of patients	% of patients
Stage-I-II	5	10
Stage-III	11	22
Stage-IV	13	26
Stage-- V	21	42



Of all patients, 5 are from CKD stage I or II, 11 from CKD stage III, 13 from CKD stage IV, 21 from CKD stage V. Of the 21 patients with CKD stage V, 17 are on maintenance hemodialysis and the remaining are on conservative management.

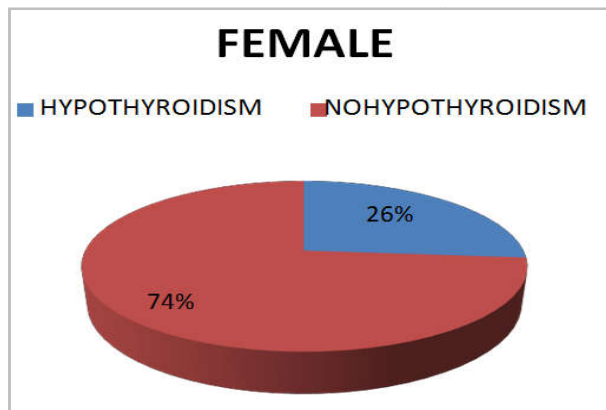
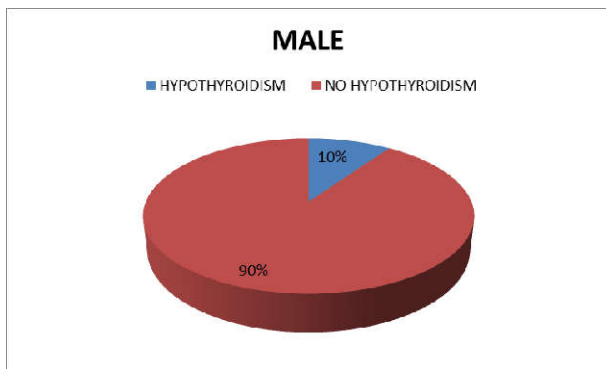
**Hypothyroidism according to CKD Stages**

CKD stage	Hypothyroidism TSH >5.5mlu/ml	Nohypothyroidism TSH < 5.5mlu/ml	% Hypothyroidism
CKD I-II	0	5	0
CKD III	1	10	10
CKD IV	2	11	18
CKD V	5	16	31
Total	8	42	19



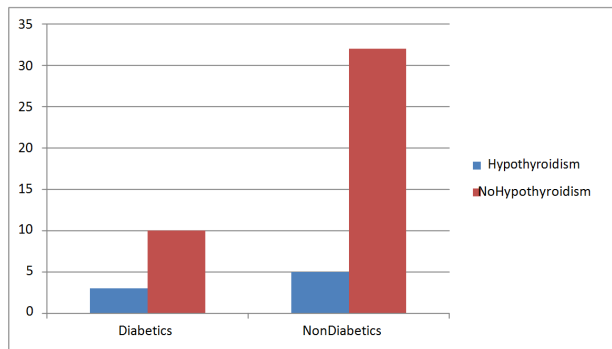
**Distribution according to SEX**

	Hypothyroidism	No hypothyroidism
Male	3	28
Female	5	14
Total	8	42



**Distribution according to diabetic status**

	Hypothyroidism	No Hypothyroidism	Total
Diabetics	3	10	13
Nondiabetics	5	32	37
Total	8	42	50



**Study characteristics**

Characteristic	Hypothyroidism	No hypothyroidism	P value
Age, mean ±SD	55.5±13.959	41.61± 14.565	0.0165
Female, N (%)	5(62.5%)	14(33.3%)	0.2317
TSH(μ IU/ml)	36.36 ±39.72	3.03 ± 1.30	R.R-2.719
TOTALT4 (μg/ml)	4.38±0.499	9.74±1.96	<0.0001
TOTALT3 (ng/ml)	0.51±0.11	1.10±0.249812	<0.0001
EGFR(MDRD) (ml/mt)	15.34 ±9.70	24.74 ±16.76	0.1326
Diabetis,N	3	10	0.413
			R.R-1.575

**DISCUSSION**

Among there presentative sample of patients with CKD, we found an increased prevalence of hypothyroidism in persons with reduced estimated GFR, independent of age and gender.

According to previous studies, like Michel Chonchol *et al*<sup>5</sup>, JoanC. Lo *et al*<sup>6</sup>, It has been estimated that the prevalence of subclinical primary hypothyroidism ranges between 4% and 10% in the general population.

Michel Chonchol *et al*<sup>5</sup> studied 3089 adults. 293 (9.5%) had subclinical primary hypothyroidism. The prevalence of subclinical hypothyroidism in patients with GFR>90ml/min/1.73m<sup>2</sup> is 7%. Whereas, in patients with aGFR<60ml/minper1.73m<sup>2</sup> the prevalence of hypothyroidism is 17.9%.(P<0.0001for trend).

JoanC.Lo, Glenn M.Chertow, Alan S. Go, and Chi-YuanHsu<sup>6</sup> studied 14,623 adults. The mean age was 48.7 years and 52.6% were women. The prevalence of hypothyroidism in different stages of CKD include-5.4% with GFR≥90, 10.9% with GFR 60-89,20.4% with GFR45-59,23.0% with GFR30-44, and 23.1% with GFR<30ml/mt/1.73m<sup>2</sup>(P <0.001for trend). There is increased prevalence as the GFR declines.

With progressively lower estimated GFR, there was agraded increased likelihood of hypothyroidism. Accordingly, there wasa significant inverse association between estimated GFR and TSH levels through out the normal and high TSH ranges.

In the present study, all the patients selected are diagnosed to have renal impairment of varying severity. Total number of patients studied-50. Average age of the patients studied-43.84±15.22 years. 33.3% are women. Whereas in the study by Joan c.lo *et al*<sup>6</sup> the the mean age was 48.7years, and 52.6% were women. In AliA.Allawi study<sup>7</sup> in Iraqi patients with CKD the mean age is 60 years, and 42% were women. In studies by Michel Chonchol *et al* and Joan C.Lo *et al*, study population are general population with varying degrees of GFR.

Whereas in the present study and AliA.Allawi study, the population selected were patients suffering from varying degrees of renal failure.

There is increasing prevalence of hypothyroidism as the severity of renal impairment increases in the present study. Percentage of hypothyroidism in CKDSTAGEIII, IV, STAGE V patients is 10%, 18%, 31% respectively in our study. These findings are consistent with previous studies like Michel Chonchol *et al*, JoanC.Lo *et al*, AliA. Allawi study. Although numerous contributing factors have been hypothesized, including altered iodine metabolism, decreased peripheral sensitivity to hormones, and auto immune thyroiditis, the exact underlying mechanisms linking advanced CKD and primary thyroid dysfunction remain unclear. In the present study, Hypothyroidism is more common in female patients with CKD compared with males. This finding is not statistically significant (Pvalue-0.2317, R.R-2.719). These findings consistent with those observed in the study by Michel Chonchol *et al*, Joan C. lo *et al*.

In the present study, hypothyroidism is more common in diabetic patients with CKD compared with nondiabetic patients with CKD. This finding is not statistically significant (Pvaue-0.413, R.R-1.575)

Previous studies have reported a higher prevalence of goiter and thyroid hormone abnormalities in persons with end-stage renal disease.

It also showed that Total T3 and Total T4 levels were lower than normal specially among patients with stage 4 & 5 CKD and a progressive reduction in values of Total T3 and

Total T4 were noticed as the severity of renal failure increased.

**Limitations**

Our study has several limitations:

1. The overall sample size is small.
2. The definition of kidney function was based on estimated GFR rather than on more precise measurement of kidney function, such as iothalamate clearance.
3. Nonthyroidal (e.g., low T3 syndrome, which is typically seen in some ill patients, including those with end-stage renal disease) and thyroidal causes of hypothyroidism were not identified.
4. Given that only TSH and total T4 (rather than free T4) levels are tested, complete assessment of thyroid function is not possible. However, TSH concentration is considered the most sensitive indicator of hypothyroidism among individuals in the absence of acute illness.
5. GFR estimated using the MDRD equation, which maybe less precise at higher GFR levels.

Further studies should explore potential causal mechanisms through which CKD maybe associated with increased TSH and reduced thyroid function, including the possible roles of auto immunity, iodine excess, and potential effects of retained solutes, such as organic acids and guanidi nocompounds, on thyroid function.

The roles of clinical or subclinical hypothyroidism on physical function, cognitive function, quality of life, and depressive illness in CKD are unknown. However, health professionals caring for patients with CKD should be cognizant that CKD and hypothyroidism may exhibit overlapping symptom complexes. Future investigations are needed to determine the value of assessing or screening for clinical and subclinical hypothyroidism among persons with CKD and ESRD.

**Summary**

Feature	Michel Chonchol et al	Joanc.Lo et al	AliA.Allawi	Present study
No.of patients	3089	14,623	50	50
Male:female	F>M	F>M	M>F	M>F
Age	54.9±16.2 yr	48.7±18.9 years	60years	43.84±15.22399
TSH(mIU/L) (hypothyroid pts)	8.19±5.72	5.30	-	36.36± 39.72
Hypothyroidpts	293	655	8	8
Hypothyroidism	17.9%in EGFR <60%	23.1%in EGFR <30(ml/mt)	21.79%in EGFR<15ml/mt	31%in EGFR<15ml/mt

**CONCLUSIONS**

1. Prevalence of hypothyroidism in chronic kidney disease patients is about 19%.
2. Prevalence of hypothyroidism increases as the severity of the renal impairment increases. Its prevalence in CKD Stage IV, V patients is 18%, 31% respectively.
3. Hypothyroidism is more common in female patients with CKD compared with males.
4. Hypothyroidism is more common in diabetic patients with CKD compared with non-diabetic patients with CKD.

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