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ORIGINAL PAPER

Prevalence of hypothyroidism in chronic kidney disease: a single centre cross-sectional study

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ABSTRACT

Background: *The kidney normally plays an important role in the metabolism, degradation and excretion of thyroid hormones. Chronic kidney disease (CKD) affects the hypothalamus pituitary thyroid axis and peripheral metabolism of thyroid hormone and thus affects thyroid function in many ways. Despite considerable overlap in the symptoms related to hypothyroidism and advanced chronic kidney disease, relatively little is known about the prevalence of thyroid abnormalities in persons with CKD. In patients with end-stage renal disease, it has been suggested that primary hypothyroidism may be more common in patients with end stage renal disease (ESRD) compared with the general population. Thus this study was conducted to estimate the prevalence of hypothyroid in CKD.* ***Objectives***: *To study the prevalence of hypothyroid in CKD and to see if prevalence increases with advancement of CKD stage.* ***Materials and methods***: *This study is a Cross-Sectional study that was conducted among nondialytic CKD patients attending Nephrology OPD of GMCH from March 2014 to Feb 2016. Out of 1742 CKD patients, 280 patients who met the study criteria were included in the study. Demographic features (age and sex) and medical history of each patient were noted at the time of diagnosis.* ***Results***: *The mean age of patients with overt hypothyroid was 59.64 years, in sub-clinical hypothyroid group was 58.14 years, and in patients with normal thyroid function was 55.51 years. We observed that prevalence of hypothyroidism was increased in patients with reduced GFR, and it increases as estimated glomerular filtration rate (eGFR) decreases ranging from 13.33% in stage 2 to 35.55% in ESRD (end stage renal disease). We also found that 68.8% of hypothyroids have sub-clinical hypothyroidism.* ***Conclusion***: *This study concludes that prevalence of hypothyroid in CKD is more than that of general population and it further increases as eGFR decreases.*

Keywords: *Hypothyroidism; CKD; end stage renal disease; sub clinical hypothyroid*

INTRODUCTION

The thyroid produces hormones (T3 and T4) have many actions including metabolism, development, protein synthesis and the regulation of many other important hormones. The kidney normally plays an important role in the metabolism, degradation and excretion of thyroid hormones. CKD affects the hypothalamus pituitary thyroid axis and peripheral metabolism of thyroid hormone and thus affects thyroid function in many ways.

Thyroid stimulating hormone (TSH) is disturbed in uraemia and the TSH response to the hypothalamic thyrotrophic releasing hormone (TRH) is reduced.[1,2] CKD affects the thyroid function by lowering levels of circulating the thyroid hormones, disrupting metabolism and elimination of thyroid hormones[3] and affect the storage of iodine in thyroid gland.[4] The concentration of serum iodine in patients with CKD is higher due to lower iodine clearance caused by reduced glomerular filtration. Elevated levels of serum inorganic iodine in patients with CKD may potentially block thyroid hormone synthesis (Wolf-Chaikoff effect), which can explain higher prevalence of diffuse goitre and hypothyroidism in these patients.[5] Despite considerable overlap in the symptoms related to hypothyroidism and advanced chronic kidney disease, relatively little is known about the prevalence of thyroid abnormalities in persons with CKD. In patients with end-stage renal disease, it has been suggested that primary hypothyroidism may be more common in patients with

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ESRD compared with the general population.[5] Thus this study was conducted to estimate the prevalence of hypothyroid in CKD.

MATERIALS AND METHODS

A Cross-Sectional study was conducted among nondialytic CKD patients attending nephrology OPD of GMCH from March 2014 to Feb 2016 to investigate for hypothyroid. A total of 1742 CKD patients attended nephrology OPD during study period. Out of 1742 CKD patients, 280 patients who met the study criteria were included in the study. Demographic features (age and sex) and medical history of diabetes mellitus, hypertension and CVD of each patient were noted at the time of diagnosis.

CKD was defined on the basis of MDRD formula. Overt hypothyroidism would be defined by a TSH >5.5 mIU/L and Free T4 <0.89 ng/dl with clinical symptoms. Subclinical hypothyroidism would be defined by a TSH >5.5 mIU/L and Free T4 >0.89 ng/dl (the lower limit of the normal range).

Inclusion Criteria

- All CKD patients (>18 years of age) not requiring dialysis
- TSH levels >5.5 mIU/L

Exclusion Criteria

- Age< 18yrs
- Patient who were on thyroid function affecting drugs like, lithium and high-dose steroids, and pregnant women were excluded from the study
- All secondary cases of hypothyroidism and subjects in whom kidney functions could not be estimated due to missing serum creatinine values or those in whom thyroid stimulating hormone (TSH) or Free T4 levels were not available.
- Patients on dialysis

RESULTS

A total of 1742 non-dialytic CKD patients had attended the Nephrology OPD during the study period. Out of 1742, two hundred and eighty patients met the study criteria and were finally included in the study. The mean age of patients with overt hypothyroid was 59.64 years, in sub-clinical hypothyroid group was 58.14 years and in patients with normal thyroid function was 55.51 years. When age in hypothyroid group (overt and sub-clinical) as a whole is compared with euthyroid group, the difference was statistically significant (p=0.023). Among the hypothyroid patients, 12% were males and 26% were females. The mean age of the patients is shown in **Table 1** and **Table 2**.

Table 1 Comparison of mean age

Condition	Mean age
Overt hypothyroid	59.64
Sub-clinical hypothyroid	58.14
Euthyroid	55.51

Table 2 Sex distribution

Sex	Hypothyroid (n=45)		Euthyroid (n=235)	
	Number	Percentage	Number	Percentage
Male	24	53.33%	175	74.46%
Female	21	46.66%	60	25.53%

The mean TSH in overt hypothyroid group was 24.55 mIU/L, in sub-clinical hypothyroid was 7.59 mIU/L, whereas in euthyroid group was 2.8 mIU/L. When TSH was compared between hypothyroid patients overall, with euthyroid, the difference was significant (p< 0.0001).

The difference in Free T4 between hypothyroid and euthyroid was also statistically significant (p< 0.0001).

Table 3 and **Figure 1** shows mean TSH and FT4.

Table 3 Mean TSH and FT4 in hypothyroid cases

	Hypothyroid	Euthyroid	p value
TSH	12.86±9.78	2.80±1.33	<0.0001
FT4	0.92±0.17	1.32±0.26	<0.0001

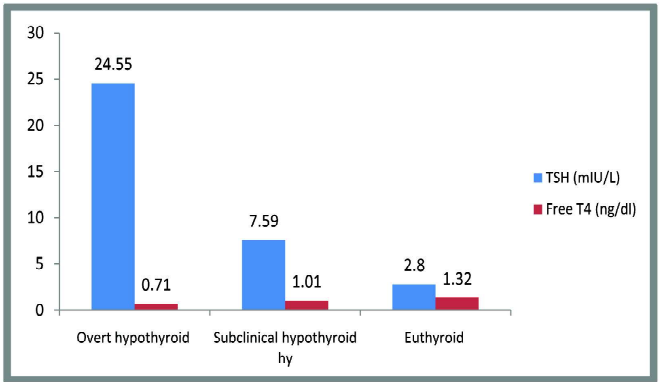

Figure 1 Comparision of mean TSH and FT4 between groups

We observed that prevalence of hypothyroidism was increased in patients with reduced GFR, ranging from 13.33% in stage 2 to 35.55% in ESRD. We found that 68.8% of hypothyroids have sub-clinical hypothyroidism.

When we compared prevalence of hypothyroid in stage 5 CKD to stage 2 CKD, we found that it was significantly higher in stage 5 CKD (P = 0.05). similarly we compared prevalence of hypothyroid in stage 3 CKD to stage 4 and stage 5 CKD, and it was significantly higher in stage 4 (p = 0.021) and stage 5 CKD (p = 0.005).

Table 4 Prevalence of hypothyroid in different CKD stages

CKD stages	Overt hypothyroid (n=14)	Sub-clinical hypothyroidn=31	Euthyroid (n=235)
CKD Stage 2	2 (14.28%)	4 (12.90%)	18 (7.65%)
CKD Stage 3	4 (28.57%)	7 (22.58%)	58 (24.6%)
CKD Stage 4	4 (28.57%)	8 (25.8%)	72 (30.63%)
CKD Stage 5	4 (28.57%)	12 (38.7%)	87 (37.02%)

DISCUSSION

The mean age of patients with hypothyroid in our study was 58.64 years, while in a study by chonchol et al,[6] the mean age was 57.9 years. Also in our study 46.66% % of patients with hypothyroid were female, while in another study by Lo et al[7] 52% of patients were female.

In our study, we found an increased prevalence of hypothyroidism in persons with reduced estimated GFR, independent of age and gender. In addition, with progressively lower GFR there was an increased likelihood of hypothyroidism. In our study we found that the prevalence of CKD in non-dialysis requiring population increases from 13% in patient with GFR > 60, to 35% in patient with GFR< 15. Also chochol et al[6] reported increase in prevalence from 11% (GFR>60) to 23% (GFR < 15). According to a study in India among ESRD patients, prevalence of subclinical hypothyroidism was 24.8 %.[8] A study by Ng et al[9] in peritoneal dialysis (PD) patients of Taiwan reported that 98(80.3 %) were having euthyroidism; 19(15.6 %) subclinical hypothyroidism; and 5(4.1 %), subclinical hyperthyroidism.[9] A study among HD patients in western Nepal showed the combined prevalence of subclinical and clinical hypothyroidism in 26.6 % patients.[10] Higher rate of thyroid dysfunction in CKD patients as observed in our study may also be due to high prevalence of thyroid autoimmunity in study population, excess iodine nutrition or iodine deficiency, and the inclusion of subjects with non-thyroidal illness.[11,12]

We observed decreasing trend for free T3 and free T4 levels (though the decrease were not significant) and increasing trend for TSH level (significant rise) across CKD stages 3–5, which suggest that TSH level increases with the progression of renal impairment (which is indicated by a decrease in GFR).

CONCLUSION

Thyroid dysfunction is common in CKD patients, as compared to person with normal kidney function. This study reveals a significant association between CKD progression and thyroid dysfunction. Hence, high degree of clinical suspicion is needed to diagnose and treat hypothyroidism in CKD.

Ethical Clearance: Taken**.**

Conflict of Interest: None.

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Contribution of Authors: The study was conceived and designed by Dr. PJ Mahanta and Dr. M Sharma; data collection and analysis by Dr. Bishal Agarwalla. All liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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