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Research Article

Thyroid Dysfunction in Chronic Kidney Disease Patients

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Abstract

Introduction: Chronic kidney disease (CKD) poses significant health risks, including early death, reduced quality of life, and higher healthcare costs. It is linked to complications like cardiovascular disease, hyperlipidemia, anemia, and metabolic bone disease. This study aims to assess thyroid function in CKD patients.

Methods: A cross-sectional study was conducted among the CKD patients and apparently healthy participants at Tribhuvan University Teaching Hospital (TUTH), Kathmandu. Demographic features were noted, and patients' blood samples were analyzed for Thyroid Stimulating Hormone (TSH), Free Thyroxine (fT4), Free triiodothyronine(fT3) and creatinine.

Result: Among the total 110 CKD patients, thyroid dysfunction was observed in 29 (26.36%) patients. The prevalence of thyroid dysfunction significantly increased with CKD progression, rising from 13.33% in stage 3 to 40.54% in stage 4. However, a decline in prevalence was observed in stage 5, with thyroid dysfunction detected in only 10 (32.25%) patients. Subclinical hypothyroidism (17.27%) was the most prevalent form of thyroid dysfunction, followed by overt hypothyroidism (3.6%). A significant inverse correlation was found between the stage of CKD and mean free T3 levels (p-value < 0.05), indicating a progressive decline in free T3 with advancing CKD.

Conclusions: This study found a strong link between CKD and thyroid dysfunction, especially hypothyroidism. The prevalence of thyroid dysfunction was higher in people with more severe CKD. This highlights the need for regular thyroid checkup in individuals with CKD.

Keywords: Chronic Kidney Disease; Thyroid Dysfunction; Subclinical Hypothyroidism; TSH

Abbreviations

AKI: Acute Kidney Injury; CKD: Chronic Kidney Disease; CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration; CVD: Cardiovascular Disease; ECI: Enhanced Chemiluminescent Immunoassay; eGFR: Estimated Glomerular Filtration Rate; fT3: Free Triiodothyronine; fT4: Free Thyroxine; GFR: Glomerular Filtration Rate; GHCC: General Health Checkup Clinic; NHANES III: Third National Health and Nutrition Examination Survey; OPD: Out Patient Department; T3: Triiodothyronine; T4: Thyroxine; TSH: Thyroid Stimulating Hormone; TUTH: Tribhuwan University Teaching Hospital; US: United States

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem associated with premature mortality and decreased quality of life [1,2]. Existing literatures suggest that Diabetes, Hypertension, Malnutrition and Acute Kidney Injury (AKI) are the risk factor for developing CKD [3-5]. Thyroid hormones are necessary for growth and development of the kidney and for maintenance of water and electrolyte homeostasis [6,7]. It is suggested that decline in kidney function is accompanied by changes in the synthesis, secretion and metabolism of thyroid hormones leading thyroid dysfunction [8,9]. Several studies have reported a higher prevalence of primary hypothyroidism, both overt and subclinical in patients with CKD [10-12].

Given that numerous studies over the years have reported reduced thyroid function in CKD, there remains a lack of sufficient research on this association in the Nepalese CKD population.

This study was carried out to find an association between thyroid function and CKD in Nepalese scenario.

Methodology

A cross sectional observational study was conducted in Tribhuvan University Teaching Hospital (TUTH), Kathmandu, Nepal. Patients diagnosed with CKD visiting Nephrology Outpatient department of TUTH were included in the study. Individuals who have come for health checkup in General health checkup Clinic (GHCC) and with normal test parameters were taken as control. A total of 110 patients with CKD and 30 healthy adults were enrolled during the period of this study from February to December 2016. Approval was taken from the Institutional Review Committee of Maharajgunj Medical Campus. Written consent was taken from each participant.

Demographic features of patients were noted and blood samples (5 ml) were drawn. CKD was defined as structural damage or GFR<60ml/min/1.73m^2 for more than three months, as per National kidney foundation guidelines.[13] Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft and Gault formula and subsequently patients were classified into 5 CKD stages. Thyroid Stimulating Hormone (TSH), Free Thyroxine(fT4) and Free triiodothyronine(fT3) were estimated using fully automated analyzer Johnson and Johnson ECI Vitros. The auto-analyzer uses enhanced Chemiluminescence (ECI) technique to measure concentration of analyte in the serum. Serum creatinine was estimated by modified Jaffe reaction, manufactured by Bio lab Reagents, France, using a fully automated chemistry analyzer, Biotecnica 1500 chemistry analyzer, Italy. Thyroid dysfunction was considered if patients thyroid hormones fall outside the reference range; serum free T3 (4.26 to 8.1 pmol/L), serum free T4 (10.2 to 28.2 pmol/L), serum TSH (0.46 to 4.68 μIU/ml). Euthyroid was considered if the thyroid hormone level lies within reference range.

Data was entered into Microsoft Excel 2011 and analyzed by SPSS version 17. One-way ANOVA and Kruskal Wallis test was applied to find differences in mean and Spearman's correlation was used to establish the correlation between study variables. Chi-square test was used to establish association between quantitative variables.

Result

Of the total of 110 patients with CKD, 69 (62.7%) were male and 41 (37.3%) were female. The number of males and females among 30 apparently healthy participants were 17 (56.7%) and 13 (43.3%), respectively. Higher number of CKD patients (37, 33.6%) belonged to stage 4, which was followed by stage 5 (31, 28.2%), stage 3 (30, 27.3%) and stage 2 (9, 8.2%). The minimum number of CKD patients were in stage 1 (3, 2.7%). All the patients with chronic kidney disease and healthy participants were tested for fT3, fT4 and TSH, and accordingly categorized into different groups of thyroid dysfunctions. The number of subjects in each group is shown in Table 1.

	CKD (n = 110)			Control (n = 30)		
Thyroid status	**Male (%)**	**Female (%)**	**Total (%)**	**Male (%)**	**Female (%)**	**Total (%)**
Euthyroid	52	29	81	16	12	28
Thyroid Dysfunction						
Hypothyroidism	2	0	2	0	0	0
Subclinical hypothyroidism	11	8	19	0	0	0
Hyperthyroidism	1	2	3	0	0	0
Subclinical hyperthyroidism	1	2	3	1	1	2
Non-thyroidal illness	2	0	2	0	0	0
Total	69	41	110	17	13	30

Table 1: Thyroid status of patients with chronic kidney disease and healthy participants.

In addition, our data shows that subclinical hypothyroidism (66%) was the most prevalent cause of thyroidal dysfunction among CKD patients. Among the total 30 control subjects selected randomly among apparently healthy individuals, only two had subclinical hypothyroidism (Figure 1).

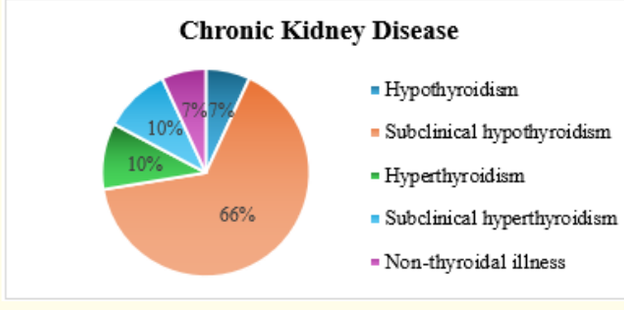

Figure 1: Thyroidal dysfunction in CKD patients.

Our result further demonstrated no significant difference in the level of fT3, fT4 and TSH in between CKD patients and the control groups. However, they had highly significant difference in the level of eGFR and creatinine (Table 2).

	CKD (n = 110)	Control (n = 30)	P-value
fT3	5.59 ± 1.4	5.79 ± 1.2	0.507
fT4	15.64 ± 4.6	15.73 ± 3.0	0.926
TSH	4.65 ± 9.9	2.38 ± 1.5	0.215
eGFR	29.26 ± 21.3	98.53 ± 8.6	0.000
Creatinine	326.18 ± 230.7	71.50 ± 13.3	0.000

Table 2: Comparison of test parameters in between patients with CKD and controls.

CKD patients were further categorized into different stages based on the values of eGFR and other parameters.[14] The frequency of patients with different stages of CKD and different thyroidal dysfunction is shown in Table 3. The most common type of thyroidal dysfunction associated with CKD patients was subclinical hypothyroidism, which was consistently predominated in patients with CKD with stages 3, 4 and 5 (Table 3).

	Stage 1 N (%)	Stage 2 N (%)	Stage 3 N (%)	Stage 4 N (%)	Stage 5 N (%)	Total N (%)
Euthyroid	3 (100)	7 (77.8)	26 (86.7)	22 (59.4)	21 (67.7)	79 (71.8)
Thyroid Dysfunction						
Hypothyroidism	0 (0)	0 (0)	0 (0)	3 (8.1)	1 (3.2)	4 (3.6)
Subclinical hypothyroidism	0 (0)	0 (0)	2 (6.7)	9 (24.3)	8 (25.8)	19 (17.2)
Hyperthyroidism	0 (0)	1 (11.1)	1 (3.3)	1 (2.7)	0 (0)	3 (2.7)
Subclinical hyperthyroidism	0 (0)	1 (11.1)	1 (3.3)	1 (2.7)	0 (0)	3 (2.7)
Non-thyroidal illness	0 (0)	0 (0)	0 (0)	1 (2.7)	1 (3.2)	2 (1.8)
Total	3 (100)	9 (100)	30 (100)	37 (100)	31 (100)	110 (100)

Table 3: Prevalence of thyroid dysfunction in different stages of CKD.

The values obtained for fT3, fT4, TSH, eGFR and Creatinine were further compared in between different stages of CKD. The result demonstrated that the level of fT3 was significantly different in between different stages (p-value 0.004), while the values of fT4 and TSH showed no difference in between different stages of CKD. The levels of eGFR followed a decreasing trend, whereas the levels of creatinine followed an increasing trend with significant differences in CKD patients when moving from stage 1 to 5 (Table 4).

Stages of CKD	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5	P-value
fT3 (pmol/L)	4.0 ± 1.6	6.2 ± 0.9	6.2 ± 1.3	5.2 ± 1.4	5.1 ± 1.3	0.004
fT4 (pmol/L)	18.8 ± 8.2	13.9 ± 3.1	16.6 ± 5.7	14.6 ± 4.5	15.5 ± 3.5	0.272
TSH (mIU/L)	2.3 ± 1.0	3.1 ± 2.9	2.5 ± 2.2	8.33 ± 16.6	4.1 ± 3.6	0.230
eGFR	103.61 ± 10.5	67.11 ± 4.8	39.96 ± 8.1	21.00 ± 3.8	10.57 ± 2.89	0.000
Creatinine	78.33 ± 18.82	116 ± 36.3	172.47 ± 40.9	290.59 ± 88.7	602.42 ± 241.9	0.000

Table 4: The values for tested laboratory parameters in different stages of CKD.

Discussion

The kidney plays an important role in the regulation of metabolism and elimination of thyroid hormones. Any alterations in the kidney may directly affect the function of thyroid glands to secret thyroid hormones. In this study, we tried to compare the levels of thyroid hormones and its relation to kidney injury with respect to the control group. Our findings demonstrated that CKD patients have high risk for developing thyroid dysfunction.

The majority of CKD patients enrolled in this study belonged to stage 4 (33.6%) followed by stage 5 (28.18%) and stage 3 (27.27%). There were only 3 (2.71%) and 9 (8.18%) patients in stage 1 and stage 2, respectively. Lower representation of CKD stage 1 and 2 in our study suggests that Nepalese patients seek medical attention only when they have symptoms and when their disease is already in advanced stages. In addition, lack of periodic general health checkup and awareness about the disease in general public may also be responsible for lower number of cases in earlier stages of CKD.

Our study showed high prevalence of thyroid dysfunction (26.36%) among CKD patients. This prevalence rate is in accordance to the study carried out by Khatiwada., *et al*. who also reported thyroid dysfunction in 38.6% of CKD patients in stages 3, 4 and 5. However, this data is very high compared to The National Health and Nutritional Examination Survey III (NHANES III) population study in US that reported thyroid dysfunction in only 5.9% of the US population. In contrary, a study from the eastern part of Nepal had previously shown high prevalence (30%) of thyroid dysfunction in Nepalese population similar to the findings of this study.[15] The differences in the prevalence rate among different study might be due to the geographical locations, inclusion criteria and endemicity of iodine deficiency in the areas where studies were performed.

Among the different types of thyroid dysfunction, subclinical hypothyroidism (17.27%) was the most common disorder associated CKD patients, while hypothyroidism only accounted for 3.63% cases in our study. NHANES III study from US has reported a different prevalence rate of hypothyroidism (4.6%) and subclinical hypothyroidism (4.3%) in the US population.[16] Existing literature suggests a varying prevalence rate of thyroidal dysfunction in general population. A study carried out in Iran reported a prevalence of subclinical hypothyroidism ranging from 1 – 20%, while the prevalence of overt hypothyroidism ranging from 1 – 2%, which is very similar to the findings of this study.[17] Also, among the different stages of CKD patients in our study, 7% in stage 3, 32% in stage 4 and 29% in stage 5 CKD patients had hypothyroidism. Our data showed that the rate of hypothyroidism increases when CKD progresses form stage 3 to 4, but it decreases when the disease progresses from stage 4 to 5. A study by Chonchol., *et al*. reported the prevalence of hypothyroidism to be 18% among CKD patients not requiring dialysis [18]. The considerable variation in data among different studies may be attributed to various genetic and environmental factors like thyroid autoimmunity and iodine deficiency or sufficiency.

A study by Lo., *et al*. showed a strong relationship between higher prevalence of hypothyroidism and a decreasing level of GFR (mL/min/1.73m^2). In their study, hypothyroidism was seen in 5.4% with GFR greater than 90, 10.9% with GFR ranging from 60-89, 20.4% with GFR ranging from 45-59, 23% with GFR 30-44, and 23.1% with GFR less than 30 mL/min/1.73m^2. Notably, subclinical hypothyroidism was significantly more prevalent than overt hypothyroidism, with its prevalence increasing steadily as GFR declined [12]. This finding aligns with the understanding that reduced renal function in CKD leads to impaired iodine clearance, resulting in elevated serum iodine levels, which can disrupt thyroid hormone synthesis [19]. A study conducted in Western Nepal by Raj Ku. Yadav., *et al*. reported a hypothyroidism prevalence of 12.07%, further emphasizing the significance of this association in the Nepalese population [20].

In the present study, hyperthyroidism was observed in 5.44% of participants, comprising 2.72% with subclinical hyperthyroidism and 2.72% with overt hyperthyroidism. This prevalence is significantly higher than that reported in the US population by the NHANES III study, which found 0.5% overt and 0.7% subclinical hyperthyroidism [16]. However, a study conducted in the western region of Nepal by Yadav., *et al*. reported a higher prevalence of overt (1.59%) and subclinical (3.05%) hyperthyroidism in a hospital-based population [20]. Interestingly, Khatiwada., *et al*. who investigated hyperthyroidism in CKD patients, observed subclinical hyperthyroidism in 3.3% but did not detect any cases of overt hyperthyroidism [21]. There is variation in the reported cases of hyperthyroidism (overt and subclinical) in population-based studies, hospital-based studies and also CKD patients. But this variation is very small and only indicates that hyperthyroidism may not be commoner condition in CKD patients than in the general population.

Non-thyroidal illness (NTI) is characterized by alterations in thyroid hormone levels despite a structurally and functionally normal thyroid gland. In the present study, NTI was observed in 1.81% of CKD patients. This finding contrasts with another study that reported low T3 syndrome as the most common thyroid dysfunction in NTI.[22] This discrepancy could be attributed to differences in patient management strategies between the studies. Furthermore, our assessment was limited to free T3 levels, whereas total T3 measurement, as suggested by Wiederkehr., *et al*. may be more sensitive in detecting low T3 syndrome [22].

The present study demonstrated a progressive decline in free T3 levels across CKD stages. Mean free T3 values were 6.2 pmol/L in stage 3, 5.2 pmol/L in stage 4, and 5.1 pmol/L in stage 5, with statistically significant differences between the stages ($p < 0.05$). This finding aligns with previous observations by Zocalli., *et al*. who also reported decreased levels of T3 and free T3 in CKD patients [23]. Several factors contribute to this decline, including diminished peripheral conversion of T4 to T3, stress-induced inhibition of TSH secretion, chronic metabolic acidosis, and inflammation [24,25]. Given the inverse relationship between T3 and TSH, an increase in TSH levels would be expected with declining T3 levels during CKD progression. In our study, mean TSH levels were 2.5, 8.3, and 4.1 µIU/mL in stages 3, 4, and 5, respectively. While a significant increase in TSH was observed from stage 3 to stage 4, an unexpected decline occurred from stage 4 to stage 5 despite continued T3 decline. This abnormal TSH response may be attributed to a blunted and delayed response of the pituitary gland to thyrotropin-releasing hormone in advanced CKD [24].

Although, this study has some important findings, it has several limitations. Firstly, the observed correlation between CKD and thyroid dysfunction does not establish a definitive cause-and-effect relationship. Secondly, the analysis was restricted to specific thyroid function tests, excluding crucial assessments such as thyroid ultrasonography and antibody levels. Iodine status, a critical factor influencing thyroid function, was not evaluated, leaving open the possibility of iodine deficiency or toxicity. Furthermore, the cross-sectional design limits the ability to determine the temporal relationship between CKD and thyroid dysfunction. Longitudinal studies with repeated measurements of thyroid hormones would be more informative, particularly in differentiating true thyroid dysfunction from transient abnormalities associated with non-thyroidal illness. Finally, the small sample size, likely due to cost constraints, may limit the generalizability of the findings. Larger, prospective studies are warranted to further investigate the association between CKD and thyroid dysfunction and to establish more robust recommendations.

Conclusion

This study demonstrates a significantly higher prevalence of thyroid dysfunction, particularly hypothyroidism (both overt and subclinical), among individuals with CKD. Furthermore, the risk of thyroid dysfunction appears to increase with the severity

of CKD, as evidenced by advanced stages or declining GFR. These findings underscore a strong association between CKD and thyroid dysfunction, emphasizing the importance of routine thyroid function assessment in individuals with CKD.

Ethical Approval

The study was approved by Institutional Review Board of Research Department of Maharajgunj Medical Campus, Institute of medicine, Tribhuvan University (Ref No. 213(6-11-E)2/92/73). Written informed consent was obtained from every participant enrolled in this study before data and sample collection.

Consent for Publication

All authors have agreed on processing this manuscript for publication.

Availability of Data and Material

The datasets obtained in this study can be made available from the corresponding author on reasonable request.

Competing Interests

All the authors declare no competing interests in publication of this article.

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Authors' Contributions

RK reviewed the literature, collected samples,performed laboratory tests,analyzed the data and wrote the manuscript. MRS designed the study and helped in drafting the manuscript. RP analyzed the data and drafted the manuscript. BJ designed the study and reviewed the manuscript. BKY designed the study, helped in data analysis and drafted the manuscript. All authors read and approved the final version of the manuscript.

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Bibliography

1. Schoolwerth AC., *et al*. "Chronic Kidney Disease: A Public Health Problem That Needs a Public Health Action Plan". *Preventing Chronic Disease* 3.2 (2006).

2. Schieppati A and Remuzzi G. "Chronic renal diseases as a public health problem: epidemiology, social, and economic implications". *Kidney International* 68 (2005): S7-S10.

3. Sharma SK., *et al*. "Burden of CKD, proteinuria, and cardiovascular risk among Chinese, Mongolian, and Nepalese participants in the International Society of Nephrology screening programs". *American Journal of Kidney Diseases* 56.5 (2010): 915-927.

4. Sharma SK., *et al*. "Community-based screening for chronic kidney disease, hypertension and diabetes in Dharan". *JNMA; Journal of the Nepal Medical Association* 52.189 (2013): 205-212.

5. Perico N and Remuzzi G. "Chronic kidney disease: a research and public health priority". *Nephrology Dialysis Transplantation* 27.3 (2012): iii19-iii26.

6. Capasso G., *et al*. "Effects of thyroid hormones on heart and kidney functions". *Mineral and Electrolyte Metabolism* 25.1-2 (1999): 56-64.

7. Kim HJ., *et al*. "Subclinical thyroid dysfunction and chronic kidney disease: a nationwide population-based study". *BMC Nephrology* 24.1 (2024): 64.

8. Iglesias P and Diez J. "Thyroid dysfunction and kidney disease". *European Journal of Endocrinology* 2009;60 (4): 503-515.

9. Mohamedali M., *et al*. "Thyroid disorders and chronic kidney disease". *International Journal of Nephrology* 2014 (2014): 520281.

10. KAPTEIN EM., *et al*. "The thyroid in end-stage renal disease". *Medicine* 67.3 (1988): 187.

11. Kaptein EM. "Thyroid hormone metabolism and thyroid diseases in chronic renal failure". *Endocrine Reviews* 17.1 (1996): 45-63.

12. Lo JC., *et al*. "Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease". *Kidney International* 67.3 (2005): 1047-1052.

13. Foundation NK. "Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification". *National Kidney Foundation* (2002).

14. Inker LA., *et al*. "KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD". *American Journal of Kidney Diseases* 63.5 (2014): 713-735.

15. Baral N., *et al*. "Thyroid dysfunction in eastern Nepal". S*outheast Asian Journal of Tropical Medicine and Public Health* 33.3 (2002): 638-641.

16. Hollowell JG., *et al*. "Serum TSH, T4, and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III)". *The Journal of Clinical Endocrinology and Metabolism* 87.2 (2002): 489-499.

17. Aminorroaya A., *et al*. "The prevalence of thyroid dysfunction in an iodine-sufficient area in Iran". *Archives of Iranian Medicine* 12.3 (2009): 262-270.

18. Chonchol M., *et al*. "Prevalence of subclinical hypothyroidism in patients with chronic kidney disease". *Clinical Journal of the American Society of Nephrology* 3.5 (2008): 1296-1300.

19. Brough R and Jones C. "Iatrogenic iodine as a cause of hypothyroidism in infants with end-stage renal failure". *Pediatric Nephrology* 21.3 (2006): 400-402.

20. Yadav RK., *et al*. "A prevalence of thyroid disorder in Western part of Nepal". *Journal of Clinical and Diagnostic Research: JCDR* 7.2 (2013): 193.

21. Khatiwada S., *et al*. "Thyroid dysfunction and dyslipidemia in chronic kidney disease patients". *BMC Endocrine Disorders* 15.1 (2015): 1.

22. Wiederkehr MR., *et al*. "Correction of metabolic acidosis improves thyroid and growth hormone axes in haemodialysis patients". *Nephrology Dialysis Transplantation* 19.5 (2004): 1190-1197.

23. Zoccali C., *et al*. "Low triiodothyronine and survival in end-stage renal disease". *Kidney International* 70.3 (2006): 523-528.

24. Wartofsky L and Burman KD. "Alterations in Thyroid Function in Patients with Systemic Illness: The Euthyroid Sick Syndrome". *Endocrine Reviews* 3.2 (1982): 164-217.

25. Verger M-F., *et al*. "Relationship between thyroid hormones and nutrition in chronic renal failure". *Nephron* 45.3 (1987): 211-215.