

A Prospective Study on Prevalence of Thyroid Dysfunction Among Chronic Kidney Disease Patients

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Abstract

Background: 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 Chronic Kidney Disease. Patients with CKD having many signs and symptoms suggestive of thyroid dysfunction like sallow complexion, edema, dry skin, cold intolerance, decreased BMR, asthenia and hyporeflexia. So in cases of CKD, it is difficult to exclude thyroid dysfunction on mere clinical background. Total number of 100 patients with Chronic Kidney Disease were selected in this prospective study. 100 patients with Chronic Kidney Disease (CKD) fulfilling the criteria for CKD who were on conservative management were studied, among these 100 patients 70 were male and 30 were female Among the 100 patients in our study 55 of them had low serum T3 levels (55%), 17 patients among the low serum T3 level also had high TSH value of >20 ILIU/ml with low T4 levels and also symptoms suggestive of hypothyroidism.

Keywords: Chronic kidney disease, thyroid dysfunction, prevalence, hypothyroidism

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Introduction

End stage renal disease is described as a terminal stage of chronic kidney disease that without replacement therapy would result in death. Despite various etiologies, CKD is the final common pathway of irreversible destruction of nephrons ultimately resulting in alteration of 'Milieu interior' that affects every system in the body. One such system in the body is thyroid hormonal system. Kidney is closely related to thyroid in the fact that it is the only other organ that competes with iodide clearance³2' Patients with CKD having many signs and symptoms suggestive of thyroid dysfunction like sallow complexion, edema, dry skin, cold intolerance, decreased BMR, asthenia and hyporeflexia. So in cases of CKD, it is difficult to exclude thyroid dysfunction on mere clinical background. Various studies have been conducted on thyroid function in CKD patients. Since the beginning, the results were inconsistent. Hyperthyroidism, hypothyroidism and euthyroidism all have been reported. The

relation between thyroid dysfunction and severity of CKD is not clear. Several previous studies report conflicting results both positive and negative. Prevalence of hypothyroidism in end stage renal disease (ESRD) has been estimated between 0 and 9%. There is also increased prevalence of goiter in patients with ESRD. In view of variability of thyroid function test in patients with CKD in previous studies, a prospective clinical and biochemical study on thyroid function in CKD patients was undertaken.

Aim

Study the prevalence of thyroid dysfunction in patients with chronic kidney disease.

Methods And Materials

Source of data Patients with chronic kidney disease admitted in Government Mohan Kumaramangalam Medical College Hospital, Salem.

Methods of collection of data Study subjects:

The present study is conducted on 100 patients of, who are diagnosed to have chronic kidney disease and being admitted in Government Mohan Kumaramangalam Medical College Hospital, Salem. These samples are selected by using simple random sampling method. Statistical parameters mean, standard deviation (SD) and correlations are used and parametric and non parametric tests are used for the analysis. Informed consent was obtained from all the patients.

Inclusion criteria:

Patients with chronic kidney disease. Patients who fulfill the criteria for CKD and who are on conservative management.

Criteria for Chronic Kidney Disease

1. Symptoms of uremia for 3 months or more
2. Elevated blood urea, serum creatinine and decreased Creatinine clearance
3. Ultra sound evidence of chronic kidney disease
 - a) Bilateral contracted kidneys - size less than 8 cm in male and size less than 7 cm in female
 - b) Poor corticomedullary differentiation
 - c) Type 2 or 3 renal parenchymal changes
 1. Supportive laboratory evidence of CKD like anemia, low specific gravity, changes in serum electrolytes, etc.,
 2. Radiological evidence of renal osteodystrophy

Exclusion criteria

1. Patients on peritoneal dialysis or hemodialysis
2. Nephrotogenic range of proteinuria
3. Low serum protein especially albumin
4. Other conditions like
 - a) Acute illness
 - b) Recent surgery, trauma or burns
 - c) Diabetes mellitus
 - d) Liver diseases
 - e) Drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, beta-blocker, estrogen pills, iodine- containing drugs. Detailed clinical history and clinical examination is undertaken with preference to thyroid and renal diseases. The following investigations were performed.
 - EI Urine routine and microscopic examination
 - Peripheral smear for anemia and burr cells

- Renal parameters like blood urea, serum Creatinine and creatinine clearance (using Cockcroft -- Gault formula)
- Serum electrolytes including calcium and phosphorous
- Serum cholesterol
- 24 hours urine protein and serum protein
- ECG, chest X-ray and 2D echo
- X ray wrist, forearm and spine for evidence of renal osteodystrophy
- USG abdomen for evidence of chronic kidney disease
- FNAC in patients presenting with thyroid swelling. After selecting the patients, fulfilling the above criteria, about 5 ml of blood sample is collected in non heparinized serum bottle and sent for thyroid profile. Components of thyroid profile in this study
- Serum triiodothyronine(T3)
- Serum thyroxine(T4)
- Serum thyroid stimulating hormone (TSH)
- Quantitative determination of T3, T4, TSH is done by Enzyme Linked Immunosorbent Assay.

The normal values:

Total T3.....0.6 to 2.1 ng/ml

Total T4..... 5 to 13 micro g/dl

TSH..... 0.4 to 7 micro IU/ml

Results

100 patients with Chronic Kidney Disease (CKD) fulfilling the criteria for CKD who were on conservative management were studied, among these 100 patients 70 were male and 30 were female, Their age varied from 25-75 years, of these 100 patients, patients who were 30 years old and below were 4 patients, of these 3 male 1 female. Age between 30- 60 years were 69 of these 46 male 23 female and patients above the age of 60 years were 27, of these 21 male 6 female in number . In our study the duration of CKD varied from 4 months - 5 years, mean duration being 11.16 months + 10.48 and the creatinine clearance varied from 6ml/min — 34ml/min. Of the 100 patients, 28 patients had GFR of <10ml/min accounting to 28%, patients had GFR ranging from 11-20 ml/min accounting for another 52% and the remaining 20 patients had GFR > 20ml/min accounting for 20%. Blood urea varied from 62 — 180 mg/dl and creatinine levels varied from 3mg - 15.6mg/dl, 24 hours urine protein excretion was <1g/day in all the patients in our study. Serum calcium and phosphorous were normal in all our patients, 80% of the patients had anemia with peripheral smear revealing normocytic normochromic anemia in 72% and hypochromic anemia in 8% of the patients Burr cells were present in 40% of the cases, three patient had pleural effusion in our study, two patients in the study showed evidence of osteodystrophy. Ultrasound abdomen showed evidence of CKD in all patients, with contracted kidney was present in all of the patients and poor corticomedullary differentiation. Among the 100 patients in our study 55 of them had low serum T3 levels (55%), 17 patients among the low serum T3 level also had high TSH value of >20[LIU/ml with low T4 levels and also symptoms suggestive of hypothyroidism.

Table 1: Age & Sex Wise Distribution

Age	Sex					
	Male		Female		Total	
	Nos.	%	Nos.	%	Nos.	%
30	3	4.29	1	3.33	4	4
31-60	46	65.71	23	76.67	69	69
>60	21	30.00	6	20.00	27	27

Among these 26 patients had low T3& and T4 value. These patients are grouped as hypothyroid syndrome in which 32 patients had low T4 levels accounting for 32% of the patients. Symptoms of hypothyroidism such as tiredness, somnolence, weight gain, cold intolerance, hoarseness of voice etc were also studied in the sample In these 42 patients with CKD did not show thyroid dysfunction, among these 2patients 28 of them had symptoms of hypothyroidism which accounts to 58.33 Patients with Hypothyroid features clinically like hypothyroid syndrome were 44 ,delayed tendon reflex 6, papilledema 1, goiter 1 and pleural effusion Hypothyroidism did not show any linear correlation with GFR .

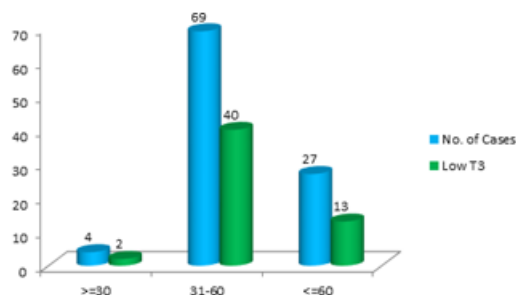


Figure 1: Age Incidence Of Low T3 Syndrome

Increased number of hypothyroid patients of about 8 in number were present in GFR 11-20ml/min and also 12 patients had hypothyroidism in GFR <10ml/min. 4 of our the patients in our study had diffuse thyroid swelling. Age incidence ,patients with age<30 , were 4 cases , patients with age<30 -60 were 69 , patients with age<60 , were 27 , In correlation of T3 level with age ,patients low T3 with the age of <30 were 2 patients , age of <30-60 were 40 patients and age of >60 were 13 patients IT showed that 2% of the CKD patients who had low T3 level were 30 years of age or below and 40% of the patients were between the ages 31-60 years and 13% of the patients were age >60, as the age increased the number of patients with low T3 also increased . Sex incidence, patients of low T3 syndrome in one study showed that 51.3% of males had low T3 and 38.7% of the females have low T4 syndrome. The T3 levels varied from 0.2 — 1.9 ng/ml. Excluding hypothyroidism T3 levels were studied in relation to GFR, mean value of serum T3 was low (0.534ng/ml) only in patients with GFR <10ml/min. The mean value was low normal in patients with GFR

>10ml/min. According to our study, number of patients with low T3 increased with increase in the severity of renal failure, in spite of low T3. The serum T4 levels varied from 0.5 — 9.514dl.(Mean value of serum T4 among 100 patients was 5.631, excluding hypothyroidism patients the mean value was 5.98pg/ml. this value is within low normal level of T4. Excluding 5 hypothyroid patients who have low T4 values, 11 other patients accounting to 22% had T4 level below normal and low T3 syndrome. Number of patients with low T4 does not correlate with the severity of renal disease The mean value of T4 excluding hypothyroidism patients was normal at all stages of CKD.

Table 2: Serum Concentration Of Thyroid Hormon

Thyroid Hormones	Normal Range	Study Range	Mean	SD	Mean excluding Hypothyroidism	SD
Serum T3	0.6-2.1	0.1-2.0	0.613	0.043	0.698	0.523
Serum T4	5-13	0.4-9.4	5.614	2.248	5.89	2.76
Serum TSH	0.4-7	0.4-27.0	6.526	0.669	5.23	4.62

None of the patients had T4 values above normal level, Studying level of TSH values varied from 0.6-24.4 RIU/ml with mean value of 7.28111U/ml, excluding hypothyroidism mean value was 4.85. This shows normal serum level of TSH. Among the 100 patients, TSH was normal in 73 patients (73%) and values between 7.1-201A1U/ml among with low T3 in 10 patients (18.18%). It was elevated >20pIU/ml with low T3 patients 10 (18.18 %) and these more present in male In 100 patients, TSH level between 7.1-201.dU/ml , with low T4 in 6 patients . It was elevated >20ttIU/ml with low T4 10 patients.

Discussion and Conclusion

Thyroid dysfunction in CKD was extensively studied by Ramirez. Apart from his study, various studies conducted in this line have showed different results. In our study, patients only on conservative management were studied. This is because thyroid profile undergoes changes due to dialysis independent of that due to chronic kidney disease. Dialysis also changes the previous serum status of thyroid hormone in the patients with renal failure. Many studies have been conducted by comparing CKD patients on conservative Management and patients on hemodialysis by Ramirez and Kayima et al. Many studies conducted in CKD patients showed low T3 values. Low T3 had been reported in Ramirez et al, Hegedus et al, Beckett et al Pon Ajil Singh et al, P Iglesias and JJ Diez and many others. Ramirez and Spector et al study showed linear correlation between mean serum T3 and T4 and severity of renal failure. As with other studies, mean T3 level in our study was reduced below normal in GFR less than 10 ml/min. In higher GFR, it was present in low normal and there was no linear correlation between T3 level and GFR, which is consistent with Avasthi et al study Mean T4 level in our study is within normal limits in all levels of GFR, but it is in low normal level and also it does not correlate with the severity of renal failure. In our study, not all the patients with CKD have low T3 and T4. It is estimated that only 52% (26 patients) of patients have Thyroid Profile abnormality. Remaining 48% of patients have normal thyroid profile. Among 52% of these patients excluding primary hypothyroidism patients 22% have only low T3 level with normal T4 level. Remaining 26% have both low T3 and T4 level. The percentage of patients having low T3 and T4 gradually increase with decrease in GFR. The patients who will develop such changes in thyroid profile is not known.

- In patients with CKD Thyroid dysfunction occurs in 52% of the patients, the alteration in the values of T3 and T4 in CKD can be viewed as protective, promoting conservation of protein.
- Prevalence of hypothyroidism is increased in patients with chronic kidney disease.
- 70 patients were male and 30 were female.
- Age varied form 25-75 years.
- Duration of CKD varied from 6 months to 5 years mean being 11.16 months + 10.48.
- Creatinine clearance varied from 6ml/min — 33ml/min.
- Urea varied from 62-180mg/dl and creatinine levels varied from 3mg/dl— 17.2mg/dl.
- The study range of serum T3 was 0.2 — 1.9 ng/ml, mean 0.665 (normal range 0.6 — 2.1), serum T4 was 0.5 — 9.54d1, mean 5.631 (normal range 5-13) and serum TSH was 0.6 — 270U/ml, mean 7.28 (normal range 0.4-7).
- 17 patients had low T3 syndrome, 11 patients had low T4 syndrome and 13 patients had hypothyroidism and 58%, 58patients had symptoms of hypothyroidism.

References

1. Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: Global dimension and perspectives. *Lancet* 2013;382:260-722.
2. Ramírez G, Jubiz W, Gutch CF, Bloomer HA, Siegler R, Kolff WJ, et al. Thyroid abnormalities in renal failure. A study of 53 patients on chronic hemodialysis. *Ann Intern Med* 1973;79:500-4
3. Castellano M, Turconi A, Chaler E, Maceiras M, Rivarola MA, Belgorosky A. Thyroid function and serum thyroid binding proteins in prepubertal and pubertal children with chronic renal insufficiency receiving conservative treatment, undergoing hemodialysis, or receiving care after renal transplantation. *J Pediatr* 1996;128:784-90
4. Gomez-Pan A, Alvarez-ude F, Yeo PB, Hall R, Evered DC, Kerr DN. Function of the hypothalamic-hypophyseal-thyroid axis in chronic renal failure. *Clin Endocrinol* 1996;2:567-74.
5. Kaptein EM, Quion-Verde H, Chooljian CJ, Tang WW, Friedman PE, Rodriguez HJ, et al. The thyroid in end-stage renal disease. *Medicine (Baltimore)* 1988;67:187-97
6. Takeda S, Michigishi T, Takazakura E. Iodine-induced hypothyroidism in patients on regular dialysis treatment. *Nephron* 1993;65:51-5.