Alteration of Thyroid Profile in Chronic Kidney Disease Patients: A Pilot Study of Thyroid Dysfunction in Chronic Kidney Disease Patients

Madhvi Trivedi[1], Gunjan Kumar Mandal[2], Arvind Trivedi[3]

ABSTRACT

Introduction: The thyroid hormones have a significant impact on chronic kidney disease patients, so it is important to consider the pathophysiological association of thyroid dysfunction in relation to chronic kidney disease. This study is based mainly to see the importance of interactions between the thyroid gland functions and renal function in chronic kidney disease patients.

Material and Methods: Thyroid Function Test, Serum urea, Serum creatinine, and eGFR (Calculated by Cockroft and Gault formula) were assayed in 100 CKD patients, in which 40 patients CKD with Thyroid dysfunction and 60 patients CKD without Thyroid dysfunction.

Results: In our study, a total of 100 patients with CKD were evaluated for a Thyroid function test out of which 40 patients had abnormal thyroid profiles, so the percent incident is 40%. Clinical variables were compared using the unpaired Student's t-test. Pearson's correlation analysis was used to determine the association between eGFR and thyroid profile. We found statistically significant increased level of Serum urea and Serum creatinine and Serum TSH, and significantly decreased level of eGFR, serum FT3 and FT4 in CKD patients with Thyroid dysfunction as compare to CKD patients without Thyroid dysfunction. We also found that eGFR was significantly negatively associated with serum creatinine, Serum TSH and a significantly positive association with FT3. No significant correlation was found with FT4.

Conclusion: This study finds thyroid dysfunction to be very common in patients with CKD and reveals the significant association between CKD and thyroid dysfunction, and may have an impact on CKD progression.

Keywords: Chronic Kidney Disease (CKD), Thyroid Dysfunction, eGFR: Estimated glomerular Filtration Rate, Thyroid-stimulating Hormone (TSH)

INTRODUCTION

Chronic kidney disease (CKD) is defined as persistent kidney damage accompanied by a reduction in the glomerular filtration rate (GFR) and the presence of albuminuria.[1] Chronic kidney disease is a worldwide health problem with increasing incidence and prevalence, poor outcome, and high cost of investigation and treatment. The kidney normally plays an important role in the metabolism, degradation, and excretion of thyroid hormones. The kidney is closely related to the thyroid as it is the only other organ that competes with base iodine clearance. Dietary iodine is reduced to iodine and absorbed in the small intestine. Circulating iodine is cleared from the blood mainly by the kidney (80%) & by the thyroid (20%).[2]

The relationship between CKD and the associated thyroid abnormalities has been studied for years but no clear-cut conclusion has been found. As of now, a variety of alterations in thyroid hormone levels and metabolism have been reported in patients with chronic kidney disease.[3,4] The thyroid hormones have a significant impact on kidney disease so it is important to consider the pathophysiological association of thyroid dysfunction in relation to chronic kidney disease.

Thyroid gland and chronic kidney disease: Abnormalities in the structure and function of thyroid gland and the metabolism and plasma conc. of thyroid hormones are common in patients with CKD. Various thyroid disorders- hypothyroidism, goiter, thyroid modules & thyroid carcinoma are seen in patients with CKD.[1,5] Based on research studies Low T3 is the most common laboratory finding[6] & subclinical hypothyroidism is most common thyroid disorder found in CKD patients.[7] TSH levels are usually normal with and altered circadian rhythm. This study is based on mainly seeing the importance of interactions between the thyroid gland functions and renal function is chronic kidney disease patients and to co-relate the levels of thyroid hormones with eGFR.

MATERIAL AND METHODS

The Hospital based cross sectioned study was conducted in the Department of Biochemistry at Santosh Medical College, Ghaziabad, Uttar Pradesh, India from January 2015 to November 2016. The Ethical Committee of the Institute gave approval to the study. A written informed consent was obtained from all patients. The study involving total 100 outdoor and indoor patients of chronic kidney

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Disease in which 40 CKD with Thyroid dysfunction (Group I), 60 CKD without Thyroid dysfunction (Group II). All outdoor and indoor patients diagnosed with CKD who are consulting for investigative check up to facilitate treatment and record maintenance will be included in the study. Patients who are too sick, undergoing peritoneal dialysis, on medications affecting thyroid function (oral contraceptives, iodine containing drugs), with known thyroid disorders and pregnant women and patients under 18 years of age were excluded from the study.

A structured questionnaire regarding the demographic data (age, sex), duration of Hypertension, BMI were measured. Blood pressure, smoking habit, kidney disease, diabetes family history and hypertension was noted down for each patient. 5 ml of blood sample was withdrawn from antecubital vein in plain vacutainer under all aseptic precautions, taken to laboratory and centrifuged. The serum was stored at 4°C and analyzed for serum urea, serum creatinine, & Thyroid profile. Serum Urea and serum creatinine were estimated by enzymatic method. All biochemical investigation was done by fully automated analyzer Turbo cam 100. Thyroid stimulating hormone (TSH), Free triiodothyronine (FT3) and Free thyroxine (FT4) levels will be estimated by immune assays (chemiluminesence) and eGFR will be estimated by Cockroft Gault equation.[8]

Thyroid dysfunction was considered if patient's thyroid hormones fall outside the reference range. Overt hypothyroidism was defined as TSH level > 5.5 µIU/mL and free T3 level < 1.40 pg/mL and free T4 level < 0.70 ng/dL. Subclinical thyroid disease is defined as serum FT4 & FT3 levels within their respective reference ranges in the presence of abnormal serum TSH levels.

Reference ranges: TSH: 0.25 - 5.5 µIU/mL, FT3: 1.40 - 4.40 pg/mL and FT4: 0.70 - 1.70 ng/dL

STATISTICAL ANALYSIS

Statistical analysis was done by using SPSS version 21 (SPSS Inc., 233, South Wacker Drive, 11th Floor, Chicago, IL, 60606-6412, USA). Thyroid function tests and renal function tests were expressed as mean ± standard deviation and were compared by unpaired Student's t-test. Pearson's correlation analysis was used to determine the association between eGFR and Thyroid Profile of CKD patients with Thyroid dysfunction. The level of significance was set as $P < 0.05$: Significant and $P > 0.05$: Non significant.

RESULTS

Total 100 patients of CKD were evaluated for Thyroid Function Test out of which 40 patients had abnormal Thyroid profile, so percent incidence is 40%, which is highest of reported literature. Various demographic data, clinical characteristics, thyroid profile were collected and subjected to statistical analysis. Average age of patients with abnormal Thyroid profile is 54.4 years, range 18 years to 75 years. Maximum number of patients in 50-70 years age (32 patients). Male to female ratio is 24/16.

Table 1 shows Clinical characteristics of CKD with Thyroid dysfunction (T. dys) patients and CKD without T. dys patients. The mean age and weight of CKD with T. dys group were 54.4±11.0 and 55.12±6.63 respectively and the

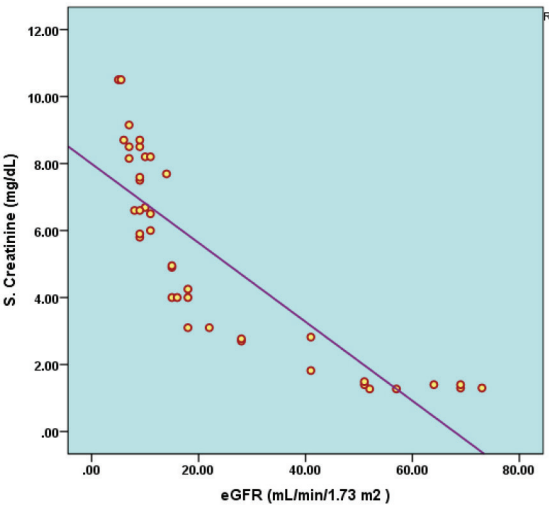

Figure-1: Negative Pearson's correlation between eGFR and Serum Creatinine

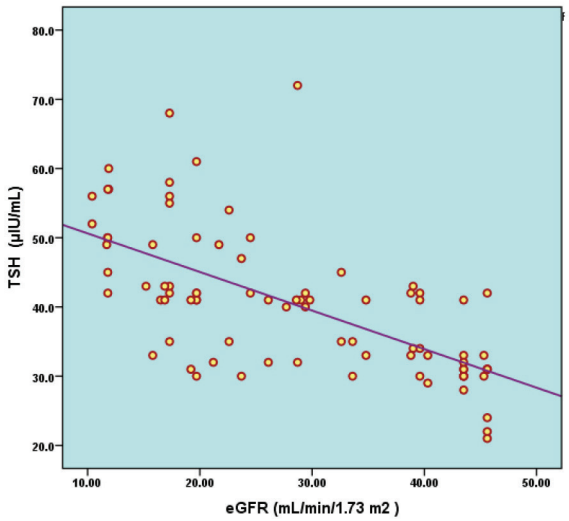

Figure-2: Negative Pearson's correlation between eGFR and Serum TSH

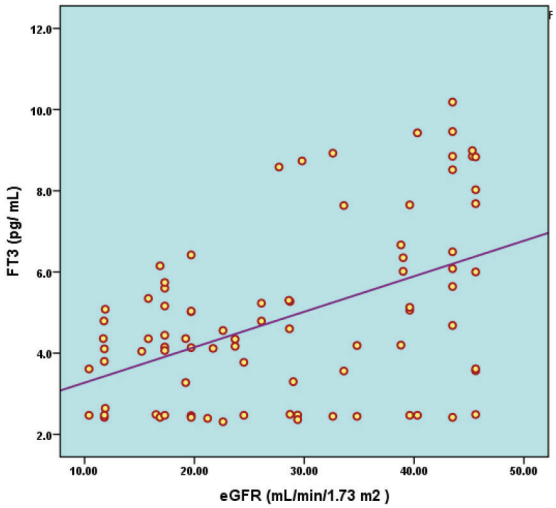

Figure-3: Positive Pearson's correlation between eGFR and FT3

Parameters	CKD with T. dys (N = 40) Mean± SD	CKD without T. dys (N = 60) Mean± SD	p value
Age (Years)	54.4±11.0	52.9±7.8	NS
Weigh (Kg)	55.12±6.63	53.9±6.63	NS
Serum Urea (mg/dL)	120.8±29.3	91.6±27.3	<0.001
Serum Creatinine (mg/dL)	9.13±2.94	5.3±1.7	<0.001
eGFR (mL/min/1.73 m^2)	22.9±21.14	44.4±8.9	<0.001
TSH (µIU/mL)	13.5 ± 24.54	4.2 ± 0.34	<0.001
FT3 (pg/mL)	1.01 ± 1.39	3.21 ± 0.21	<0.001
FT4 (ng/dL)	0.89 ± 1.82	1.48 ± 1.61	<0.05
P < 0.05: Significant, P < 0.001: Highly significant. T. dys: Thyroid dysfunction patients, eGFR: Estimated glomerular filtration rate, TSH: Thyroid stimulating hormone, FT3: Free triiodothyronine and FT4: Free thyroxine.			

Table 1: Comparison of Clinical characteristics of CKD with T. dys patients and CKD without T. dys patients (Mean± SD)

Parameters	r	P
Serum Creatinine (mg/dL)	−0.845**	<0.001
TSH (µIU/mL)	−0.429**	<0.001
FT3 (pg/mL)	0.381*	<0.05
FT4 (ng/dL)	0.206	NS
P < 0.05: Significant, P < 0.001: Highly significant. eGFR: Estimated glomerular filtration rate, TSH: Thyroid stimulating hormone, FT3: Free triiodothyronine and FT4: Free thyroxine		

Table-2: Pearson's correlation coefficient (r) between eGFR, and serum creatinine, thyroid Profile of CKD with Thyroid dysfunction patients

CKD without T. dys group were 52.9±7.8 and 53.9±6.63 respectively. There was no significant difference in age and weight between the two groups. Serum urea levels and Serum creatinine levels significantly increased (P < 0.001) as compared to CKD without T. dys patients, whereas eGFR by Cockroft and Gault formula was significantly lower (P < 0.001) compare than CKD without T. dys patients.

In Patients with Thyroid dysfunction, we found Serum TSH level was significantly increased (P < 0.001), whereas serum FT3 and FT4 levels were significantly decreased compared to CKD without T. dys group. The data indicates the high risk of hypothyroidism in patients suffering from CKD.

Table 2 shows Pearson's correlation coefficient (r) between eGFR and Thyroid Profile of CKD with Thyroid dysfunction patients. The results showed that eGFR was significantly negative associated with serum creatinine (r = −0.845, P < 0.001) shown in [Figure 1], serum TSH (r = −0.429, P > 0.001) shown in [Figure 2] and significantly positive association with FT3 (r = 0.381, P < 0.05) shown in [Figure 3]. No significant correlation was found with FT4.

DISCUSSION

Serum creatinine values range from 1.27 to10.5 mg/dL, with mean of 5.12± 2.93 mg/dL. eGFR by Cockroft and Gault formula ranged from 4 ml to 69 mL/min/1.73m2. Majority of patients in eGFR less than 15 mL/min/1.73 m2 (20/40 patients). THE mean GFR observed is 22.9±21.14. The proportion of diabetic patients in the study group is 16/40. Among the etiology of CKD, diabetic kidney disease constituted 16/40 = 40%. Other causes included Hypertensive, Nephrosclerosis, Chronic Glomerulonephritis, Obstructive Uropathy, Bladder outlet Obstruction, Renal Calculus Disease. Important accompanying illness included Dilated Cardiomyopathy in 4 patients, Sepsis in 2 patients, Hemiparesis CVA in 2 patients, Hyperuricemia in 4 patients, Chronic Liver Disease in 2 patients.

Patients were either from OPD or admitted indoors. Most of our study patients were advanced chronic kidney disease (stage 5) and were on dialysis or were offered dialysis. Various patterns of abnormal Thyroid Function tests were observed in patients with deranged Thyroid Function Test.

In our study thyroid dysfunction was found in 40% of patients with CKD, the most common Hypo functioning of Thyroidal Gland in 20 patients (50%), patterns observed were: Isolated Low FT3, Low FT3, and Low FT4, Low FT3, FT4, and high TSH. Followed by subclinical hypothyroidism observed in 6 patients, Low FT3 with High TSH in 4 patients, two patients had low values of all three FT3, FT4, and TSH hormones. Our result is consistent with the finding of several previous studies.[9-11] A small study in hemodialysis patients showed the combined prevalence of subclinical and clinical hypothyroidism in 26.6% of patients.[12] Study by Lo et al found that the prevalence of hypothyroidism increased with lower levels of eGFR, occurring in 5.4% of subjects with eGFR greater than or equal to 90, 10.9% with eGFR 60–89, 20.4% with eGFR 45–59, 23.0% with eGFR 30–44, and 23.1%with eGFR < 30 (p < 0.001 for trend).[13] In a study in India among end-stage renal failure (ESRD) patients, the prevalence of subclinical hypothyroidism was 24.8%.[14]

In our study subclinical hyperthyroidism was observed in 2 patients. Two patients had high values for FT3 and FT4 hormones. Our study is in variance with previous literature about higher values of T3 and T4 and Lower values of TSH hormones being reported.[11]

A high incidence of abnormal Thyroid Function Test of 40% is not reported by earlier studies. Isolated low FT4 was not observed. Most patients exhibited low functioning of the Thyroid in one or other combinations. It is said low thyroid function in CKD is an adaptation to reduce catabolism and preserve body mass. It may be good for the untreated disease of CKD, but with the wide availability of treatment options like Maintenance Dialysis and Renal Transplant, every component should be treated for optimal results and to reduce the rate of CKD progression. Thyroid

Hormone replacement should be given to selected patients of CKD; there is literature to show benefits of treatment, like improvement in cardiac output and increased Renal Blood Flow, translating into increased GFR.[15,16] Our study serves the purpose of a pilot study for further large-scale controlled studies to evaluate thyroid function tests and chronic kidney disease at various stages, association, and causation.

CONCLUSIONS

In summary, thyroid dysfunction was found to be very common in CKD patients by this study. Also, this study reveals the significant association between thyroid dysfunction and the progression of CKD. An attempt will be made to see the correlation between different stages of CKD and the degree of thyroid distinction. Treatment of thyroid dysfunction will definitely improve hemodynamic factors involved with renal insufficiency. It is observed that treatment of hypothyroid state in CKD patients will improve hemodynamic factors for renal perfusion leading to some improvement in GFR. So estimation of Thyroid Function Tests should be recommended in the evaluation of CKD patients and Physicians should offer the benefit of diagnosis and treatment of abnormal TFT in CKD patients. Symptomatology of CKD patients and hypothyroid patients have a lot of similarities and diagnosis of hypothyroidism in CKD patients on clinical grounds alone may be difficult and routine testing of thyroid function test is likely to overcome problems of under-diagnosis of Thyroid dysfunction in CKD patients.

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