ORIGINAL ARTICLE

A Study of Thyroid Profile and Lipid Profile in Patients with Chronic Kidney Disease with or without Hemodialysis in a Tertiary Care Hospital

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Abstract

Background: Chronic kidney disease (CKD), due to increasing frequency and prevalence, has become one of the leading public health issues. The Kidney Disease Outcome Quality Initiative (KDOQI) defines CKD as kidney injury or a reduction in the glomerular filtration rate (GFR) to <60 mL/minute/1.73 m^2 for at least 3 months. This study aims to compare the effects of decreased renal function on thyroid profile and lipid profile in CKD patients.

Materials and methods: This is a prospective cross-sectional observational study conducted among the patients attending Outpatient Department/Inpatient Department (OPD/IPD) at the School of Medical Sciences & Research, Sharda Hospital, Greater Noida, Uttar Pradesh, India, in known cases of CKD, irrespective of the treatment/stage of CKD. All patients of >18 years of age with CKD were included in the study.

Result: A total of 200 patients who met the inclusion criteria were included after obtaining detailed informed consent, of which 100 were cases and 100 were controls. The mean age of patients in the study was 47.74 years, with the mean age in patients with CKD 52 years, and the control was 43 years. The mean level of triglycerides (TGs) was significantly higher among the cases, and the high-density lipoprotein (HDL) was significantly lower among cases compared to controls ($p < 0.05$). Pearson's correlation between thyroid-stimulating hormone (TSH) with creatinine showed a weak albeit significant positive association ($r = 0.200$; $p < 0.05$).

Conclusion: Our study shows a higher incidence of alteration in thyroid profile and dyslipidemia among the patients with CKD compared to controls. There is a necessary need to screen routinely for hypothyroidism and dyslipidemia among patients with CKD. Importantly, thyroid hormone levels and their effects on the progression of CKD have not been studied exhaustively.

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Introduction

As a consequence of ever-rising life expectancy, CKD has become one of the foremost challenges to the public health system. Its frequency and prevalence have increased over the past decades. K/DOQI defines CKD as kidney injury or a decrease in GFR of <60 mL/minute/1.73 m^2 for a period of 3 months.[1,2]

Chronic kidney disease (CKD) patients, especially those who have end-stage renal disease (ESRD) and who are managed with either intermittent hemodialysis (HD), peritoneal dialysis, or renal transplantation, have a greater risk of developing cardiovascular disease (CVD).[3] Patients with CKD are more likely to die because of CVD than due to complications arising out of ESRD and renal replacement therapy (RRT).[3,4] When compared to the general population, the incidence of CVD is significantly higher in patients with CKD. This is due to numerous risk factors frequently associated with CKD.[5] The risk factors can be the ones that are usually linked with CVD in the universal population, like age, gender, diabetes, obesity, hypertension, and dyslipidemia. There are also certain risk factors that are exclusive to patients of CKD; these are uremia, anemia, hyperhomocysteinemia, mineral bone disease-CKD with hyperparathyroidism, increased oxidative stress, hypoalbuminemia, and chronic inflammation.[3,4]

It has been frequently observed that a decrease in renal function usually affects the function of the thyroid gland. However, the association between thyroid hormone levels and the progression of CKD has not been studied exhaustively. CKD disrupts the working of the hypothalamus-pituitary-thyroid axis and also affects the peripheral metabolism of thyroid hormone. Previous studies have shown that a low triiodothyronine (T3) and subclinical hypothyroidism are the most frequent thyroid gland disorder which is seen in patients of CKD.[6]

Another common complication of CKD is dyslipidemia. Lipid profile is greatly affected by the grade of kidney function (GFR) and the extent of proteinuria.[7,8] Hypertriglyceridemia due to an increase in TG-rich lipoproteins [very-low-density lipoprotein (VLDL), chylomicrons, and their fragments] is typically seen in patients with CKD.

The mechanism which is most prominent in the raised levels of TG levels is delayed catabolism which occurs because the action of hepatic TG lipase and peripheral lipoprotein lipase is reduced. An increase in hepatic production of TG-rich lipoproteins also contributes to hypertriglyceridemia.[9,10]

Low-density lipoprotein (LDL) particles that are smaller, denser, and more atherogenic are not usually elevated in patients with CKD. However, oxidized LDL and intermediate-density lipoproteins, which are atherogenic, are increased.[10–12]

Materials and Methods

Study Type

Prospective cross-sectional observational study.

Study Site

Patients attending the School of Medical Sciences and Research, Sharda Hospital, Greater Noida, Uttar Pradesh, India.

Study Duration

September 2019–July 2020.

Study Participants

A total of 100 newly diagnosed and known CKD cases were involved in the study, along with an equivalent number of controls after taking informed consent from the patients (cases) and the controls.

After the approval of the Institutional Ethics Committee, this study was conducted on different age groups of patients who have

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CKD, are attending the OPD, or IPD admitted at Sharda Hospital.

Inclusion Criteria

- All patients of CKD aged >18 years with a history of or newly diagnosed CKD.
- CKD patients on either HD or conservative management.

Exclusion Criteria

- Patients with acute kidney injury or a history of renal transplantation.
- History of any hematological disorder.
- Patients with a history of any renal malignancy or on chemotherapy.
- Patients with autoimmune disorders.
- Patients in any stage of pregnancy.
- Patients with a history of use of nephrotoxic drugs/lipid-lowering agents/thyroid hormone-altering medications.

Statistical Analysis

All the patient's data was recorded in a patient *pro forma* sheet and entered in Microsoft Excel. The demographic details of the patients were summarized as frequency, percentage, mean, and standard deviation (SD). The data is represented using tables, figures, etc., as per need (Table 1). The statistical difference between the continuous variable was analyzed using the student's *t*-test, and categorical variables were analyzed using the Chi-squared test. Pearson's correlation was used to analyze the strength of the association between the continuous variables. A *p*-value of <0.05 was considered statistically noteworthy, and all the statistical analysis was executed by means of Statistical Package for the Social Sciences version 21, operating on Windows 10.

Results

A total of 200 subjects were enrolled after obtaining informed consent which included 100 patients with CKD and 100 healthy controls. The average age of subjects in the present study was 47.74 years, with the mean age in patients with CKD being 52 years and for control was 43 years (Table 2 and Fig. 1).

In studying the gender distribution among the study subjects, it was found that among the enrolled subjects, 40.5% were females, and 59.5% were males (Fig. 2).

The distribution of CKD patients in the study according to the mode of management with or without HD. Amongst the 100 enrolled cases of CKD, 44 patients were on maintenance HD, while 66 patients were taking medical management (Table 3).

On comparing the mean of urea and creatinine between the two study groups, it was observed that a higher proportion of patients with CKD had raised urea and creatinine values as equated with the control group (Table 4 and Fig. 3).

On comparing the thyroid profile between the study groups, the mean value of T3, thyroxine (T4), and TSH was found to be 3.3 ng/mL, 9.9 µg/mL, and 6.6 µIU/mL, respectively, in the CKD patients (Table 5 and Fig. 4).

On comparing the lipid profile between the two study groups, dyslipidemia was more prevalent amongst the patients with CKD as compared to the control group (Table 6 and Fig. 5).

A total of 200 study subjects were involved in the study after obtaining informed consent. Cases were 100 patients with CKD,

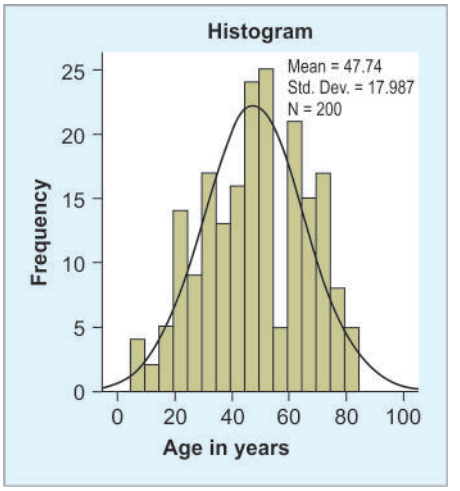

Fig. 1: Histogram showing the mean age distribution of patients enrolled in the study

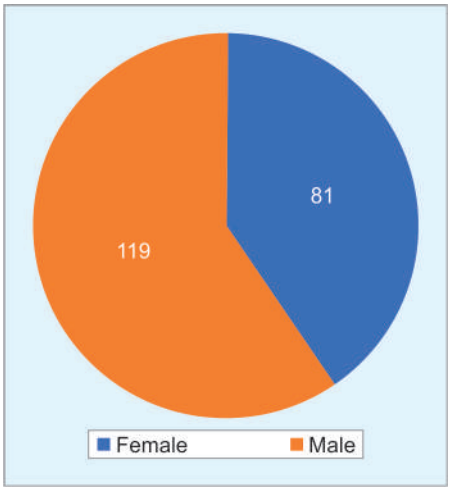

Fig. 2: Gender distribution among the study participants

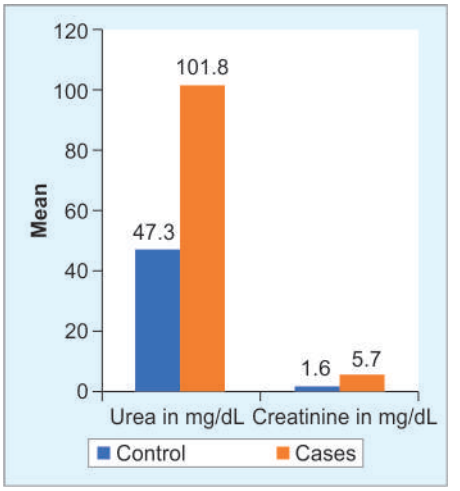

Fig. 3: Comparison of mean of urea and creatinine between the study groups

Table 1: CKD classification based upon GFR and albuminuria[19]

GFR stages	*GFR(mL/minute/1.73 m²)*	*Terms*
G1	≥90	Normal or high
G2	60–89	Mildly decreased
G3a	45–59	Mildly to moderately decreased
G3b	30–44	Moderately to severely decreased
G4	15–29	Severely decreased
G5	<15	Kidney failure (add D if treated by dialysis)
Albuminuria stages	*AER(mg/day)*	*Terms*
A1	<30	Normal to mildly increased (may be subdivided for risk prediction)
A2	30–300	Moderately increased
A3	>300	Severely increased (may be subdivided into nephrotic and nonnephrotic for differential diagnosis, management, and risk prediction)

Table 2: Showing the mean age of patients

	N	*Minimum*	*Maximum*	*Mean*	*SD*
Age in years	200	18	80	47.74	17.98

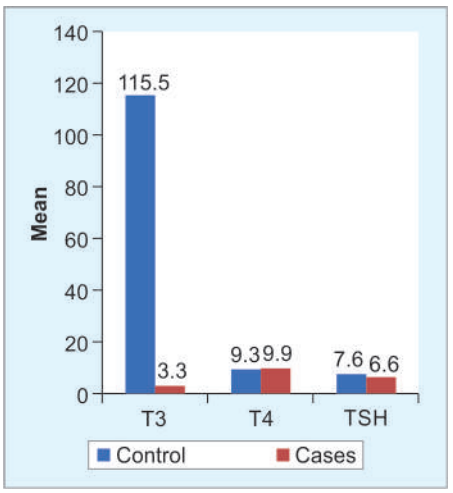

Fig. 4: Comparison of the thyroid profile between the study groups

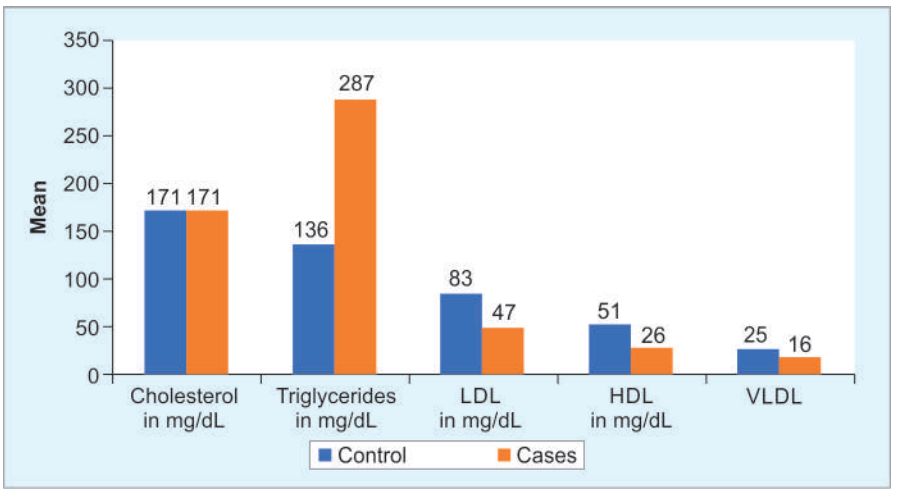

Fig. 5: Comparison of the lipid profile between the study groups

Table 3: Table showing the distribution of CKD patients according to the mode of management

Patients on maintenance HD	*Patients not on maintenance HD*
44	66

Table 4: Comparison of mean of urea and creatinine between the study groups

	Control		*Cases*		*p-value*
	Mean	*SD*	*Mean*	*SD*	
Urea in mg/dL	22.39	0.07	66.34	50.65	<0.001**
Creatinine in mg/dL	0.88	0.29	4.75	3.23	<0.001**

**, statistically significant

Table 5: Comparison of the thyroid profile between the study groups

	Control		*Cases*		*p-value*
	Mean	*SD*	*Mean*	*SD*	
T3	115.5	29.0	3.3	1.4	0.01**
T4	9.3	2.4	9.9	3.6	0.146
TSH	7.6	1.4	6.6	2.9	0.01**

**, statistically significant

Table 6: Comparison of lipid profile between the two study groups

	Control		*Cases*		*p-value*
	Mean	*SD*	*Mean*	*SD*	
Cholesterol in mg/dL	171	13	171	46	0.99
TGs in mg/dL	136	19	287	99	0.01**
LDL in mg/dL	83	7	47	11	0.01**
HDL in mg/dL	51	8	26	7	0.01**
VLDL	25	3	16	7	0.01**

**, statistically significant

and controls were 100 healthy controls. The mean age of participants in the present study was 47.74 years. The mean age was 51.18 ± 11.03 and 62.52 ± 11.95 years in control and CKD patients, respectively. Among 100 CKD patients, 40% ($n = 40$) were females, and 60% ($n = 60$) were males.

Among the study participants (cases and controls), the majority were male patients (59.5%), and 40.5% were female patients. The male-to-female ratio was found to be 1.46:1.

The levels of urea and creatinine increased significantly in CKD patients when compared to the control population. Blood urea in CKD patients was 66.34 ± 50.65 mg/dL ($p < 0.0001$), and serum creatinine was 4.75 ± 3.23 mg/dL ($p < 0.0001$), whereas, in control, blood urea was 22.39 ± 0.07 mg/dL and serum creatinine was 0.88 ± 0.29 mg/dL. Serum proteins were also significantly decreased in the CKD group 5.40±7.03 gm/dL ($p<0.0001$) vs 7.44±0.53 gm/dL in controls.

In studying the correlation between the lipid profile amongst CKD patients to healthy controls in the current study, we found that there was a greater occurrence of dyslipidemia in the patients diagnosed with CKD. The value of TGs in the controls (mean value 136 ± 19) was found to be lower as compared to patients with CKD (mean value 287 ± 99) ($p > 0.05$).

On studying the thyroid profile in the two study groups, it was concluded that a positive correlation exists between thyroid dysfunction and CKD (low T3 levels in the CKD patients with a mean value of 3.3 ± 1.4, $p < 0.01$) as compared to the study subjects (mean value of T3 in the study subjects 115.5 ± 29).

In a 2013 study conducted by Rajagopalan et al., it was found that in patients with CKD, the levels of T3 and T4 were significantly reduced, while the TSH levels remained unchanged when compared to healthy controls. In this study, they also found that there was a significant negative association between thyroid hormones and blood urea and creatinine levels.[13]

In another study conducted by Khatiwada et al. in Nepal, it was found that patients with CKD had abnormal thyroid functions. In this study, subclinical hypothyroidism was found to be strongly associated with CKD. This study also found a significant association between the progression of CKD and abnormalities of thyroid function.[14]

In another study conducted by Rajeev et al., it was found that in patients with CKD,

Table 7: Showing Pearson's correlation between TSH and creatinine among the study participants

		Creatinine in mg/dL
TSH	Pearson's correlation	0.200**
	Significant	0.004

**, statistically significant

the levels of total T3, total T4, albumin, and serum protein are significantly reduced when compared to controls. TSH levels were found to be significantly raised in the same study. These results are similar to the present study. We concur that patients with CKD have significant thyroid abnormalities, and these should be interpreted carefully.[15]

In the present study, the Pearson's correlation of TSH with creatinine was found to be a weak significant positive association, with $r = 0.200$, $p < 0.05$ (Table 7). In the study by Srivastava et al., Pearson's correlation coefficient revealed a nonsignificant relationship between the levels of urea in blood and serum TSH ($r = 0.236$, $p = 0.069$) and the creatinine clearance and serum TSH ($r = 0.206$, $p = 0.114$). There is a weak positive association between creatinine levels and TSH ($r = 0.248$, $p = 0.049$). Thyroid hormone levels were found to be significantly lower in nondialyzed CKD patients compared to healthy controls.[16]

Dyslipidaemia was seen among the patients with CKD. The mean level of TGs was significantly higher among the cases, and the HDL was significantly lower among the cases as compared to controls ($p < 0.05$).

In the study by Aryee et al., the TG, total count, LDL, HDL, VLDL, and TSH levels did not show any significant difference among the stages of CKD among the study subjects. However, the free-T4 (FT4) and free-T3 (FT3) levels were meaningly different between the stages of CKD. The study concluded that higher levels of FT3 and FT4 were associated with the occurrence of CKD and estimated GFR decline among the patients with CKD.[17]

In a 2013 study conducted by Chen et al., it was found that dyslipidaemias and their certain levels were independently associated with a need for RRT and rapid progression of CKD in stages 3–5. This study which was conducted on 1,080 subjects, concluded that an assessment of lipid profile might help to identify patients at risk of developing a rapidly progressive renal dysfunction.[18]

Strengths of Study

Dyslipidemia and thyroid hormone dysfunction are major contributors to the early progression and increased complications in patients with CKD. These are two easily attainable parameters and, therefore, if managed timely, can slow the progression of the disease.

The presence of an equal number of healthy subjects provides more credibility to the observations made.

Limitations of Study

Small sample size and single-centric study. The study has large potential to globalize the findings and strengthen the results by conducting similar observations at multiple centers with a larger sample size which includes an equal number of males and females.

Conclusion

A prospective cross-sectional study was conducted on a total of 200 study subjects at the School of Medical Sciences and Research, Sharda Hospital, Greater Noida, Uttar Pradesh, India, on 100 CKD patients and 100 healthy controls.

Blood samples for thyroid profile, lipid profile, and kidney function test were taken.

The study documented a higher incidence of alteration in thyroid profile and dyslipidemia among the patients with CKD compared to controls.

Clinicians must exercise extreme caution in patients with CKD, and regular screening for thyroid dysfunction and dyslipidemia should be carried out.

This, in turn, may contribute to decreased CVD risk in patients with CKD so that timely intervention and proper preventive measures can be undertaken.

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