Section: General Medicine

Original Research Article

STUDY OF THYROID AND LIPID PROFILE IN CHRONIC KIDNEY DISEASE

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Received : 25/10/2024
Received in revised form : 06/12/2024
Accepted : 20/12/2024

Keywords:
Chronic kidney disease, Lipid profile, Thyroid function, Glomerular filtration rate, Cardiovascular disease, HDL.

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DOI: 10.47009/jamp.2024.6.6.128

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 675-679

Abstract

Background: Chronic kidney disease leads to a progressive decline in GFR. CKD is associated with lipid and thyroid dysfunction, including elevated triglyceride, low HDL, and altered thyroid hormone levels. This study aimed to determine the thyroid and serum lipid profiles of patients with CKD and compare them with those of healthy controls. **Materials and Methods:** This prospective cross-sectional study included 100 patients with CKD admitted to the Department of General Medicine, Tirunelveli Medical College and Hospital for one year. The details of the patient were obtained, and routine laboratory investigations, thyroid function tests, and lipid profiles were obtained. **Result:** Most patients were aged 41-50 years (28%). Of these patients, 66% were male and 34% were females. Diabetes and hypertension were prevalent in 66% and 68% of the patients, respectively. There were significant differences between serum T3 ($p = 0.001$), T4 ($p = 0.006$), and THS levels ($p = 0.001$). Serum creatinine levels increased significantly with CKD severity, (4.94 ± 1.75) in Grade V ($p = 0.001$). The eGFR also showed a significant difference of (67 ± 1.41) in grade II to (11.75 ± 2.41) in grade V ($p = 0.001$). Total cholesterol in grade V CKD was (255.25 ± 34.94) and low in Grade II (182.58 ± 17.67), with a significant increase as CKD severity progressed ($p = 0.001$). **Conclusion:** CKD progression correlates with lower T3 and T4 levels, higher TSH levels, reduced HDL levels, and elevated triglyceride, total cholesterol, LDL, and VLDL levels. The negative correlation between HDL and GFR affects lipid metabolism in renal dysfunction.

INTRODUCTION

Chronic kidney disease (CKD) encompasses a group of distinct pathophysiological processes associated with abnormal kidney function that progressively reduce the Glomerular Filtration rate (GFR).[1] Various pathological processes in CKD ultimately result in the loss of renal metabolic, excretory, endocrine, and synthetic functions owing to the accumulation of various protein-nitrogenous substances.[2] The most widespread cause of mortality in patients with CKD is a spectrum of cardiovascular diseases. The prevalence of cardiovascular morbidity in patients age group 25-34 years with CKD is 500 times higher than that in people without CKD in similar age groups and races.[3] Primary Care Physicians mostly manage the initial stages of CKD and play a pivotal role in delaying the progression of CKD to ESRD by addressing various comorbidities associated with CKD by identifying and intervening early.[4]

Two important comorbidities in patients with CKD are lipid and thyroid dysfunctions. Hyperlipidaemia, an abnormally high level of lipids in the blood, is a well-known risk factor for early atherosclerosis, which causes various cardiovascular diseases and is frequently seen in patients with CKD.[3] Indian studies demonstrating the pathophysiological relationship of CKD with Lipid profile have quoted almost no lipid profile abnormalities in CKD to pathophysiological significant alterations in lipid profile in patients with CKD, such as high triglycerides and low HDL levels.[5] Shah and Nair studied the occurrence of lipid profile abnormalities in CKD and demonstrated significant hypertriglyceridemia in CKD patients.[6] Increased levels of triglycerides, total cholesterol, and low levels of HDL-C in patients with CKD managed conservatively have been shown in a study by Sumathi.[7]

There is also evidence of thyroid hormone dysfunction in CKD patients, which causes alterations in the synthesis, secretion, metabolism, and elimination of thyroid hormones. Iodine, an important element in synthesizing thyroid hormones, is removed from the circulation by glomerular filtration under physiological conditions.[8] In CKD, progressively decreasing GFR leads to the accumulation of iodine in the blood, which ultimately

ISSN (O): 2687-5365; ISSN (P): 2753-6556

leads to decreased thyroid hormone synthesis by the 'Wolff Chaikoff effect.' This results in subnormal serum total and free T3 concentrations and normal reverse T3 and free T4 levels. However, the TSH levels were mostly unaltered in patients with CKD. Patients with CKD may also present with hypothyroidism in CKD. Previous studies have demonstrated all types of thyroid abnormalities, including hypothyroidism, hyperthyroidism, and euthyroidism, in patients with CKD, with a prevalence of hypothyroidism of 0.9%. Goitre is also noted in patients with CKD.[9]

Aim

This study aimed to determine the thyroid and serum lipid profiles of patients with CKD and compare them to those of healthy controls.

MATERIALS AND METHODS

This prospective cross-sectional study included 100 patients with CKD admitted to the Department of General Medicine, Tirunelveli Medical College and Hospital for one year. This study was approved by the Institutional Ethics Committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

Patients admitted to the Department of Medicine, Tirunelveli Medical College Hospital, and diagnosed with chronic kidney disease were included.

Exclusion Criteria

Patients with known cases of thyroid dysfunction and dyslipidemia, those undergoing dialysis, and pregnant women were excluded.

Methods: The details of the patient were obtained, and routine laboratory investigations, thyroid function tests, and lipid profiles were obtained.

Statistical Analysis: Data are presented as mean, standard deviation, frequency, and percentage. Continuous variables were compared using ANOVA. Significance was defined as $p < 0.05$ using a two-tailed test. Data analysis was performed using IBM-SPSS version 21.0 (IBM-SPSS Corp., Armonk, NY, USA).

RESULTS

The age distribution varied; most patients were between 41-50 years (28%) and 51-60 years (26%), with lower percentages of < 30 years (13%), 31-40 years (15%), and > 60 years (18%). Of the patients, 66% were male and 34% were females. Most patients (66%) had grade IV CKD, 20% had grade III CKD, 12% had Grade V CKD, and only 2% had Grade II CKD [Table 1].

Diabetes was present in 66% of the patients, and 68% had hypertension. Thyroid function tests showed that 88% of patients had normal serum T3 levels, while 12% had low T3 levels. The serum T4 levels showed that 89% of the patients were normal and the low T4 level was 11%. TSH levels were low at 88%, and 12% had normal TSH levels. Regarding lipid profiles, 74% had high total cholesterol levels, while 26% were within the normal range. The triglyceride levels in normal patients were 87% and in high patients were 13%, respectively. For HDL, 56% of patients had normal levels, whereas 44% had low levels. Among patients with abnormal LDL levels, 62% had abnormal patients, and 38% had normal LDL levels. In terms of VLDL levels, abnormal patients were 61%, and normal were 39% [Table 2].

Males in grade IV had a higher number of patients with 43 and females also had a higher number of patients in grade IV with 23 patients. Of the patients with diabetes, 12 had Grade III CKD, 45 had Grade IV CKD, and 9 had grade V CKD, with no patients having Grade II CKD. The highest number of patients with hypertension was grade IV CKD, with 43 patients [Table 3].

The mean age of the patients was high in CKD grade II (64 ± 5.65) and low in Grade III (43.95 ± 14.35), with no significant differences ($p = 0.179$). Blood urea levels in grade V CKD at an average of 142.44±25.6, followed by grade IV had 140.38 ± 40.04, grade III had 130.85 ± 69.74, and grade II with a low average of 93±12.72, which was not significantly differences ($p = 0.505$).

Grade V CKD showed a high serum creatinine level (4.94 ± 1.75), followed by grade IV CKD (3.44 ± 0.69), grade III (1.9 ± 0.3), and grade II CKD (low level) (1.2 ± 0), with the serum creatinine levels increasing significantly ($p = 0.001$). eGFR in grade II CKD was 67 ± 1.41, in grade III was 42.14 ± 8.49, in grade IV, was 19.33 ± 3.84, and in grade V with a low eGFR was 11.75 ± 2.41, which was significantly different ($p = 0.001$) [Table 4].

The mean of serum T3 levels in grade II CKD was 1.5 ± 0.14, followed by grade III had 1 ± 0.26, grade IV had 0.82 ± 0.34, and low in grade V had 0.76 ± 0.29. The mean serum T4 level in grade II CKD was 7.05 ± 0.77, grade III was 3.79 ± 0.72, grade IV was 2.59 ± 1.07, and the lowest level in grade V was 2.48 ± 0.99.

The mean serum TSH levels in grade V CKD was 11.39 ± 2.17, followed by grade IV had 10.87 ± 2.45, grade III had 9.1 ± 2.78, and low in grade II had 7.92 ± 0.59. There were significant differences in serum T3, T4, and TSH between CKD grades ($p = 0.001$), ($p = 0.006$), and ($p = 0.001$), respectively [Table 5].

The mean total cholesterol level was high in CKD Grade V 255.25 ± 34.94 and low in Grade II (182.58 ± 17.67), with a significant difference ($p = 0.001$). Triglycerides in Grade V were 195.33 ± 13.32, and low in Grade II were 148 ± 5.65, which was not significant ($p = 0.171$).

The mean HDL levels decreased significantly in CKD grades, with high levels in grade II 52.6 ± 5.65 and low levels in grade V 31.08 ± 3.47 ($p = 0.001$). LDL levels were also high in grade V 163.3 ± 22.76 and low in Grade II 132.5 ± 17.67, which was not significant ($p = 0.199$). The mean of VLDL level, grade V had a high 63.33 ± 15.66, while grade II had a low level of 16.5 ± 2.12, which was not a significant difference ($p = 0.423$) [Table 6]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 1: Demographic details.

		Frequency (%)
Age in years	< 30	13%
	31-40	15%
	41-50	28%
	51-60	26%
	> 60	18%
Sex	Male	66%
	Female	34%
CKD Grade	Grade II	2%
	Grade III	20%
	Grade IV	66%
	Grade V	12%

Table 2: Prevalence of co-morbidity and the thyroid and serum lipid profiles in CKD

		Frequency (%)
Diabetes	Present	66 (66%)
	Absent	34 (34%)
Hypertension	Present	68 (68%)
	Absent	32 (32%)
Serum T3	Normal	88 (88%)
	Low	12 (12%)
Serum T4	Normal	11 (11%)
	Low	89 (89%)
Serum TSH	Normal	12 (12%)
	Low	88 (88%)
Total cholesterol	Normal	26 (26%)
	High	74 (74%)
Triglycerides	Normal	87 (87%)
	High	13 (13%)
HDL	Normal	56 (56%)
	Low	44 (44%)
LDL	Normal	38 (38%)
	Abnormal	62 (62%)
VLDL	Normal	39 (39%)
	Abnormal	61 (61%)

Table 3: Comparison of sex, diabetes, and hypertension between grades of CKD

		CKD Grade			
		Grade II	Grade III	Grade IV	Grade V
Sex	Male	1 (1%)	18 (18%)	43 (43%)	4 (4%)
	Female	1 (1%)	2 (2%)	23 (23%)	8 (8%)
Diabetes	Present	0	12 (12%)	45 (45%)	9 (9%)
	Absent	2 (2%)	8 (8%)	21 (21%)	3 (3%)
Hypertension	Present	1(1%)	15 (15%)	43 (43%)	9 (9%)
	Absent	1 (1%)	5 (15%)	23 (23%)	3 (3%)

Table 4: Comparison of age, and renal parameters between grades of CKD

	CKD Grade				P value
	Grade II	Grade III	Grade IV	Grade V	
Age in years	64 ± 5.65	43.95 ± 14.35	48.55 ± 13.94	49.75 ± 10.21	0.179
Blood urea (mg/dL)	93 ± 12.72	130.85 ± 69.74	140.38 ± 40.04	142.44 ± 25.6	0.505
Serum creatinine (mg/dL)	1.2 ± 0	1.9 ± 0.3	3.44 ± 0.69	4.94 ± 1.75	0.001
eGFR (mL/min)	67 ± 1.41	42.14 ± 8.49	19.33 ± 3.84	11.75 ± 2.41	0.001

Table 5: Comparison of thyroid profile between grades of CKD

	CKD Grade				P value
	Grade II	Grade III	Grade IV	Grade V	
Serum T3 (ng/mL)	1.5 ± 0.14	1 ± 0.26	0.82 ± 0.34	0.76 ± 0.29	0.001
Serum T4 (µg/dL)	7.05 ± 0.77	3.79 ± 0.72	2.59 ± 1.07	2.48 ± 0.99	0.006
Serum TSH (µIU/mL)	7.92 ± 0.59	9.1 ± 2.78	10.87 ± 2.45	11.39 ± 2.17	0.001

Table 6: Comparison of lipid profile between the grades of CKD

	CKD Grade				P value
	Grade II	Grade III	Grade IV	Grade V	
Total cholesterol (mg/dL)	182.58 ± 17.67	202.55 ± 19.28	236.79 ± 35.96	255.25 ± 34.94	0.001
Triglycerides (mg/dL)	148 ± 5.65	162.3 ± 32.79	181 ± 52.99	195.33 ± 13.32	0.171
HDL (mg/dL)	52.6 ± 5.65	40.2 ± 10.79	36.35 ± 3.18	31.08 ± 3.47	0.001
LDL (mg/dL)	132.5 ± 17.67	144.55 ± 19.76	151.76 ± 29.04	163.3 ± 22.76	0.199
VLDL (mg/dL)	16.5 ± 2.12	38.85 ± 8.46	56.52 ± 17.21	63.33 ± 15.66	0.423

ISSN (O): 2687-5365; ISSN (P): 2753-6556

DISCUSSION

In our study, of the 100 patients with CKD,66 were males and 34 were female. The age distribution varied; most patients were between 41-50 years (28%) and 51-60 years (26%), with lower percentages of < 30 years (13%), 31-40 years (15%), and > 60 years (18%). Spector DA studies have found that most patients (72%) were between 30-60 years. The remaining two age groups (< 30 and > 60 years) had a similar proportion of cases (13% and 15%, respectively). 32 (60.4%) patients were males and 21 (39.6%) were females. Approximately two-thirds of the patients were males, while only one-third were females.[10]

In our study, thyroid function tests showed that 88% of patients had normal serum T3 levels, while 12% had low T3 levels. The serum T4 levels showed that 89% of the patients were normal and the low T4 level was 11%. TSH levels were low at 88%, and 12% had normal TSH levels. Regarding lipid profiles, 74% had high total cholesterol levels, while 26% were within the normal range.

Hardy et al. showed mean serum TSH level was significantly higher in the dialysis patients, although 35 of 40 patients had levels within the normal range. The remaining 5 patients had slightly increased TSH levels, the highest being 5.4 mlU/L, but these 5 patients did not have significantly lower thyroid hormone levels than the patients with normal TSH values.[11] Singh et al. reported a significant decrease in the levels of T3, T4, total protein, and albumin levels in CRF patients when compared to control.[12]

Iglesias and Diez reviewed that chronic kidney disease is accompanied by notable effects on the hypothalamus-pituitary–thyroid axis. The secretion of pituitary thyrotropin (TSH) is impaired in uremia. Contrary to other non-thyroidal chronic diseases, in uraemic patients it is not unusual to observe the sick euthyroid syndrome with low serum triodothyronine (T3) without elevation of reverse T3 (rT3).[13] Spector et al. reported a linear correlation between mean serum T3 and T4 levels and the severity of CKD.[10] Studies by Quionverde et al. showed a high prevalence of hypothyroidism in CKD. It is estimated to be approximately 5% in patients at the final stage of CKD.[14]

In our study, none of the patients showed clinical or biochemical features of hyperthyroidism. The symptoms of hypothyroidism were equally distributed in both hypothyroid and CKD patients. Kaptein et al. showed that the prevalence of primary hypothyroidism was approximately 2.5 times higher in patients with chronic kidney disease and dialysis than in the normal population.[15]

In our study, the mean T3 level decreased in patients with a GFR < 15 ml/min. In patients with reduced GFR, T3 level was found to be reduced and it shows that there was a straight-line relationship between levels of T3, T4, and GFR, which is consistent with Fitzgerald et al. study.[16]

In our study, none of the patients had a goiter. But Ramirez et al. showed a high prevalence of goiter in patients with CKD, especially in those undergoing chronic dialysis.[17] In addition, a study conducted by Hegedus et al. showed that the thyroid gland volume was significantly increased in patients with CKD.[18]

In our study, 56 of the 100 patients with CKD had low HDL levels. The low HDL levels in patients with CKD were matched with Lee et al., who studied the abnormalities of lipid profiles in CRF patients.[19] This Low HDL cholesterol level was also an isolated independent risk factor for the development of CKD in the Framingham Spring Study.[20]

In our study, triglyceride levels were higher, and abnormal triglyceride values were found in 13 out of 100 patients. This demonstrates that CRF is commonly accompanied by lipid dysfunction, manifesting as hypertriglyceridemia. Chan et al. showed that hypertriglyceridemia was the major abnormality in their studies. Hypertriglyceridemia may be an early feature of renal failure.[21]

In our study, LDL levels were elevated, and LDL cholesterol levels were significantly higher in patients with CKD stages IV and V, and 61 of 100 patients had elevated LDL levels. Most studies point out that uremic patients commonly have normal to slightly decreased concentrations of LDL-C levels and exhibit significant disturbance in the density distribution of the LDL subfraction, which is characterised by the presence of predominantly small dense LDL particles.[22]

In our study, total cholesterol levels increased in 74 of the 100 patients with CKD, resulting in acquired LDL receptor deficiency, which plays a vital role in the cause of associated hypercholesterolemia, consistent with the study by Vaziri et al.[23]

CONCLUSION

CKD progression was associated with an increasing trend of low T3 and T4 levels and elevated TSH levels, indicating a higher incidence of hypothyroidism as renal function deteriorates. Additionally, advancing age and lower GFR were correlated with an increased incidence of low T3 syndrome. Lipid profile analysis revealed decreased HDL levels and elevated triglyceride, total cholesterol, LDL, and VLDL levels in CKD patients compared to controls, with significant differences in increases in triglycerides, LDL, and VLDL in advanced CKD stages (Grades III, IV, and V). A significant negative correlation was observed between HDL level and GFR, underscoring the impact of renal dysfunction on lipid metabolism.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556

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ISSN (O): 2687-5365; ISSN (P): 2753-6556