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Original Research Article

Thyroid and lipid profile in chronic kidney disease in Southern India

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ABSTRACT

Background: The progression of chronic kidney disease (CKD) is linked to a multitude of comorbidities, such as thyroid dysfunction, dyslipidemia, and cardiovascular disease. Objective were to determine the thyroid and serum lipid profile of CKD patients and to establish correlation between severity of renal disease with these 2 metabolic parameters.
Methods: This was a prospective study conducted among the 100 CKD patients over 1 year admitted in the department of urology and nephrology at our hospital.
Results: There were 66 (66%) male patients and 36 (36%) female patients among the 100 patients. There were no patients in grade 1, whereas there were 2, 20, 66, and 12 patients in grades 2-5 CKD, respectively. In each grade of CKD, the mean age, eGFR, urea, creatinine, thyroid profile, and lipid profile were computed individually. The levels of urea, creatinine, and eGFR differed significantly across CKD grades 2-5. The thyroid profile differed significantly across CKD grades 2-5. The lipid profile differed significantly across CKD grades 2-5, with p=0.000, >0.05, 0.000, >0.05, >0.05 for total cholesterol, triglycerides, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) levels, respectively.
Conclusions: The number of patients increases with decreasing T3 and T4 and increasing thyroid stimulating hormone (TSH) proportionate to the severity of the renal failure. In addition, hypothyroidism is becoming more common in people with chronic renal disease. Serum triglycerides, LDL, and VLDL levels rise statistically significantly in CKD grades 3-5 patients.

Keywords: Dyslipidemia, CKD, Hemodialysis, Thyroid function test

INTRODUCTION

Chronic kidney disease (CKD) encompasses a group of distinct pathophysiological processes which are associated with abnormal kidney functioning and progressively reducing glomerular filtration rate (GFR).[1] Various pathological processes in CKD ultimately results in loss of renal metabolic, excretory, endocrine, and synthetic functions due to the accumulation of various protein nitrogenous substances.[2] The initial stages of CKD are mostly managed by primary care physicians and they have a pivotal role in delaying the progression of CKD to ESRD by addressing various comorbidities associated with CKD by identifying and intervening them early. Two of such important co-morbidities are lipid dysfunction and Thyroid dysfunction in patients with CKD. Hyperlipidemia, an abnormally high level of lipids in the blood, is a well-known risk factor for early atherosclerosis causing various cardiovascular diseases, is frequently seen in patients with CKD.[3] Indian studies demonstrating the patho-physiological relationship of CKD with lipid profile have quoted almost nil lipid profile abnormalities in CKD to patho-physiologically significant alterations in lipid profile in patients with CKD like high triglycerides and low HDL level. Shah et al studied the occurrence of lipid profile abnormalities in CKD and have demonstrated significant hyper triglyceridemia in patients with CKD.[4] Increased level of triglycerides, total cholesterol and low levels of HDL-C in patients with CKD managed conservatively has been shown in a study by Sumathi et al.

There is also evidence of thyroid hormone dysfunction in patients with CKD.[5] CKD causes alteration in synthesis, secretion, metabolism and elimination of thyroid hormones. Iodine an important element in the synthesis of thyroid hormone removed from circulation by glomerular filtration under physiological conditions. In CKD, progressively decreasing GFR leads to accumulation of iodine in the blood which ultimately leads to decreased thyroid hormone synthesis by 'Wolff Chaikoff effect'. This results in subnormal levels of serum total and free T_3 concentration and normal reverse T_3 and free T_4 levels. But, TSH level is mostly unaltered in CKD. Patients may have symptoms of hypothyroidism in CKD.[6,7]

Objectives

Objectives of the study were to determine the thyroid and serum lipid profile of CKD patients and to establish a correlation between the severity of renal disease with these two metabolic parameters.

METHODS

A prospective cross-sectional study of 100 CKD patients enrolled to Narayan medical college's department of urology and nephrology was undertaken from April 2019 to March 2020. Routine laboratory investigations, thyroid function tests and lipid profiles are done. Inclusion criteria were Patients diagnosed as CKD patients. Exclusion criteria were patients already known cases of thyroid dysfunction, dyslipidemia, patients undergoing dialysis and pregnant women. Informed consent was obtained from each patient. The study had institute ethical committee (IEC) approval. Hundred CKD cases admitted to nephrology and urology departments at our institute were enrolled on the study. The data were statistically analyzed using SPSS version 22. For continuous variables, the data were presented as the mean +SD or the median within range and means were compared using one-way analysis variance. For categorical variables, the data were presented as counts and percentages and the differences were analyzed using the chi-square test.

RESULTS

Out of 100 patients, 66 (66%) were male patients and 36 (36%) were female patients. No patients in grade 1, while 2, 20, 66 and 12 patients in grade 2-5 CKD respectively. Diabetes mellitus was present in 66 (66%) cases of CKD. Hypertension was present in 68 (68%) cases of CKD.

Mean age, eGFR, urea, creatinine, thyroid profile and lipid profile in each grade of CKD is mentioned in Tables 1-4.

There was a significant difference in the urea, creatinine and eGFR levels between CKD grades 2-5 with p>0.05, <0.0001, <0.0001 respectively (Table 5).

There was a significant difference in the thyroid profile between CKD grades 2-5 with p=0.006, 0.000, >0.05 for T3, T4 and TSH respectively (Table 6).

There was a significant difference in the lipid profile between CKD grades 2-5 with p=0.000, >0.05, 0.000, >0.05, >0.05 for total cholesterol, triglycerides, HDL, LDL and VLDL levels respectively (Table 7).

Table 1: Descriptive statistics of grade 2 CKD.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	2	60	68	64.00	4.657
eGFR	2	66.00	68.00	67.0000	1.41421
Urea	2	84.00	102.00	93.0000	12.72792
Creatinine	2	1.20	1.20	1.2000	0.00000
T3	2	1.40	1.60	1.5000	0.14142
T4	2	6.50	7.60	7.0500	0.77782
TSH	2	7.50	8.34	7.9200	0.59397
Total cholesterol	2	170.00	195.00	182.5000	17.67767
Triglycerides	2	144.00	152.00	148.0000	5.65685
HDL	2	48.00	56.00	52.0000	5.65685
LDL	2	120.00	145.00	132.5000	17.67767
VLDL	2	15.00	18.00	16.5000	2.12132

Table 2: Descriptive statistics of grade 3 CKD.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	20	10	70	43.95	14.358
eGFR	20	31.00	58.00	42.1500	8.47457
Urea	20	15.60	328.00	130.8550	69.74827
Creatinine	20	1.39	2.30	1.9015	0.30278
T3	20	0.60	1.90	1.0060	0.26573
T4	20	2.50	5.00	3.7910	0.72357

Continued.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
TSH	20	6.60	16.70	9.1075	2.78036
Total cholesterol	20	163.00	263.00	202.5500	19.78696
Triglycerides	20	102.00	241.00	162.3000	32.79297
HDL	20	15.00	57.00	40.2000	10.79279
LDL	20	120.00	178.00	144.5500	19.76300
VLDL	20	21.00	55.00	38.8500	8.46836

Table 3: Descriptive statistics of grade 4 CKD.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	66	14	89	48.95	13.949
eGFR	66	15.00	29.00	19.3333	3.84841
Urea	66	21.20	204.00	140.3894	40.04487
Creatinine	66	2.17	4.56	3.4459	0.69412
T3	66	0.30	1.80	0.8258	0.34788
T4	66	0.20	4.90	2.5923	1.07250
TSH	66	5.80	109.00	10.8788	12.45530
Total cholesterol	66	120.00	300.00	236.7879	35.69551
Triglycerides	66	126.00	574.00	181.0000	52.99289
HDL	66	31.00	44.00	36.3485	3.18889
LDL	66	119.00	276.00	151.7424	29.04867
VLDL	66	21.00	556.00	56.5152	67.21429

Table 4: Descriptive statistics of grade 5 CKD.

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age (Years)	12	39	74	49.75	10.217
eGFR	12	6.00	14.00	11.7500	2.41680
Urea	12	95.70	292.00	142.4417	56.10251
Creatinine	12	3.60	10.10	4.9433	1.75646
T3	12	0.30	1.20	0.7667	0.29336
T4	12	0.60	4.20	2.4842	0.99048
TSH	12	8.40	14.60	11.3917	2.17400
Total cholesterol	12	203.00	297.00	255.2500	34.94704
Triglycerides	12	175.00	214.00	195.3333	13.32348
HDL	12	25.00	35.00	31.0833	3.47611
LDL	12	125.00	187.00	163.3333	22.70896
VLDL	12	38.00	80.00	63.3333	15.66892

Table 5: Comparison of means of EGFR, urea and creatine between CKD grades by ANOVA.

Variables	Mean	SD	F value	P value
Urea				
CKD grade 2	93.000	12.727	0.785	>0.05
CKD grade 3	130.85	69.750		
CKD grade 4	140.90	40.044		
CKD grade 5	142.44	56.102		
Creatinine				
CKD grade 2	1.200	0.0000	39.008	<0.0001
CKD grade 3	1.902	0.303		
CKD grade 4	3.445	0.694		
CKD grade 5	4.943	1.756		
eGFR				
CKD grade 2	67.000	1.414	180.815	<0.0001
CKD grade 3	42.150	8.474		
CKD grade 4	19.333	3.850		
CKD grade 5	11.750	2.416		

Table 6: Comparison of means of thyroid profile between CKD grades by ANOVA.

Variables	Mean	SD	F value	P value
T3				
CKD grade 2	1.50	0.141	4.468	0.006
CKD grade 3	1.90	1.006		
CKD grade 4	0.825	0.347		
CKD grade 5	0.767	0.293		
T4				
CKD grade 2	7.05	0.777	19.524	0.000
CKD grade 3	5.00	3.791		
CKD grade 4	2.59	1.072		
CKD grade 5	2.48	0.990		
TSH				
CKD grade 2	7.920	0.593	0.221	>0.05
CKD grade 3	16.70	9.107		
CKD grade 4	10.88	12.455		
CKD grade 5	11.39	2.174		

Table 7: Comparison of means of lipid profile between CKD grades by ANOVA.

Variables	Mean	SD	F value	P value
Total cholesterol				
CKD grade 2	182.50	17.68	9.279	0.000
CKD grade 3	202.55	19.78		
CKD grade 4	236.78	35.69		
CKD grade 5	255.25	34.95		
Triglycerides				
CKD grade 2	148.00	5.66	1.705	>0.05
CKD grade 3	162.30	32.79		
CKD grade 4	181.00	52.99		
CKD grade 5	195.33	22.71		
HDL				
CKD grade 2	52.00	5.65	11.571	0.000
CKD grade 3	40.20	10.79		
CKD grade 4	36.34	3.18		
CKD grade 5	31.08	3.47		
LDL				
CKD grade 2	132.50	17.68	1.579	>0.05
CKD grade 3	144.55	19.76		
CKD grade 4	151.74	29.04		
CKD grade 5	163.33	22.70		
VLDL				
CKD grade 2	16.50	2.12	0.942	>0.05
CKD grade 3	38.85	8.46		
CKD grade 4	56.51	67.21		
CKD grade 5	63.33	15.66		

DISCUSSION

To determine the pathological interrelationship between thyroid dysfunction and severity of renal disease, numerous studies were conducted about thyroid function abnormality and severity of CKD and different results have been shown. In our study, only those CKD patients on the conservative line of therapy were studied. This can be attributed to the fact that thyroid profile changes due to dialysis independent of the present due to CKD. Numerous studies have been studied by comparing CKD patients on the conservative line of management and patients on HD by Ramirez et al and Kayima et al.[8,9] In our study, 100 patients of CKD, who were on conservative management fulfilling the criteria for CKD were studied, among these 100 patients, 66 were males and 34 were females, their age distribution varied from less than 30 years to more than years. Among these 100 patients, patients were categorized into less than 30 years, 31-40 years, 41-50 years, 51-60 years, more than 60 years.

Of the 100 patients, the mean eGFR ranged from 67 ml/min in stage II CKD to 11.75 ml/min in stage V CKD in our study. The blood urea means value ranged from 93 mg/dl in stage II CKD to 142.44 mg/dl in stage V CKD. The creatinine mean value varied from 1.2 mg/dl in stage II CKD to 4.9 mg/dl in stage V CKD. In our study out of 100 patients, 12 patients had low serum T3 levels (12%), 89 patients had low T4 levels (89%), 88 patients had low TSH (88%) and 12 had normal range TSH. In our study, the decreasing trend in T4 and increasing trend in TSH showed a linear correlation with progressing stages of CKD. One study done by Ramirez et al, Spector et al, Dudani et al and Karunanidhi et al showed abnormality in the hypophyseal mechanism of TSH release in patients with uremia as the TSH response to the TRH was reduced.[8,10-12] Ramirez et al and Spector et al study exposed the linear correlation between mean serum T3 and T4 and severity of CKD.[8,10] A detailed study by Kaptein et al showed the prevalence of primary hypothyroidism was about 2.5 times much higher in CKD and dialysis than in the normal population.[13] The incidence of hypothyroidism in CKD was estimated to range between 0 and 9.5%. Kaptein et al study also calculated the presence of an anti-thyroid antibody titer in 6.7% of CKD.[13] The symptoms of hypothyroidism were distributed equally in both hypothyroid and CKD patients in our study. So, diagnosis of hypothyroidism in CKD, more importantly, depends on TSH level which must be very high (>20 µIU/dl) with a low level of serum T4. In this study, none of the patients had clinical or biochemical features of hyperthyroidism. As a go with other studies, the mean T3 level in our study was decreased in GFR less than 15 ml/min.

Goiter

A study by Ramirez et a1 showed a high prevalence of goiter in patients with CKD especially those undergoing chronic dialysis.[8] The incidence was found to be raised in end-stage renal disease. The possible explanation could be due to the accumulation of iodides in the Thyroid gland due to reduced renal clearance in CKD patients. Other than goiter, a study conducted by Hegedus et al showed the volume of the thyroid gland was significantly increased in patients with CKD.[14] In our study, no patient had a goiter.

CKD and lipid

In our study, the most frequent lipid abnormalities documented were low HDL levels and hypercholesterolemia.

Decreased high-density lipoprotein levels

In our study, 56 out of 100 patients with CKD had low levels of HDL. The low HDL levels in patients with CKD in our study were in a match with Diana et al who studied the abnormalities of lipid profile in CRF patients.[15] This low HDL cholesterol level was also an isolated independent risk factor for the development of CKD in the Framingham spring study.[16] Several pathological processes may underlie the reductions in HDL cholesterol levels, which is usually an indication of dysfunctional reverse cholesterol transport. Apo AI, which is the activator of lecithin cholesterol acyltransferase (LACT), is decreased in CKD due to inverse regulation of hepatic Apo AI genes causing a decline in the function of LACT, which leads to decreased cholesterol esterification and abnormality in HDL maturation. The activity of LACT is persistently decreased in CKD, so there is reduced HDL levels. In a study by MDRD, low HDL levels in CKD patients were one of the independent risk factors for the progression of kidney disease. In our study, the mean value was significantly lower than the age-matched healthy controls.

Elevated triglycerides

Triglyceride levels were essentially elevated in our study than in the control group. Abnormal triglyceride values were found in 13 out of 100 patients in our study. The present study demonstrates that CRF is commonly accompanied by lipid dysfunction manifesting as hypertriglyceridemia. This is in co-ordinance to the observations made in Western studies and recent Indian studies by Gupta et al, Das et al and Bagdae et al. Elevated triglyceride levels are implicated to impaired activity lipoprotein lipase (LPL) and direct inhibitory action of various uremic 'toxins' on the enzymes involved in lipid metabolism pinpointing the most important pathophysiological mechanisms causing the development of hypertriglyceridemia in renal failure.[17-19] Chan et al also showed hypertriglyceridemia was the major abnormality in their studies. Hypertriglyceridemia may represent an early feature of renal failure.[20]

Elevated LDL and VLDL

LDL was essentially elevated compared to that of controls in our study. We found that 61 of 100 patients showed elevated LDL levels. Most studies point out that uremic Patients commonly have normal to slightly decreased concentrations of LDL-C levels and they exhibit significant disturbance in the density distribution of LDL subfraction that is characterized by the presence of predominantly small dense LDL particles.[21] In the present study, we find significantly high levels of LDL cholesterol in the group with CKD stages IV and V.

Total cholesterol

Total cholesterol levels were raised in 74 out of 100 patients in our study group with CKD results in acquired LDL receptor deficiency, which plays a vital role in the cause of associated hypercholesterolemia consistent with Vaziri et al study.[22]

Limitations

The majority of the patients in our research had advanced CKD (3-5). The study's sample size was small, further

large-scale studies should be undertaken to confirm the findings of our study. The study was conducted in a low-income area where patients' conditions [nutrition status, sickness status, thyroid autoimmunity status, genetic components] may differ slightly from those seen in other areas of the world.

CONCLUSION

There is a progressive increase in the count of patients with a decreasing T3 and T4 and increasing TSH proportional to the severity of the renal failure. There is also an increase in the incidence of hypothyroidism found in patients with CKD. As the age progresses, there is an increase in the incidence of low T3 syndrome in patients with CKD. In patients with low GFR the serum T3, T4 levels were found to be low. This shows a direct linear relationship between GFR and T3, T4 levels. There is a statistically significant rise in the level of serum triglycerides, serum LDL, serum VLDL in CKD grade 3-5 patients. All lipid abnormalities found in CKD have reduced HDL levels in serum along with significant rise in serum triglyceride, serum cholesterol serum LDL level and serum VLDL level.

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