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RESEARCH ARTICLE

A STUDY OF THYROID PROFILE AND FASTING LIPID PROFILE IN CHRONIC KIDNEY DISEASE

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Abstract

Background: Chronic kidney disease [CKD] is associated with specific abnormalities in the thyroid and lipoprotein metabolism both in the early and in the advanced stages of chronic renal failure. Regardless of age, heart disease is a major cause of morbidity and mortality among patients with renal failure.Our study aimed at to estimate thyroid profile and dyslipidemia in CKD patients on conservative management,on haemodialysisand to compare with healthy controls.

Methods: This was a prospective study conducted among the 100 CKD patients and controls over 18 months admitted in the department of general medicine at our hospital.

Results: Hundred CKD cases with 70 male and 30 female in a M: F ratio of 2.3:1 were found to be in different stages CKD (12, 29 and 59 in stage-3 to stage-5 respectively). In 59 cases of stage-5 CKD, 32 were on HD and 27 on conservative management. 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 3-5.The thyroid profile differed significantly across CKD grades 3-5. The lipid profile differed significantly across CKD grades 3-5, 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 TSH proportionate to the severity of the renal failure, hypothyroidism is becoming more common in people with chronic renal disease.All lipid abnormalities found in CKD on HD have reduced HDL levels in serum along with significant rise in serum triglyceride, serum cholesterol serum LDL level and serum VLDL level.Dyslipidemia in CKD worsened as patientsprogresssed to severe stages with significant increase in TG, TC, VLDLc and TC/HDLc

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confirming presence of atherogenic lipid profile needing early intervention to prevent cardiovascular complications.

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Introduction:-

Chronic kidney disease (CKD) is an important, chronic, non-communicable epidemic disease that affects world including, India.[1,2]

It is characterized by irreversible deterioration of renal function resulting in impairment of excretory, metabolic and endocrine functions with progressively reducing glomerular filtration rate leading to development of clinical syndrome of uremia.[3]

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.[4]

Hyperlipidemia is a well-known risk factor for early atherosclerosis causing various cardiovascular diseases, is frequently seen in patients with CKD.[5]

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.[6]

There is also evidence of thyroid hormone dysfunction in patients with CKD.CKD causes alteration in synthesis, secretion, metabolism and elimination of thyroid hormones. 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 T3 concentration and normal reverse T3 and free T4 levels. But, TSH level is mostly unaltered in CKD. Patients may have symptoms of hypothyroidism in CKD.[7,8]

Our study aimed at to estimate thyroid profile and dyslipidemia in CKD patients on conservative management,onhaemodialysis and to compare with healthy controls.

Objectives:-

1. To study Thyroid profile of CKD patients and compare them with healthy controls .
2. To study Fasting Lipid profile of CKD Patients and compare them with healthy controls .

Materials and Methods:-

A cross-sectional study was conducted on the in-patients and out-patients attending department of General Medicine, Basaveshwara Teaching and General Hospital which is attached to MahadevappaRampure Medical College, Kalaburagifor a period of 18 monthsi.e., from 1 March 2021- 1 August 2022.

Inclusion Criteria:

1. Patients with established chronic kidney disease were selected irrespective of the etiology
2. Patients who were on conservative or dialytic treatment for chronic kidney disease.
3. Age >18 yrs.
4. Established renal failure was ensured by radiological evidence (bilateral shrunken kidney/ loss of cortico-medullary differentiation)or biochemical evidence(elevated blood urea, serum creatinine) for more than 3 months.

Exclusion Criteria:

1. Known case of thyroid dysfunction
2. Known case of dyslipidemia
3. Patients with Acute renal failure and Nephrotic Syndrome.

4. Pregnant women
5. Who are on drugs affecting lipid metabolism like β blockers, statins and oral contraceptive pills.
6. Acute illness of any nature, recent surgery, trauma or burns;
7. Those on drugs altering thyroid profile such as amiodarone, steroids, dopamine, phenytoin, beta-blocker, estrogen pills, iodine-containing drugs.

Sample size:
100 (study subjects were selected arbitarily based on inclusion and exclusion criteria).

Method of collection of data:
A cross-sectional study was performed on the out patients and inpatients admitted in Basaveshwara Teaching and General Hospital attached to MahadevappaRampure Medical College Kalaburagi for a period of 18 months after Ethical committee approval. After obtaining informed consent, a detailed history wascollected from qualifying patients using a pre-designed, structured proforma. Further, general examination and a detailed systemic examination, followed by relevant investigations were conducted and the results were noted.

Statistical Analysis:
Data was analyzed by IBM SPSS 25.0 version software. Collected data were spread on excel sheet and prepared master chart. Through the master chart tables and graphs were constructed. For quantitative data analysis ANOVA, Correlation coefficient and Un-paired t-tests were applied. For qualitative data analysis chi-square test and Fisher exact probability tests were applied for testing of statistical significance. If P-value was less than 0.05 considered as significant.

Results:-

Out of 100 patients, 70 were male patients and 30 were female patients.

Majority of patients 59 (59.0%) were diagnosed Grade-5, followed by 29 (29.0%) of patients were diagnosed Grade-4, 12 (12.0%) of patients were diagnosed Grade-3.

The history of hypertension was seen in 71% patients, diabetes mellitus was present in 42%.

Mean age, eGFR, urea, creatinine, thyroid profile and lipid profile in each grade of CKD is mentioned in (Tables 1-3).

There was a significant difference in the urea, creatinine and eGFR levels between CKD grades 3-5 with p>0.05,**<0.01, <0.05** respectively (Table 4).

Study observed that 32%of grade 5 CKD cases were seen on Dialysis management and 27% of grade 5, 29% of grade 4 and 12% of grade 3 were seen on conservative management(Table 5).

There was a significant difference in the thyroid profile between CKD grades 3-5 with p=**<0.05** for T3, T4 and TSH (Table 6).

There was a significant difference in the lipid profile between CKD grades 3-5 with p=**0.00**, >0.05, **0.00**, >0.05, >0.05 for total cholesterol, triglycerides, HDL, LDL and VLDL levels respectively (Table 7).

Table No.1:- Descriptive statistics of Grade 3 CKD.

Variables	No. of patients	Minimum	Maximum	Mean	SD
Age	12	21	75	45.33	17.48
eGFR	12	31	46	36.08	4.53
Urea	12	86	311	146.16	57.93
Creatinine	12	1.4	2.8	2.11	0.42
T3	12	0.2	1.8	0.90	0.41
T4	12	0.6	8.2	4.46	1.91
TSH	12	2.5	11.2	6.81	4.12

Total Cholesterol	12	114	209	185.54	41.37
Triglycerides	12	103	280	194.58	43.41
HDL	12	29	40	38.73	4.35
LDL	12	85	180	127.25	31.69
VLDL	12	21	79	47.00	16.16

Table No.2:- Descriptive statistics of Grade 4 CKD.

Variables	No. of patients	Minimum	Maximum	Mean	SD
Age	29	19	76	47.06	17.86
eGFR	29	15	28	19.93	3.73
Urea	29	86	311	142.34	45.74
Creatinine	29	2.2	5.0	3.40	0.67
T3	29	0.2	1.1	0.75	0.33
T4	29	0.6	5.7	3.94	1.87
TSH	29	1.3	16.7	7.04	3.95
Total Cholesterol	29	128	276	218.65	39.02
Triglycerides	29	82	322	197.89	62.82
HDL	29	15	51	36.52	6.74
LDL	29	67	196	126.72	36.91
VLDL	29	17	65	41.86	13.21

Table No.3:- Descriptive statistics of Grade 5 CKD.

Variables	No. of patients	Minimum	Maximum	Mean	SD
Age	59	20	84	54.23	15.00
eGFR	59	3	14	7.49	3.08
Urea	59	100	310	147.86	37.72
Creatinine	59	3.3	15.8	8.39	8.39
T3	59	0.2	1.6	0.69	0.24
T4	59	0.4	8.3	3.05	1.54
TSH	59	2.3	26.0	9.49	4.73
Total Cholesterol	59	130	317	221.89	40.63
Triglycerides	59	74	501	196.30	65.14
HDL	59	30	53	35.29	5.46
LDL	59	79	238	130.77	35.30
VLDL	59	15	100	42.98	15.45

Table No.4:- Comparison of patient's Blood urea, Srcreatinine and eGFR with respect to CKD Grades.

CKD Grades	Blood urea	Srcreatinine	eGFR
	Mean ± SD	**Mean ± SD**	**Mean ± SD**
Grade-3	143.71 ± 45.96	5.69 ± 3.31	15.67 ± 10.17
Grade-4	154.61 ± 36.88	6.96 ± 3.19	12.46 ± 10.01
Grade-5	149.40 ± 20.80	10.24 ± 3.79	5.60 ± 2.41
Total Mean ± SD	146.06 ± 43.07	6.19 ± 3.48	14.53 ± 10.27
ANOVA-test and P-value	**F = 1.014, P = 0.390 NS**	**F = 4.174, P = 0.008 HS**	**F = 2.759, P = 0.046 S**

NS= not significant, **S=significant, HS=highly significant**

Table No.5:- Distribution of patients on conservative and haemodialysis management in study population.

Management	Number of patients	Percentage
Conservative	68	68.0
Hemodialysis	32	32.0
Total	100	100.0

Table No.6:- Comparison of thyroid profile of T3, T4 and TSH with respect to CKD Grades.

CKD Grades	T3	T4	TSH
	Mean ± SD	Mean ± SD	Mean ± SD
Grade-3	0.90 ± 0.39	4.46 ± 1.91	6.81 ± 3.26
Grade-4	0.75 ± 0.33	3.94 ± 1.87	7.04 ± 3.95
Grade-5	0.69 ± 0.27	3.05 ± 1.54	9.49 ± 4.73
Total Mean ± SD	0.76 ± 0.35	4.01 ± 1.89	8.46 ± 4.55
ANOVA-test and P-value	**F = 3.410, P = 0.032 S**	**F = 2.974, P = 0.045 S**	**F = 3.872, P = 0.024 S**

Table No.7:- Comparison of lipid profile with respect to CKD Grades.

Lipid profile	Grade-3	Grade-4	Grade-5	ANOVA-test, P-value & Significance
	Mean ± SD	Mean ± SD	Mean ± SD	
Total cholesterol	185.54 ± 41.37	218.89 ± 39.02	221.89 ± 40.63	**F = 4.561, P = 0.019 S**
Triglyceride	194.58 ± 43.41	197.89 ± 62.82	196.30 ± 65.14	**F = 0.13, P = 0.987 NS**
LDL	127.25 ± 31.69	126.72 ± 36.91	130.77 ± 35.30	**F = 1.442, P = 0.531 NS**
HDL	38.73 ± 4.35	36.52 ± 6.74	35.29 ± 5.46	**F = 3.282, P = 0.0293 S**
VLDL	47.00 ± 16.16	41.86 ± 13.21	42.98 ± 15.45	**F = 0.495, P = 0.611 NS**

Discussion:-

Of late globally increasing trend of CKD has put the health care facilities around the world under tremendous strain. Increase CVD morbidity and mortality in CKD is caused by dyslipidemia, thyroid dysfunction in CKD is another area of concern.

Study observed thatmean age of CKD patients (study group) was 51.09 years and mean age of control group was 54.53 years. Out of 100 CKD patients;70 male and 30 female in a M: F ratio of 2.3:11 were found to be in different stages CKD (12, 29 and 59 in stage-3 to stage-5 respectively). In 59 cases of stage-5 CKD, 32 were on HD and 27 on conservative management.Study observed that; the prevalence of DM in CKD patients was 42 (42.0%), prevalence of HTN in CKD patients was 71 (71.0%).

In our study out of 100 patients, 37 patients had low serum T3 levels (37%),73 patients had low T4 levels (73%), 92 patients had high TSH (92%) and 12 had normal range TSH.

One study done by Spector [10] and Ramirez et al [9]Dudaniet al[11], Karunanidhi et al[12]. These studies showed abnormality in hypophyseal mechanism of TSH release in patients with Uraemia as the TSH response to the TRH was reduced.

Low T3 had also been reported in Ramirez et al[9], Hegedus et a1, Beckett et al, PonAjil Singh et al, P Iglesias and JJ Diez and many others.

Ramirez and Spector et a1 [10] study exposed the linear correlation between mean serum T3 and T4 and severity of CKD Studies by Quionverdeet a1 [13] showed high preponderance of hypothyroidism in CKD. It was roughly estimated to be about 5% in patients with final stage of CKD.

In the present study, we found that stage 4 and 5 patients had significantly high risk for thyroid dysfunction as compared to stage 3 patients, which is consistent with the findings of Lo et al., who observed increased risk for hypothyroidism with the decrease in GFR.In our study, the decreasing trend in T3 and T4 and increasing trend in TSH showed a linear correlation with progressing stages of CKD.

Chronic kidney disease (CKD) results in profound lipid disorders, which stem largely from dysregulation of high density lipoproteins (HDL) and triglyceride-rich lipoprotein metabolism. Specifically, maturation of HDL is impaired and its composition is altered in CKD.

Lipid changes in CKD patient on conservative management

1. The characteristic plasma lipid abnormality in CRF patients is moderate hypertriglyceridemia - this is due to impaired carbohydrate tolerance leading to increased hepatic synthesis of VLDL and decreased activity of lipoprotein lipase and hepatic triglyceride lipase leading to decreased fractional catabolic rate of triglycerides.
2. Decrease in HDL cholesterol level - this is due to the deficiency of LCAT which is essential for esterification of cholesterol. LCAT plays an important role in HDL mediated cholesterol uptake from the extra hepatic tissues and serves as a main determinant of HDL maturation and plasma HDL cholesterol level. Decrease in HDL level is also contributed by elevation of CETP.
3. Normal or slightly increased total cholesterol level.
4. Normal or slightly increased LDL cholesterol level.

Observation on lipid profile changes of CKD patients on conservative management the final results revealed tohave reduced HDL levels in serum along with significant rise in serum triglyceride, serum cholesterol serum LDL level and serum VLDL level.

The significant decrease in HDL could be due to various reasons mentioned earlier (decrease in LCAT, hepatic lipase activity, increase in ACAT, decrease in apoA-I and apoAII) .

In a study by Attman PO et al [14] revealed increased VLDL ; remnants and intermediate density lipoproteins; prolonged persistence of postprandial chylomicrons and accumulation of noncardioprotective acute phase HDL in renal disease patients. Another study by Bagdade, casaretto A, Albers J showed the same effects of chronic uremia on lipid profile.[15]

Lipid changes in CKD patients on Haemodialysis

1. Moderate increase in triglyceride levels
2. Decrease in HDL levels
3. Normal / slightly elevated total cholesterol, LDL cholesterol
4. Increased Lp(a)
5. Increased apoB and apoA-IV and decreased apo A-I

In addition to factors responsible for renal dyslipoproteinemia the other contributing factors in a CKD-HD patient are

1. Reduced lipolytic activity following repeated heparinisation. The exact reason is not understood but may be due to functional insulin deficiency or insulin resistance, and also due to the presence of non dialyzable factor of lipolytic enzyme (lipoprotein lipase), in the plasma of CKD-HD patients. The changes are more pronounced with the use of conventional heparin than low molecular weight heparin.
2. The presence of Acetate in the dialysate which gets converted to long chain fatty acids and later to cholesterol in the liver.
3. Carnitine deficiency results in impaired fatty acid oxidation.

Observation on lipid profile changes of CKD- HD showed the following

Results:-

The mean age of the hemodialysis group was 43.09 yrs.

Observation on lipid profile changes of CKD patients on HD the final results revealed tohave reduced HDL levels in serum along with significant rise in serum triglyceride, serum cholesterol serum LDL level and serum VLDL level.

In a study by Deighan CJ, Caslake MJ, McConnel revealed tha same lipid changes in dialysis patients. Shoji T , and Huttunnen JK tested the role of heparin in the pathogenesis of HD induced dyslipidemia revealed the same changes[16,17]. But According to ATP III guidlines 55.7% would require treatment based on LDL >100.

Early diagnosis of dyslipidemia is indicated and potential therapeutic approaches (therapeutic life style changes and pharmacotherapy) should be initiated to limit the long term consequences of cardiovascular disease in this population of patients, whose longevity is anticipated to increase with dialysis.

Conclusion:-

The number of patients increases with decreasing T3 and T4 and increasing TSH proportionate to the severity of the renal failure, hypothyroidism is becoming more common in people with chronic renal disease.All lipid abnormalities found in CKD on HD and on conservative management have reduced HDL levels in serum along with significant rise in serum triglyceride, serum cholesterol , serum LDL level and serum VLDL level.Dyslipidemia in CKD worsened as patientsprogresssed to severe stages with significant increase in TG, TC, VLDLc and TC/HDLc confirming presence of atherogenic lipid profile needing early intervention to prevent cardiovascular complications.

Limitations:

The majority of the patients in our research had advanced CKD(3-5). 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.

References:-

1.Lok CE, Huber TS, Lee T, Shenoy S, Yevzlin AS, Abreo K, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. Vol. 75, American journal of kidney diseases : the official journal of the National Kidney Foundation. United States; 2020. p. S1164.

2.Gupta S, Uppal B, Pawar B. Is soluble transferrin receptor a good marker of iron deficiency anemia in chronic kidney disease patients? Indian J Nephrol. 2009 Jul 1;19:96–100.

3.Strippoli GFM, Craig JC, Manno C, Schena FP. Hemoglobin targets for the anemia of chronic kidney disease: a meta-analysis of randomized, controlled trials. J Am Soc Nephrol. 2004;15(12):3154–65.

4.National Kidney Foundation K-DOQI: Clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Clinical Reviews in Bone and Mineral Metabolism.2007;5(1):53-67.

5. Macdonald G. Harrison's Internal Medicine, 17th edi byFauci AS, Kasper DL, Longo DL, Braunwald E, Hauser SL, Jameson JL et al. Internal Med J. 2018;38(12):932.

6. Sumathi ME, Tembad MM, Jayaprakash Murthy DS, Preethi BP. Study of lipid profile and oxidative stress in chronic renal failure. Biomed Res. 2010;21:451-6.

7. Lim VS, Fang VS, Katz AL. Thyroid dysfunction in chronic renal failure-A study of pituitary thyroid axis and peripheral turn over kinetics of thyroxine and triiodothyronines. J Clinic Investig. 1977;60(3):522- 34.

8. Lim VS, Zavala DC, Flanigan MJ, Freeman RM. Blunted peripheral tissue responsiveness to thyroid hormone in uremic patients. Kidney Inter. 1987;31(3):808-14.

9. Ramirez G et al. Thyroid abnormalities in renal failure. A study of 53 patients on chronic dialysis.Ann Internal Medicine, 1973; 79, 500-4.

10. Spector DA et al. Thyroid function and metabolic rate in chronic renal failure. Ann Intern Med. 1976; 85: 724-30.

11. Dudani RA et al. Thyroid dysfunction in Ureaemia J Assoc Physicians India.1981; 29: 1037-40.

12. Karunanidhi A et al. Thyroid function in patients with chronic renal failure. Indian J Med Research, 1979; 69: 792-7.

13. Quion-verde et al. Prevalence of thyroid disease in chronic renal failure and dialysis patients. IXt1' mtCongr of Nephrol, 1984; 120.

14. Attman PO, Knight-Gibson C ,TavellaM,SamuelssonO,Alaupovic p; NephrolDisl Transplant 13;2833-2841,1998

15. Bagdade J, Casaretto A, Albers J, Effects of chronic uremia, hemodialysis and renal transplantation on plasma lipids J Lab Clin Med 87;38-48 ,1976.

16. Shoji T, Nishizawa Y, Nishitani H, Yamakawa M, Morii H. Impaired metabolism of high density lipoprotein in uremic patients. Kidney Int 1992; 41: 1653-61.

17. Huttunen JK, Pasternack A, Vanttinen T, Ehnholm C, Nikkila EA. Lipoprotein metabolism in patients with chronic uremia. Effect of hemodialysis on serum lipoproteins and postheparin plasma triglyceride lipases.Acta Med Scand 1978; 204: 211-8.