

THYROID FUNCTION AND LIPID PROFILE IN NEWLY DIAGNOSED CASES CHRONIC KIDNEY DISEASE

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ABSTRACT:

Introduction:- Chronic kidney disease (CKD) is a clinical syndrome due to irreversible renal dysfunction leading to excretory, metabolic and synthetic failure culminating in the accumulation of non-protein nitrogenous substances and present with various clinical manifestations. The thyroid hormones are essential for kidney growth and development and maintaining electrolytes and water homeostasis. The kidney plays an important role in thyroid hormone metabolism, degradation and excretion. CKD is associated with a higher prevalence of overt and subclinical primary hypothyroidism. Patients with CKD have elevated levels of triglycerides level because of reduction in the activity of lipoprotein lipase and the direct inhibitory effect of various uremic toxins on the enzymes involved in lipid metabolism. Thyroid dysfunction and dyslipidemia in CKD increase risk of CVD which further leads to increased mortality and morbidity. **Material and methods:-** We have conducted a hospital-based prospective study on 127 newly diagnosed patients of CKD, admitted to MBGH, RNT Medical College Udaipur. Patients are selected as per the standard definition of CKD. We have performed thyroid profiles, lipid profiles, and other routine investigations in these patients. EGFR is calculated using the MDRD equation. **Results:-** In this study out of 127 patients, 70 patients had normal TSH values, while 57 patients had elevated TSH values. The prevalence of low T3 was 87.4 % and for low T4 was 47.24 %. Out of 70 patients who had normal TSH values 62 patients have low T3 which is 88.57 % and 33 patients have low T4 which is 47.14 %. The most common thyroid abnormality was subclinical hypothyroidism which is found in 35.43 % of patients and 9.45 patients had overt hypothyroidism. Thyroid dysfunction was more in females than in males. The most common lipid abnormality was low HDL in 66 patients which is 51.97 %, the second most common was elevated TG values in 41.73 % of patients. Total cholesterol was elevated in 18.9 % of patients while LDL was elevated in 26.77% of patients. **Conclusion:-** The most common thyroid dysfunction found was subclinical hypothyroidism in 35.43 % of patients and overt hypothyroidism in 9.45 % of patients. The Most common lipid abnormality was low HDL followed by elevated TG values. There was an increased incidence of thyroid dysfunction and lipid abnormality in patients with CKD

Keywords:- CKD, T3, T4, TSH, HDL, LDL, TG, Total cholesterol, Thyroid, Hypothyroidism

INTRODUCTION:

Chronic kidney disease (CKD) is a clinical syndrome due to irreversible renal dysfunction leading to excretory, metabolic and synthetic failure culminating into accumulation of non-protein nitrogenous substances and present with various clinical manifestations.^{1,2} Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR).² End stage renal disease is described as a terminal stage of chronic kidney disease that without replacement therapy would result in death. Despite

various etiologies, CKD is the final common pathway of irreversible destruction of nephrons ultimately resulting in alteration of the 'Milieu interior' that affects every system in the body and having a number of complications including thyroid dysfunction and dyslipidemia.³ The functions of thyroid and kidneys are interrelated. The thyroid hormones are essential for growth and development of kidney and for maintaining electrolytes and water homeostasis. On the other side The kidney plays an important role in the metabolism, degradation and excretion of thyroid hormones.^{4,5} CKD affects thyroid function in many ways, including low circulatory thyroid hormone

levels, altered peripheral metabolism, insufficient binding to carrier proteins, reduced thyroid hormone content and altered iodine storage in the thyroid gland. Thus, in CKD thyroid hormone metabolism is impaired.⁶ Iodine is an important element in the synthesis of thyroid hormone which is removed by glomerular filtration under physiological condition. In CKD there is progressively decrease in GFR which leads to accumulation of iodine in blood which leads to decrease in thyroid hormone synthesis by Wolff Chaikoff effect.⁷ CKD is associated with a higher prevalence of primary hypothyroidism, both overt and subclinical but not with hyperthyroidism. Prevalence of primary hypothyroidism mainly in the subclinical form increases as GFR decreases⁸. Hyperlipidemia, an abnormally high level of lipids in blood, is a well-known risk factor for early atherosclerosis which causes cardiovascular diseases are frequently seen in patients with CKD. Several factors contributes in the development of dyslipidemia in CKD. Patients with CKD have elevated levels of triglycerides level because of reduction in activity of lipoprotein lipase⁹ and direct inhibitory effect of various uremic toxins on the enzymes involved in lipid metabolism.¹⁰ This leads to interference with uptake of triglycerides, apolipoprotein b containing lipoproteins by the liver and peripheral tissues. Which increases circulation of these atherogenic lipoproteins.³ Progression of CKD is accompanied by the development of specific alterations of the lipoprotein metabolism.¹¹ There is growing evidence that abnormalities in lipid

metabolism may contribute in renal disease progression.¹²

AIMS AND OBJECTIVES:

1. To evaluate the thyroid function in newly diagnosed cases of CKD
2. To evaluate the lipid profile in newly diagnosed cases of CKD.

MATERIAL AND METHODS:

SOURCE OF DATA : Diagnosed cases of chronic kidney disease who will be admitted in MBGH, RNT MEDICAL COLLEGE, Udaipur

Design of the study :- Hospital based Prospective observational study

Duration :- 1 Year ,From November 2021 to October 2022

Inclusion Criteria:-

1. Willing to give informed consent for the study
2. Newly diagnosed cases of CKD

Exclusion Criteria:-

1. Patients not giving consent for the study
2. Patients with nephrotic range proteinuria
3. Patients who have been already diagnosed with thyroid disorders
4. Patients on lipid lowering agents
5. Established cases of CKD

OBSERVATION AND RESULTS:

Table 1: Age and Sex wise Distribution of Cases

Age group (years)	Female		Male		Total
	No.	%	No.	%	
10-20	3	8.33%	2	2.20%	5
21-30	3	8.33%	11	12.09%	14
31-40	4	11.11%	14	15.38%	18
41-50	8	22.22%	20	21.98%	28
51-60	10	27.78%	17	18.68%	27
61-70	5	13.89%	18	19.78%	23
71-80	3	8.33%	8	8.79%	11
81-90		0.00%	1	1.10%	1
Total	36	100.00%	91	100.00%	127

Table 2: CKD Stage-wise Distribution of Cases

CKD Grade	Female		Male		Total	
	No.	%	No.	%	No.	%
Grade 1	0	0%	0	0%	0	0%
Grade 2	0	0%	0	0%	0	0%
Grade 3	0	0%	0	0%	0	0%
Grade 4	5	13.89%	11	12.09%	16	12.60%
Grade 5	31	86.11%	80	87.91%	111	87.40%
Total	36	100.00%	91	100.00%	127	100.00%

Table 3: Distribution of T3 in Study Population

T3	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Low	87	86.14%	24	92.31%	111	87.40%
Normal (1.3 – 3.10 nmol/L)	14	13.86%	2	7.69%	16	12.60%
Total	101		26		127	100.00%

Out of 127 patients in this study prevalence of low T3 is 87.4 % which consist of 111 patients. Most of the DM patients (92.31) also have low T3. Low T3 is the most common abnormality found in CKD patients

Table 4: Distribution of Low T3 Among various Levels of TSH

TSH level	Low T3		Normal T3	
	No.	%	No.	%
Normal (0.27 – 4.2 nmol/L)	62	55.86%	8	50.00%
High (>4.2)	49	44.14%	8	50.00%
Total	111	100.00%	16	100.00%

In table no.4 low T3 is compared with various levels of TSH. Out of 70 patients who have normal TSH values 62 have low T3 values. Of 57 patients with TSH values,>4.2 49 have low T3 values.

Table 5: Distribution of T4 in Study Population

T4	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Low	44	43.56%	16	61.54%	60	47.24%
Normal (66 – 181 nmol/L)	57	56.44%	10	38.46%	67	52.76%
Total	101		26		127	100.00%

In this study of 127 patients prevalence of low T4 is 47.24% which consists of 60 patients of which 44 are non-diabetic and 16 are diabetic.

Table 6: Distribution of Low T4 in Among various Levels of TSH

TSH level	Low T4		Normal T4	
	No.	%	No.	%
Normal (0.27 – 4.2 nmol/L)	33.00	55.00%	37.00	55.22%
High (>4.2)	27.00	45.00%	30.00	44.78%
Total	60.00	100.00%	67.00	100.00%

Low T4 values are compared with various levels of TSH. In normal TSH 33 patients have low T4 while when TSH values are >4.2 27 patients have low TSH values.

Table 7: Analysis of T3, T4 and TSH Excluding Hypothyroidism (TSH >4.2) (n=70)

	Low		Normal	
	No.	%	No.	%
T3	62.00	88.57%	8.00	11.43%
T4	33.00	47.14%	37.00	52.86%
P value = <0.001 Highly significant				

In this study, we have 70 patients who have normal TSH values and 57 patients who have TSH values >4.2. In the above table, we have compared values of T3 and T4 in patients with normal TSH values. Out of 70 patients, 62 patients have low T3 values and 33 patients have low T4 values. From this, we can conclude that Low T3 is not due to hypothyroidism alone and due to uremia despite Low T4 TSH values are failed to raise. These values of Low T3 and T4 in patients with Normal TSH are highly significant (p=0.001)

Table 8: Analysis of Thyroid Dysfunction According to Sex

TSH	FEMALE		MALE		Total	
	No.	%	No.	%	No.	%
0-4.2	15.00	41.67%	55.00	60.44%	70.00	55.12%
4.2-10	14.00	38.89%	31.00	34.07%	45.00	35.43%
>10	7.00	19.44%	5.00	5.49%	12.00	9.45%
Total	36.00	100.00%	91.00	100.00%	127.00	100.00%
P value = <0.03 , Significant						

In this study out of 36 female patients, 15 are in a euthyroid state 14 are having subclinical hypothyroidism and 7 are having overt hypothyroidism. While in 91 male patients, 55 have a euthyroid state 31 individuals have subclinical hypothyroidism and 5 are having overt hypothyroidism. Females are having more thyroid dysfunction as compared to male patients with CKD (p=<0.03, significant)

Table 9: Distribution of Lipid Profile in Diabetic Patients

Lipid Profile	Non-Diabetic		Diabetic		P value
	Mean	SD	Mean	SD	
TC	146.12	54.35	156.61	58.27	0.404
TG	143.43	72.84	209.85	155.46	0.036 (S)
HDL	36.49	14.71	36.74	20.55	0.953
LDL	76.85	37.72	82.07	45.30	0.587

The above table is showing mean values of Total cholesterol, TG, HDL, and LDL in CKD patients, and these values are compared in patients with and without DM. The mean values of TG are significantly higher in patients with DM (p=0.036) while the rest of the values are not significant

Table 10: Distribution of TC in Study Population

TC	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Normal (<200 mg/dL)	85.00	84.16%	18.00	69.23%	103.00	81.10%
High	16.00	15.84%	8.00	30.77%	24.00	18.90%
P value = 0.22, not significant						

The above table shows us that total cholesterol values are high in only 18.9 % of patients with CKD and the rest of the patients are having normal cholesterol levels.

Table 11: Distribution of TG in Study Population

TG	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Normal (30-150 mg/dL)	62.00	61.39%	12.00	46.15%	74.00	58.27%
High	39.00	38.61%	14.00	53.85%	53.00	41.73%
P value = 0.373 , not significant						

The above table shows that Triglyceride values are high in 53 patients prevalence is 41.73 %. Diabetes does not affect TG values in CKD patients (p=0.373, not significant)

Table 12: Distribution of HDL in Study Population

HDL	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Low (<35 mg/dL)	54.00	53.47%	12.00	46.15%	66.00	51.97%
Normal (35-55 mg/dL)	35.00	34.65%	11.00	42.31%	46.00	36.22%
High	12.00	11.88%	3.00	11.54%	15.00	11.81%
P value = 0.099, Not significant						

As per the above table, HDL was low in 66 patients, normal in 46 patients and HDL values are high in 15 patients. The prevalence of low HDL was 51.97 % in patients with CKD. When these values are compared in patients with and without DM the values are insignificant (p=0.099)

Table 13: Distribution of LDL in Study Population

LDL	Non-Diabetic		Diabetic		Total	
	No.	%	No.	%	No.	%
Normal (0-99 mg/dL)	76.00	75.25%	17.00	65.38%	93.00	73.23%
High	25.00	24.75%	9.00	34.62%	34.00	26.77%
P = 0.599, Not significant						

The above table shows the Distribution of LDL in patients with DM and patients without diabetes mellitus. In Non-diabetic out of 101 patients, 25 have high LDL values while in 26 patients with DM 9 patients are having high LDL values. Hence in CKD most of the patients are having normal LDL values and diabetes does not affect LDL values in CKD (p=0.599, not significant)

DISCUSSION:

This study is conducted to study the thyroid profile and lipid profile in newly diagnosed cases of CKD. For

which 127 patients are enrolled over 1 year. Many such studies were conducted about thyroid dysfunction, lipid profile abnormalities and severity of CKD for which different results have been shown. In this study total 127 patients with newly diagnosed CKD were studied among these 91 are male and 36 are female their ages varied from 19 to 84 years. Most patients are from the age group 40-70 years.

Ramirez et al.¹³ conducted a study and study shows that in patients on dialysis, mean serum thyroxine and triiodothyronine levels are lower than normal. In our study mean values of T₃ and T₄ are 0.94 and 70.72 which are low. The low serum T₃ is not due to increased T₃ degradation or to decreased thyroidal T₃ secretion but is a result of impaired extrathyroidal T₄ to T₃ conversion.¹⁴

In this study out of 127 patients 111 patients which is 87.4% have low T₃ values in which 96 patients are in stage 5 of CKD while 15 are in stage 4 of CKD. There was a higher frequency of reduced free T₄ values in our study (47.24) which is consistent with the study done by **Kaptein et al.**¹⁵ in which they found reduced T₄ in 24% and **Avasthi et al.**¹⁶ in which low T₄ was found in 33% of patients. Out of 60 patients, 7 patients are in stage 4 of CKD while 7 are in stage 5 of CKD. The reduction in T₄ is attributed to the presence of circulating inhibitors, which impair the binding of T₄ to thyroxine-binding globulin.¹⁴

In our study, out of 127 patients 70 patients have normal TSH values. 45 patients have TSH values between 4.2 to 10 μ IU/ml and 12 patients are having overt hypothyroidism TSH values >10 μ IU/ml. Out of 57 patients who are having TSH values >4.2 49 patients have low T₃ while 8 have normal values and 27 patients have low T₄ values. which can be explained by the normal feedback regulation of the pituitary thyroid axis. This result is similar to a study conducted by Joseph et al. in 175 patients of CRF who had low T₃, T₄, and fT₄ but had high TSH levels suggests maintenance of the pituitary thyroid axis.

Of 70 patients who are having normal TSH value 62 patients have low T₃ and 33 patients are having low T₄ values so these 62 patients are having normal TSH values despite low T₃ this show abnormality in the hypothalamic pituitary axis of TSH release in uremic patients as the TSH response to TRH was blunted. These results are consistent with the study of Spector et al. and Ramirez et al. reported normal levels of serum TSH in patients of CRF despite low serum T₃ levels.

In this study most common thyroid abnormality found was low T₃. **Khawwaja et al.**¹⁷ conducted a study on 360 newly diagnosed patients of CKD. They found 61.4 % of patients euthyroid, 27.2 % have subclinical hypothyroidism, 8.1% have overt hypothyroidism and 3.3 % have subclinical hypothyroidism. They have compared these patients in stage 3,4 and 5 of CKD and found that the majority of patients are from stages 4

and 5 of CKD. A study conducted by **Lo et al.**¹⁸ found that the prevalence of hypothyroidism increased with the severity of renal disease, they found 5.4 % of subjects in stage 1, 10.9 % in stage 2, 20.4 % in stage 3a, 23.0 % stage 3b, and 23.1 % in stage 4 of CKD ($p < 0.001$ for trend). They also reported that 56 % of hypothyroidism cases were subclinical. **Shanta GPS et al.**¹⁹ also conducted a study on 137 ESRD patients and found the prevalence of hypothyroidism was 24.8 %

Rajeev G et al.²⁰ conducted a study on 45 patients of CKD and 45 controls and they found Serum total T₃ and total T₄ levels were significantly less and TSH values are significantly increased in the study patients compared with the controls. Low T₃ was found in 40 patients, low T₄ in 15 patients, and TSH values are elevated in 27 patients

In this study we found the prevalence of Low T₃ is 87.4 %, Low T₄ is 47.24%, subclinical hypothyroidism is 35.4 %, and overt hypothyroidism in 9.44 % of patients. Some studies have reported that subclinical hypothyroidism is associated with an increased risk of coronary heart disease and there appears to be a significant increase in a cluster of metabolic CVD risk factors among people with subclinical hypothyroidism^{21,22}

In this, we also studied the Lipid profile in CKD and the impact of diabetes mellitus on it. The most frequent abnormality was low HDL. CKD affects lipoprotein metabolism, leading to hypercholesterolemia, hypertriglyceridemia, and excess LDL cholesterol.²³

In our study out of 127 patients low HDL was found in 66 patients which consist of 51.97 % and the mean HDL was 36.62. This is the most common lipid abnormality found in CKD patients

Piperi c et al.²⁴ also conducted a study on 140 patients of CRF and they also found a significant decrease in HDL values. These low HDL cholesterol levels were also an isolated independent risk factor for the development of CKD in the Framingham spring study. These mean values are studied in both the patients with and without DM but they are not significant. The prevalence of elevated Triglyceride is 41.73 % which is the second most common abnormality found in CKD patients. Hypertriglyceridemia is one of the most common quantitative lipid abnormalities in patients with CKD. 21,22. The mean value of triglyceride in patients with DM is 209.85 while in without DM is 143.43 which is statistically significant hence diabetes also affects triglyceride values in CKD patients. LDL values were high in 26.77 % of patients and the mean value of LDL is 77.92. Total cholesterol was high in 18.9 % of patients in our study group. **Khawwaja et al.**¹⁷ conducted a study on 360 newly diagnosed patients of CKD and found low HDL in 34.1%, high LDL in 34.1%, hypercholesterolemia in 34.4 %, and hypertriglyceridemia in 36.6 %.

Poudel B et al²⁵ also conducted in CKD patients and found low HDL cholesterol, high LDL cholesterol, and hypertriglyceridemia were present in 33.75, 32.5, 38.03 and 35.58 % of CKD patients respectively, and they also concluded that CKD patients had higher odds of developing dyslipidemia as compared to non-CKD controls.

In our study we found low HDL in 51.97 %, elevated triglyceride in 41.73 %, high LDL in 26.7 %in, and elevated total cholesterol in 18.9% of patients.

Dyslipidemia have a significant impact on cardiovascular disease in patients with CKD.²⁶ A large number of studies have suggested that dyslipidemia has an independent role in cardiovascular morbidity and mortality in the general population .²⁷ But, the role of dyslipidemia in the pathophysiology of atherosclerotic disease in patients with CKD remains controversial. Some studies have shown a positive association between cholesterol values and the risk for cardiovascular events in CKD individuals, while others failed to find any significant correlation. There is significant deviation from what is seen in the general population but the exact cause for which has not been established, but may be due to the presence of phenomena such as protein energy wasting (conditions very common in ESRD patients) or inflammation may significantly affect the relationship between the traditional risk factors for CVD and mortality in CKD patient .²³A study conducted by Chen et al. demonstrated that certain levels of dyslipidemia were independently associated with renal replacement therapy and rapid renal progression in CKD stages 3–5. Hence, assessment of lipid profile in CKD patients may help identify high risk groups and their adverse renal outcomes. Dyslipidemia is the leading risk factor for CVD in CKD patients, and CVD is the leading cause of death in CKD patients. Kidney Disease Outcomes Quality Initiative (K/DOQI) working group has also suggested that all adults and adolescents with CKD should be evaluated for dyslipidemias because of the high risk for CVD.²⁸

CONCLUSION:

- There is an increase the in the incidence of hypothyroidism in patients with CKD.
- The prevalence of thyroid dysfunction in CKD patients is 44.8 %
- The prevalence of subclinical hypothyroidism is 35.43 % while 9.45 % of patients are having overt hypothyroidism
- The most common abnormality found was low T3; the prevalence for low T3 is 87.4 %
- Low T4 was found in 47.24 % of patients
- In 70 patients with normal TSH values, 88.57 % of patients have low T3 and 47.14 % of patients have low T4
- Thyroid dysfunction was found more in females than males.

- Diabetes mellitus has no impact on thyroid dysfunction in CKD patients
- The most common lipid abnormality found was low HDL
- The prevalence of low HDL is 51.97 %
- The second most common lipid abnormality was elevated TG, which is found in 58.27 %
- High LDL was found in 26.77 % of patients while total cholesterol values are elevated in 18.9 % of patients
- Diabetes mellitus increases triglycerides values quantitatively as compared to nondiabetic patients of CKD.

SUMMARY:

- This study was conducted on 127 newly diagnosed patients of CKD for thyroid and lipid profile
- Out of 127 patients 36 are female and 91 are male.
- 16 patients were in stage 4 of CKD and 111 patients are in stage 5 of CKD.
- 26 patients had DM which is 20.47 %
- 121 patients had hypertension
- The mean value of blood urea was 92.67 and 169.03 in stage 4 and 5 of CKD respectively
- The mean value of serum creatinine was 3.27 and 9.35 in stage 4 and 5 of CKD respectively
- The mean value of T3, T4, and TSH was 0.95, 70.72, 5.51 in 101 nondiabetic and 0.87,70.76,4.73 in 26 patients of DM.
- Out of 127 patients, 111 patients had a low T3 value which is 87.4 %
- Out of 111 patients with low T3, 62 patients had normal TSH values while 49 have high TSH value
- Out of 111 patients with low T3,96 patients are in stage 5 of CKD and 15 patients were in stage 4 of CKD
- In this study of 127 patients, 60 patients have low T4 values which is 47.24 % , in which 33 patients had normal TSH and 27 patients have high TSH values.
- Out of 60 patients with low T4 , 53 patients were in stage 5 of CKD and 7 are in stage 4 of CKD.
- In this study 70 patients had normal TSH value and 57 have high TSH value
- The prevalence of subclinical hypothyroidism was 35.43 % and 9.45 % for overt hypothyroidism. Females are more prone for hypothyroidism than male patients (p<0.03)
- Total cholesterol values were elevated in 18.9 % of patients
- Triglyceride values were elevated in 41.73 % of patients.
- HDL values were decreased in 51.97 % of patients

- LDL values were elevated in 26.77 % of patients
- Mean values of TC, TG, HDL, and LDL are 146.12, 143.43, 36.49, 76.85 in nondiabetic and 156.61, 209.8, 36.74 and 82.07 in patients with DM
- Triglyceride values were significantly elevated in diabetic patients of CKD.

LIMITATION OF STUDY:

In this study majority of patients are in ESRD. Most IPD patients are in stages 4 and 5 of CKD. We have enrolled the majority of patients on an IPD basis. Hence we are unable to compare the severity of renal disease and its impact on thyroid and lipid profile due to selection bias

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