

Original Research Article

A cross-sectional study of thyroid dysfunction in patients of chronic kidney disease in Goa medical college

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ABSTRACT

Background: Thyroid hormones are essential for regulating metabolism, development, protein synthesis, and other hormone functions. CKD has been linked to changes in the pituitary-thyroid axis and peripheral thyroid hormone metabolism.

Methods: A cross-sectional study was conducted in 100 subjects from September 2019 to September 2021 in the department of medicine, Goa Medical College, a tertiary care hospital in Goa.

Results: Most of the CKD patients in study population are in the Age group of 41-70 years. 70% were male. 54% patients were diabetic and 46% patients were non diabetic, majority of them 87% patients were hypertensive, majority of them were DM and HTN With 88% and few patients belonged to other diseases. 8% patients with high TSH level, 6% with low TSH level, 86% with normal TSH level. TT4 levels were low in 28% patients and normal in 72% patients, TT3 levels were high in 3% patients, low in 60% and normal in 37% patients. FT4 levels were high in 5% patients and low in 7%, normal in 88% patients. FT3 levels were high in 1% patients, low in 49%, normal in 50% patients. 55% patients belong to euthyroid state and 7% patients belongs to hypothyroid state and 36% patients belong to sick euthyroid state and 2% belongs to subclinical thyrotoxicosis.

Conclusions: Most of the participants in this study were euthyroid. The most common thyroid hormone derangement was low T3 values (non-thyroidal illness). The prevalence of hyperthyroidism in this study was 2% and hypothyroidism 7%.

Keywords: Chronic kidney disease, Thyroid hormone

INTRODUCTION

It's crucial to keep metabolic functions in all body organs in a state of balance or homeostasis. Inside a human body Hormones are important regulatory proteins help to attain this balance. Thyroid hormones influence cellular growth and differentiation, as well as other processes. It influences key physiological activities in almost all human tissues.¹

Chronic kidney disease (CKD) is a broad term that refers to a variety of conditions affecting the kidneys

pathophysiologic processes linked to a developing kidney disease and impaired kidney function glomerular filtration rate decreases (GFR). It is a worldwide public health issue that is linked to premature death, reduced quality of life, and expensive healthcare costs.² A trend towards an increase in its incidence and prevalence has been reported worldwide with epidemic proportions in some countries.³⁻⁵

Currently, over 2 million people worldwide depend on dialysis or kidney transplants for their survival; however, this may only account for 10% of the global population whose survival truly depends on treatment.⁶

Thyroid hormones play a role in cellular growth and differentiation, as well as the management of metabolism. All human tissues, including the kidney, have physiological roles and are involved in maintenance of water and electrolyte equilibrium. As a result, thyroid dysfunction can be caused by a variety of factors. Water metabolism changes are associated with hypothyroidism or hyperthyroidism.⁷ On the other hand, the kidney is an essential target organ for thyroid hormone effects as well as thyroid hormone metabolism and removal. Abnormalities in the kidney function are linked to abnormalities in the physiology of thyroid hormones. CKD affects both hypothalamus-pituitary-thyroidal axis and thyroid hormone peripheral metabolism. Kidney disease can cause a variety of problems, hypothyroidism, hyperthyroidism, sick euthyroid disease.

Thyroid hormone levels and how they impact the course of chronic kidney disease (CKD) are among the most significant conditions that have received less attention. Certain levels of thyroid hormone have been observed to coexist with disorders related to renal function. The purpose of this study is to clarify the significance of the relationships between kidney disease and thyroid function.⁸

The objective of this study was to study the thyroid dysfunction in patients of chronic kidney disease for the prevalence of thyroid dysfunction.

METHODS

We carried out a prospective cross-sectional study over 2 years-time period on patients attending outpatient department of general medicine and admitted in medicine ward of Goa Medical College, Goa, India.

A total number of 100 patients were included in this study after fulfilling the inclusion criteria. An informed consent was taken from all the cases before their inclusion into the study.

Inclusion criteria

All the patients of chronic kidney disease above the age of 18 years were included.

Exclusion criteria

Family history of thyroid disorder, past history of any medication for thyroid disease, history of any surgery or any radiological intervention to thyroid gland.

A total of 100 study participants with CKD were recruited. Demographic and medical data were obtained from the participants using a questionnaire designed for this study. Estimation of glomerular filtration rate was done using the 4-variable modification of diet in renal disease (MDRD) formula with subsequent staging of chronic kidney disease. Thyroid stimulating hormone

(TSH), total thyroxine (T4), total triiodothyronine (T3), free triiodothyronine (f T3), and free thyroxine (fT4) were estimated using enzyme immunoassay on these patients with CKD.

Detailed clinical history with special reference to: 1) presenting complaints; 2) past history of diabetes, hypertension, ischemic heart disease; 3) treatment history of CKD, DM, HTN; and 4) clinical examination (both general and systemic).

Statistical analysis

Descriptive analysis of the collected data was done and association of various parameters with the presence or absence of thyroid disorder was studied using chi square test and correlation with taking 5% as level of significance (p value <0.001) The statistical analysis was performed using SPSS software version 20.

RESULTS

Our study comprised of 100 cases of chronic kidney disease. Various demographic data, clinical characteristics, thyroid profile were collected and subjected to statistical analysis.

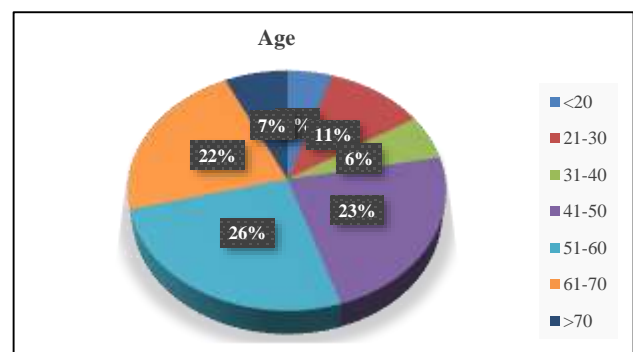


Figure 1: Pie diagram showing age wise distribution of CKD patients.

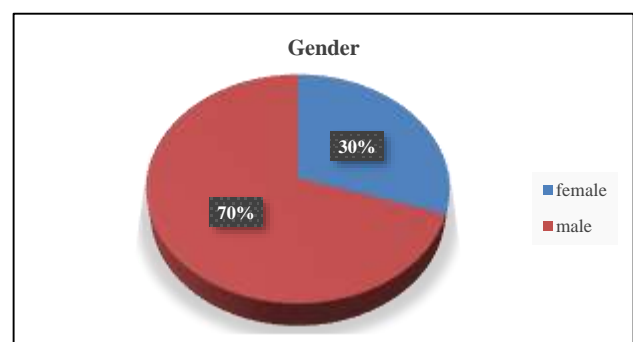


Figure 2: Pie diagram showing gender distribution of CKD patients.

Total patients were divided into 7 age groups: <20 years, 21-30 years, 31-40 years, 41-50 years, 51-60 years, 61-70

years. Most of the CKD patients in study population were in the age group of 41-70 years. Among them 26% belong to 51-60 years, 23% belong to 41-50 years, 22% belong to 61-70 years (Figure 1).

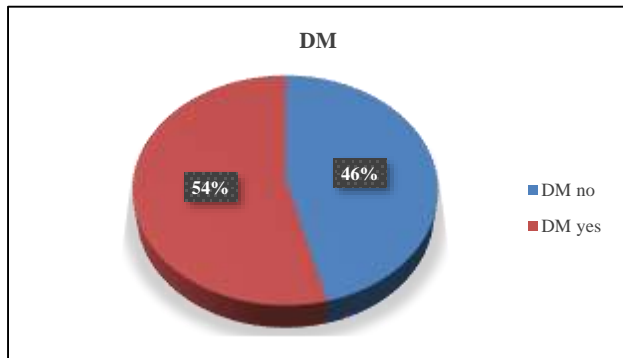


Figure 3: Pie diagram showing CKD patients with diabetes mellitus.

Out of 100 patients 70% are male and 30% are female (Figure 2). 54% patients were diabetic and 46% patients were non diabetic (Figure 3), 87% patients were hypertensive and 13% patients were non hypertensives.

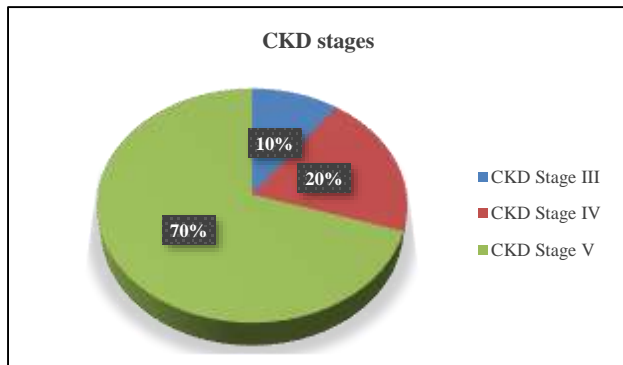


Figure 4: Pie diagram showing stage wise distribution.

Majority of them (88%) were DM and HTN, few patients belonged to other diseases such as poly cystic kidney disease, glomerulonephritis, tubulointerstitial nephritis, focal glomerulosclerosis, autoimmune disorder, vasculitis, infectious causes.

Clinically CKD is divided into 5 stages, out of 100 patients, 10% belong to stage III, 20% of them belong to stage IV, and rest 70% belong to stage V (Figure 4).

TSH levels were studied among them. 8% patients had high level, 6% had low level, 86% had normal level. TT4 levels were low in 28% patients and normal in 72% patients. TT3 levels were high in 3% patients, low in 60% and normal in 37% patients.

FT4 levels were high in 5% patients and low in 7%, normal in 88% patients. FT3 levels were high in 1% patients, low in 49%, normal in 50% patients.

Table 1: CKD patients distribution based on category.

Category	Count		Column %
	Euthyroid	55	
	Hypothyroid	7	
	Sick euthyroid	36	
	Subclinical thyrotoxicosis	2	

55% patients belonged to euthyroid state, 7% patients belonged to hypothyroid state and 36% patients belonged to sick euthyroid state and 2% belonged to subclinical thyrotoxicosis (Table 1).

TSH levels in majority of the patients were normal, TT4 levels in majority of the patients were normal, TT3 levels in majority of the patients were low, FT4 levels in majority of the patients were normal, FT3 levels in majority of the patients were normal or low.

Table 2: Comparison of TSH category in CKD stages.

Crosstab						
			CKD Stages			Total
			Stage III	Stage IV	Stage V	
TSH CAT	High	Count	1	3	4	8
		% within CKD stages	10.0	15.0	5.7	8.0
	Low	Count	1	1	4	6
		% within CKD stages	10.0	5.0	5.7	6.0
	Normal	Count	8	16	62	86
		% within CKD stages	80.0	80.0	88.6	86.0
Total	Count		10	20	70	100
	% within CKD stages		100.0	100.0	100.0	100.0
Chi-square tests		Value	df	P value (<0.05 is significant)		
Pearson chi-square		2.221	4	0.695		

Table 3: Comparison of TT4 category in CKD stages.

Crosstab						
			CKD Stages			Total
			Stage III	Stage IV	Stage V	
TT4 CAT	Low	Count	3	6	19	28
		% within CKD stages	30.0	30.0	27.1	28.0
	Normal	Count	7	14	51	72
		% within CKD stages	70.0	70.0	72.9	72.0
Total	Count		10	20	70	100
	% within CKD stages		100.0	100.0	100.0	100.0
Chi-square tests		Value	df		P value (<0.05 is significant)	
Pearson chi-square		0.085	2		0.958	

Table 4: Comparison of TT3 category in CKD stage.

Crosstab						
			CKD stages			Total
			Stage III	Stage IV	Stage V	
TT3 CAT	High	Count	0	1	2	3
		% within CKD stages	0.0	5.0	2.9%	3.0
	Low	Count	5	9	46	60
		% within CKD stages	50.0	45.0	65.7%	60.0
	Normal	Count	5	10	22	37
		% within CKD stages	50.0	50.0	31.4%	37.0
Total	Count		10	20	70	100
	% within CKD stages		100.0	100.0	100.0	100.0
Chi-square tests		Value	df		P value (<0.05 is significant)	
Pearson chi-square		3.827	4		0.430	

Table 5: Comparison of FT4 category in CKD stage.

Crosstab						
			CKD stages			Total
			Stage III	Stage IV	Stage V	
FT4 CAT	High	Count	2	1	2	5
		% within CKD stages	20.0	5.0	2.9	5.0
	Low	Count	1	4	2	7
		% within CKD stages	10.0	20.0	2.9	7.0
	Normal	Count	7	15	66	88
		% within CKD stages	70.0	75.0	94.3	88.0
Total	Count		10	20	70	100
	% within CKD stages		100.0	100.0	100.0	100.0
Chi-square tests		Value	df		P value (<0.05 is significant)	
Pearson chi-square		12.883	4		0.012	

Comparison of CKD with thyroid parameters using chi square test showed 88% of stage V had normal TSH, 80% of stage IV had normal TSH, 80% of stage III had normal TSH. Low TSH in stage V 5.7%, stage IV 5%, stage III 10%, high TSH in stage V 5.7%, stage IV 15%, stage III 10% (Table 2).

72.9% of stage V, 70% of stage IV, 70% of stage III had normal TT4. Low TT4 in stage V 27.1%, stage IV 30%, stage III 30% (Table 3).

31.4% of stage V, 50% of stage IV, 50% of stage III had normal TT3. Low TT3 in stage V 65.7%, stage IV 45%, stage III 50%, high TT3 in stage V 2.9%, stage IV 5%, stage III 0% (Table 4).

94.3% of stage V, 75% of stage IV, 70% of stage III had normal FT4. Low FT4 in stage V 2.9%, stage IV 20%, stage III 10%. High FT4 in stage V 2.9%, stage IV 5%, stage III 20% (Table 5).

Table 6: Comparison of thyroid category in CKD stage.

Crosstab						
			CKD Stages			Total
			Stage III	Stage IV	Stage V	
Category	Euthyroid	Count	6	11	38	55
		% within CKD stages	60.0	55.0	54.3	55.0
	Hypothyroid	Count	1	2	4	7
		% within CKD stages	10.0	10.0	5.7	7.0
	Sick euthyroid	Count	3	7	26	36
		% within CKD stages	30.0	35.0	37.1	36.0
	Sub thyrotoxicosis	Count	0	0	2	2
		% within CKD stages	0.0	0.0	2.9	2.0
Total	Count	10	20	70	100	
	% within CKD stages	100.0	100.0	100.0	100.0	
Chi-square tests		Value	df	P value (<0.05 is significant)		
Pearson chi-square		1.591	6	0.953		

47.1% of stage V, 60% of stage IV, 50% of stage III had normal FT3. Low FT3 in stage V 51.4%, stage IV 40%, stage III 50%. High FT3 in stage V 1.4%, stage IV 0%, stage III 0% (Table 6).

Euthyroid patients in CKD stage V-54.3%, stage IV 55%, stage III 60%. Hypothyroid patients in CKD stage V 5.7%, stage IV 10%, stage III 10%. Sick euthyroid patients in CKD stage V 37.1%, stage IV 35%, stage III 30%. Sub clinical thyrotoxicosis patients in CKD stage V 2.9%, stage IV 0%, stage III 0%.

DISCUSSION

A total of 100 participants were recruited in the study which evaluated distribution of chronic kidney disease patients among age group, gender, diabetic and hypertensive patients. And it also examined disturbance of TT3, TT4, FT3, FT4, TSH profile and thyroid category in CKD patients.

Demographic distribution of the study population

In our study we evaluated the distribution of CKD patients according to age group. Majority of the patients in the study group were in the age group of 41-50, 51-60 and 61-70 years (Figure 1). This finding is consistent with the other studies done in Canada, increase in age associated with increase in incidence and progression to Chronic renal failure.⁹ The study conducted in Canada shows low incidence of CKD in young age group where as in our country CKD in young age group (less than 40 years) was 23%.

In our study majority of them are male patients (Figure 2) with male =70% and female =30%, whereas study done in Milan Italy showed prevalence in male and female to be almost the same, but in our study male incidence more than twice the females, this may be due to the fact that

females do not seek early health care in the course of disease.¹⁰ Sex differences in onset, duration, and severity of some risk factors, such as albuminuria, diabetes, cardiovascular disease, obesity, and socioeconomic status, may also explain part of the excess risk in men.

Distribution of CKD patients in Diabetic patients

In our study among 100 patients, diabetic patients were 54% and non-diabetic patients were 46% (Figure 3), this is consistent with the other study done in New jersey USA which says the prevalence of CKD in T2DM was 58.7% in patients aged ≥ 65 years, 25.7% in patients aged < 65 years.¹¹ This may be secondary to uncontrolled diabetes leading to proteinuria, diabetic nephropathy which progressed to chronic renal failure.

Distribution of CKD patients in hypertensive patients

In our study among 100 patients majority of them were hypertensive patients compared to non-hypertensive patients. This is consistent with study done in Imperial College London, UK which says HTN confers excess risk of incidence of CKD or ESRD.¹² Delayed identification of HTN, lack of poor control of pressure leads to hypertensive nephropathy which progresses to chronic renal failure.

Figure 4 shows the stage wise distribution of CKD patients in our study majority of CKD patients belong to stage V- 70% and rest belongs to stage IV- 20%, stage III 10% as we have conducted our study in tertiary care centre nephrology unit where stage IV and stage V were most commonly found. This is similar to a study done in Kenyatta national hospital Kenya where, majority of the participants 40.9% (n=56) were classified as CKD stage IV, stage III- 29.9%, stage V- 27.5% and only 2 participants (1.5%) were classified as stage 2, and none was in CKD stage I.¹³

Table 2 shows study of TSH levels in CKD patients, majority of the CKD patients were having normal TSH levels corresponds to 86% and only few of them had low TSH 6% and high TSH 8%. This is consistent with a study done in Kenyatta national hospital Kenya which showed normal TSH level in 80.3%, low TSH in 4.4%, where as in their study high TSH level were found in 15.3% in our study high TSH level were found in only just 8%.¹³

Table 3 shows study of TT4 levels in CKD patients, majority of CKD patients were having normal TT4 levels corresponding to 72% and few of them are with low TT4 level 28%. This is consistent with a study done in Kenyatta national hospital Kenya where normal TT4 level were seen in 65%, low TT4 in 24%, and high TT4 in 10.9 % whereas in our study high TT4 is seen in 0%.¹³

Table 4 shows study of TT3 levels in CKD patients, majority of CKD patients, 60% were having normal TT3 levels and few of them, 37% were with low TT3 level and very few 3% had high TT3 level. This is consistent with a study done in Kenyatta national hospital Kenya which shows normal TT3 level in 85.4%, low TT3 in 19%, and high TT3 in 0.7%.¹³

Table 5 shows study of FT4 levels in CKD patients, majority of CKD patients were having normal FT4 levels corresponds to 88% and few of them are with low FT4 level 7% and few with high FT4 level 5%. This is consistent with a study done in Kenyatta national hospital Kenya where normal FT4 levels were found in 66.4%, low FT4 in 22.6% and high FT4 in 10.9%.¹³

Tables 1 and 6 shows study of thyroid category in CKD patients, majority of CKD patients belonged to euthyroid state 55%, 36% of CKD patients belong to sick euthyroid state, 7% of CKD patients belong to hypothyroid state and only 2% CKD patients belong to subclinical hyperthyroid state. This is consistent with the study done in Kenyatta national hospital Kenya where 58% CKD patients belong to euthyroid state, 14% CKD patients belong to sick euthyroid state, 15% of CKD patients belong to hypothyroid state, 2% CKD patients belong to subclinical hyperthyroid state, primary hyperthyroidism and secondary hyperthyroidism 2% and 8% respectively where as in our study primary and secondary hyperthyroidism 0%.¹³ The sick euthyroid patients incidence was very high that is 36% which indicates decreased peripheral conversion of T4 to T3 leads to low T3 with normal TSH.

In this study, the levels of T3 and fT3 were found to be low and these were noted to decrease as the renal insufficiency progresses. This is mostly due to a decrease in T4 to T3 conversion in peripheral tissues. Reduced fT3 appears to indicate a real selective T3 shortage caused by a T4 to T3 conversion problem. The lack of an increase in TSH in patients with non-thyroidal illness as a result of low T3 and fT3 concentrations could be due to stress

regulation of TSH secretion by the pituitary.¹⁴ TSH response to thyroid releasing hormone (TRH) has been shown to be muted and delayed in patients with chronic renal failure, and chronic metabolic acidosis in ESRD may also lead to low fT3 levels.¹⁵

Subclinical hypothyroidism was frequent, especially among older persons, according to studies; laboratory testing revealed decreased thyroid function in 4% to 10% of the general population. Thyroid abnormalities were more common in ESRD patients, and newer studies reveal a higher proportion of subclinical hypothyroidism in CKD patients who do not need continuous dialysis.¹⁶

The concentration of serum iodine in patients with CKD was higher due to lower iodine clearance caused by the reduced glomerular filtration. Increased levels of serum inorganic iodine in patients with CKD may impede thyroid hormone synthesis, explaining why these patients have a higher prevalence of diffuse goitre and hypothyroidism.¹⁷

Thyrotoxicosis is caused by an imbalance in the hypothalamus pituitary and peripheral responses to systemic thyroid hormones.¹⁸ However not many studies have been done on hyperthyroidism in CKD.

Thyroid function tests may be muddled by pharmacologic medications given to patients with chronic kidney disease (CKD). Glucocorticoids reduce TSH secretion, down-regulate T4 to T3 conversion via 5 α -deiodinase, and decrease TBG concentration and hormone binding ability in the hypothalamic-pituitary thyroid axis on many levels.¹⁹

At therapeutic levels, furosemide has little or no effect on thyroid parameters; nevertheless, at large doses, the displacement of T4 from TBG causes a transitory increase in free T4 and a drop in T4. This shift is influenced by serum albumin levels, which bind furosemide as well.¹⁹ In this study, some patients were on steroids and antihypertensives including furosemide which were considered a limitation to the study.

Because the clinical symptoms of thyroid dysfunction are frequently hidden by uraemia, thyroid function tests in CKD patients may be necessary on a regular basis. Early detection and treatment of thyroid illness in CKD stage 5 patients awaiting renal replacement therapy lowers morbidity and death. Low T3 and fT3 levels before a renal transplant have been linked to lower graft survival, therefore early detection and maybe treatment should be sought to enhance the result.²⁰

It was single-centre research with few participants. A larger sample size may give more insight about thyroid dysfunction in CKD. Despite these limitations, this study strengthens the valid scientific evidence about thyroid dysfunction in CKD. A multicentre study involving larger numbers of patients is required to know the clinical

characteristics, biochemical derangement in thyroid dysfunction and to form a standard monitoring and treatment protocol.

CONCLUSION

Majority of the study population consisted of males. The mean age of presentation was between 41-70 years. DM and HTN were the most prevalent factor in the study population. Most of the participants in this study were euthyroid. There were abnormalities in the thyroid hormone profiles in 45% of the participants. The most common thyroid hormone derangement was low T3 values (non-thyroidal illness). Non-thyroidal illness increased with the severity of chronic kidney disease. The prevalence of hyperthyroidism in this study (2%) and hypothyroidism 7%. These study findings reinforce the current knowledge, understanding and management in the field of thyroid dysfunction in CKD.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Goa Medical College, Goa

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