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Original Article

Evaluation of Thyroid Hormones in Chronic Kidney Disease Patients in Tertiary Care Hospital

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Abstract

Background and Objectives: Chronic kidney disease (CKD) is a global burden and its prevalence is rising exponentially. CKD is associated with increased morbidity and mortality and also with increased threat of cardiovascular disease, heart failure, and increase healthcare expenditure. CKD encompasses a spectrum of different pathophysiological process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR)<60 mL/min per 1.73 m^2). Kidneys participate in the metabolism and elimination of the thyroid hormones. The function of the thyroid is affected in many ways due to CKD. The overall prevalence of CKD in India is 17.2% and the prevalence of CKD stages 1, 2, 3, 4, and 5 are 7%, 4.3%, 4.3%, 0.8%, and 0.8%, respectively. The prevalence of hypothyroidism in end-stage renal disease (ESRD) has been estimated between 0 and 9%.

Materials and Methods: A casecontrol study was done, in which 50 healthy controls (Group 1) and 50 patients with CKD on Stage 5 (Group 2) were included in the study. Serum fT3, fT4, thyroid-stimulating hormone TSH was estimated by chemiluminescence immunoassay, serum urea by Kinetic enzymatic method, creatinine by Modified Jaffe"s and GFR calculated using modification of diet in renal disease Equation in all the cases and controls. Data were analyzed using Graph pad prism version 8.2.1.

Results: Serum fT3 levels were significantly decreased in Group 2. The Serum fT3 in Group 1 was 2.486 ± 0.7087 pg/ml and in Group 2 was 1.346 ± 0.6732 pg/ml. The difference in mean of cases and controls was statistically significant with a *P* = 0.0001. The mean ± standard deviation (SD) of serum TSH in Group 1 was 2.972 ± 0.9072 uIU/ml and in Group 2 was 6.938 ± 3.842 uIU/ml. The difference in mean of cases and controls was significant with a *P* = 0.0001The mean ± SD of Serum fT4 in Group 1 was 1.018 ± 0.234 ng/dl and in Group 2 was 1.014 ± 0.3739 ng/dl. The difference in mean of cases and controls was not statistically significant with a *P* = 0.9465.

Conclusion: In this study, thyroid dysfunction was observed in Stage 5 patients of CKD most common was low fT3 levels. Low thyroid hormone levels (i.e. free triiodothyronine) have been associated with adverse cardiovascular sequelae in CKD patient. Periodical screening reduce the morbidity and mortality in CKD patients

Key word: Chronic kidney disease, Creatinine, Thyroid hormones, Urea

INTRODUCTION

Chronic kidney disease (CKD) is a global burden and its prevalence is rising exponentially.[1,2] CKD is associated with increased morbidity and mortality and also with increased threat of cardiovascular disease, heart failure, and increased healthcare expenditure.[3,4] CKD encompasses a spectrum of different pathophysiological process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR)<60 mL/min per 1.73 m^2). CKD is an abnormality of kidney structure or function regardless of cause or specific clinical presentation and proposed a staging system based on the level of GFR. The guidelines also suggested a conceptual model for the natural history of CKD that often begins with initial kidney damage and progresses through the stages of CKD towards the outcome of kidney failure.

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Kidneys participate in the metabolism and elimination of thyroid Hormones,[5] the function of the thyroid is affected in many ways due to CKD. Thus in CKD, thyroid hormone metabolism is Impaired.[6,7] Worldwide 5-7% of the population is affected by CKD. CKD is common in

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developing countries.[8] The overall prevalence of CKD in India is 17.2% and prevalence of CKD stages 1, 2, 3, 4, and 5 are 7%, 4.3%, 4.3%, 0.8%, and 0.8%, respectively.

The prevalence of hypothyroidism in ESRD has been estimated between 0 and 9% CKD upsets thyroid function in many ways, including low circulating thyroid hormone concentration, insufficient binding to carrier proteins, and altered iodine storage in the thyroid gland.[10,11] Low fT3 is the hallmark of main disturbance.[12] Hence, presence study was done to evaluate to thyroid hormones in patients with CKD.

Aims and Objectives

1. To study thyroid hormones in CKD patients
2. To measure thyroid hormones in CKD patients
3. To assess the association of thyroid hormones in CKD patients.

MATERIALS AND METHODS

It was a hospital-based casecontrol study conducted in Osmania General Hospital in January 2020. The study included100 subjects who were divided into two groups.

Group 1 with 50 healthy subjects as controls and Group 2 with 50 patients on stage 5 CKD cases. Suffering from CKD disease who were taking treatment in hemodialysis nephrology unit. After taking informed consent, patients underwent history recording, and clinical examination. Laboratory investigations included Serum fT3, fT4, thyroid-stimulating hormone (TSH), serum urea, and serum creatinine. The GFR calculated using modification of diet in renal disease (MDRD) formula

Criteria used for Diagnosis of CKD:

- GFR of <60 ml/min/1.73 m^2.
- Evidence of kidney damage (radiologic or pathologic findings).

Levels of urinary albumin excretion above 30 mg/day (or urinary albumin to creatinine ratios of 17 mg/g or higher for men or 25 mg/g or higher for women) on at least 2 measurements, regardless of the level of GFR. The individual venous blood samples taken from each subject after overnight fast of 12 h. Four ml of venous blood was collected under aseptic precautions into serum vacutainers. Blood was allowed to clot and serum was separated after centrifuging at 3000 rpm for 5 min. The serum was stored in Eppendorf tubes at −800°C. Hemolysed and lipemic samples were not included and Serum fT3, fT4, TSH were estimated by chemiluminescence immunoassay, serum urea by Kinetic enzymatic method, creatinine by Modified Jaffe‟s and GFR calculated using MDRD equation. In all the cases and controls. Data were analyzed using Graph pad prism version 8.2.1.

Inclusion Criteria

- Patients with established CKD irrespective of etiology.
- Symptoms of uremia for 3 months or more.
- Elevated blood urea, creatinine.
- Age – 30 years–70 years
- Age and sex-matched healthy controls were taken

Exclusion Criteria

- Patients on thyroxine supplementation.
- Patients on antimetabolites, antiviral drugs.

RESULT

Fifty patients with chronic renal failure (CRF) who were on conservative management were studied among 50 patients, 10 patients were female and 40 patients were male. The age varied from 30 to 70 years among 50 cases 80% were males and 20% were female. In our study males preponderance was more in ckd cases.

The duration of CRF in this study varied from 3 months to 5 years. The glomerular filtration varied from 4 ml/min to 23 ml/min. 15 patients had GFR <10 ml/min/1.73 m^2 accounting for 30%, 30 patients GFR 11–20 ml/min/1.73 m^2 accounting for another 60% remaining five patients accounting for 10% and more than 20 ml/min/1.73 m^2 mean of GFR was 12.25 ml/min/1.73 m^2 most of cases are DN (48%) and hypertension(40%).

In this study, the Mean ± standard deviation (SD) of serum urea was increased in cases when compared to controls. The Mean ± SD of urea in cases were found to be 96.92 ± 54.18 and in controls 26.10 ± 4.390.

The Mean ± SD of Serum creatinine was increased in cases when compared to controls. The Mean ± SD of creatinine in cases were found to be 4.671 ±2.038 and in controls 0.5502 ± 0.1207.

The Mean ± SD of GFR was decreased in cases when compared to controls. The Mean ± SD of GFR in cases were found to be 12.25 ± 4.991 and in controls 117.7 ± 10.74.

In order to assess the significance of the differences observed in the mean values of different parameters observed in different groups studied, the data is subjected to unpaired *t* - test. The significance of difference of mean values of different groups is represented by *P* values and $P < 0.05$ is considered as significant.

Thyroid Hormonal Status in Group 1 and Group 2

parameters	Group 1 (control)			Group 2 (cases)		
	Mean	±SD	SEM	Mean	±SD	SEM
Serum fT3	2.486	0.7087	0.1002	1.346	0.6732	0.09521
Serum fT4	1.018	0.2340	0.0330	1.014	0.3739	0.0528
Serum TSH	2.972	0.9072	0.1283	6.938	3.842	0.5434

The Mean ± SD of Serum fT3 was decreased in cases when compared to controls.

The Mean ± SD of fT3 in cases were found to be 1.346 ± 0.6732 and in controls 2.486 ± 0.7087. The Mean ± SD of Serum fT4 was no difference in cases when compared to controls. The Mean ± SD of fT4 in cases was found to be 1.014 ± 0.3739 and in controls 1.018 ± 0.2340. The Mean ± SD of TSH was increased in cases when compared to controls. The Mean ± SD of TSH in cases were found to be 6.938 ± 3.842 and in controls 2.972 ± 0.9072.

Unpaired *t*-test between Group 1 and Group 2

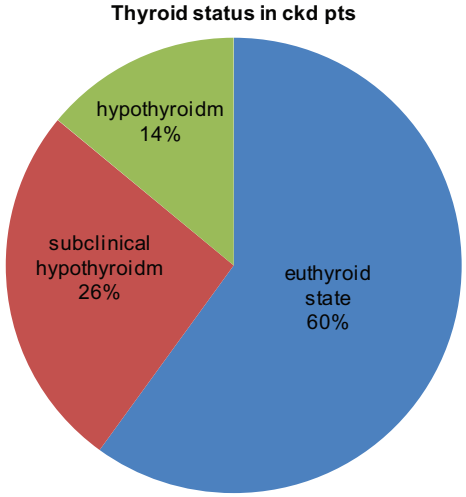
Parameter	*t*-value	*P* value	Degree of freedom (df)
Serum fT3	8.247	<0.0001	98
Serum fT4	0.06733	0.9465	98
TSH	7.103	<0.0001	98

P value was significant in (fT3, TSH)

Thyroid Status of CKD Patients

Thyroid status	No of ckd pts	%
Euthyroid state	30	60
Subclinical hypothyroidism	13	26
Hypothyroidism	7	14

In this study, fT3 was significantly decreased in 60% of patients. The subclinical hypothyroidism was observed in 26% and hypothyroidism seen in 14% cases.



DISCUSSION

CKD is defined as persistent kidney damage accompanied by a reduction in the GFR and the presence of albuminuria.[13]

The term ESRD represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys results in the uremic syndrome. This syndrome leads to death unless the toxins are removed by renal replacement therapy, using dialysis, or kidney transplantation.

The progression of metabolic and cellular dysfunction both systemically and locally within kidney tissue is linked to many diverse and complex pathways, which in particular include heightened production of proinflammatory cytokines.

CKD is a global threat to health in general and for developing countries in particular, because therapy is expensive and life-long. Individuals with CKD should be included in the highest-risk group for cardiovascular disease and therefore receive aggressive preventive measures to reduce the prevalence and severity of cardiovascular disease. Death from cardiovascular disease is a substantially more common endpoint of CKD than progression to dialysis. Identifying and treating risk factors for early CKD may be the best approach to prevent and delay adverse outcome. The adverse outcomes of CKD are universal, as are the underlying science and evidence-based strategies for prevention, detection, evaluation, and treatment.

ESRD is the advance form of Stage 5 CKD that can be treated with renal replacement therapy. Endocrine abnormalities are common in CKD. In the present study the mean ± SD of Serum fT3 in Group 1 was 2.486 ± 0.7087 pg/ml and in Group 2 was 1.346 ± 0.6732 pg/ml. The difference in mean of cases and controls was significant with a $P = 0.0001$. The mean ± SD of serum TSH in Group 1 was 2.972 ± 0.9072 uIU/ml and in Group 2 was 6.938 ± 3.842 uIU/ml. The difference in mean of cases and controls was significant with a $P = 0.0001$. The mean ± SD of serum fT4 in Group 1 was 1.018 ± 0.234 ng/dl and in Group 2 was 1.014 ± 0.3739 ng/dl. The difference in mean of cases and controls was not significant with a $P = 0.9465$.

In the present study, we found that the serum fT3 concentration were lower than the normal value in 30 (60%), out of 50 CKD patients. The low fT3 was predominantly found in stage 5 CKD patients. Reduced fT3 concentration indicating that the prevalence of low T3 was higher in stage 5 CKD patients. In our study, the median values of fT3 were

significantly low among control. Subclinical hypothyroidism was observed in 26% of cases hypothyroidism was14%These findings are justified by earlier studies done by several authors in which they have reported that one third to one-half of ESRD cases had low T3 values.[13]

In this study, we found that the low fT3 was commonly seen in the advanced stage (stage 5 CKD). This is similar to the study done by Vanani *et al.* The kidney plays an important role in the degradation and excretion of thyroid hormones. CKD upsets thyroid function in many ways, including low circulating thyroid hormone concentration, insufficient binding to carrier proteins, and altered iodine storage in the thyroid gland. Low fT3 is the hallmark of main disturbance.[13].

The major cause of reduction in fT3 levels had been linked to impaired conversion of T4 to T3 despite the normal production of T3 by the thyroid gland.

According to Singh *et al.*, the underlying mechanism behind the impaired conversion of T4 to T3 may be mediated by malnutrition and humoral factors including cytokines that are generally associated with CRF, which is an irreversible deterioration in renal function as seen in stage 5 CKD with requirements of some form of renal replacement therapy. Moreover, other factors such as chronic metabolic acidosis and increased excretion of bound and free T4 in urine of CRF patients were also among the contributors of low T3 concentrations.[10,14]

Thyroid hormone metabolism is disturbed at multiple critical steps in CKD patients including iodine accumulation in the thyroid gland and altered de-iodination. It was also hypothesized that the sub-normal fT3 in ESRD may be due to the accumulation of substances that inhibits binding of T3 to the solid-phase matrices.[14]

Limitations of the Study

This study had limitations which were listed below.

- At first, the sample size was small. The study should have been carried out on a larger group of population.
- The state of diet (calorie intake or dietary composition) or cardiac status influencing thyroid hormonal status were not considered

Recommendation

- As low T3 is important predictor of mortality in CKD patients, Nephrologists should revise the management protocol of CKD patients
- Future investigations are needed to determine the importance of evaluating or for clinical and subclinical hypothyroidism in different stages of CKD.

CONCLUSION

In this study thyroid dysfunction was observed in stage 5 patients of CKD most common was low fT3 levels. Low thyroid hormone levels (i.e. free triiodothyronine) have been associated with adverse cardiovascular sequelae in CKD patient. Periodical screening reduce the morbidity and mortality in CKD patients.

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