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Original Article

Study of Thyroid hormone (T3, T4, TSH) level in dialyzed Chronic Kidney Disease (CKD) Patients

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Abstract
Objective: *This study was undertaken to investigate the effect of renal function, on the thyroid hormone (T3, T4 and TSH) level in dialyzed chronic kidney disease (CKD) patients in both sex and different age group.*
Background: *Present study designed to analyze the thyroid hormone level in dialyzed CKD patients. Chronic kidney disease (CKD) is associated with a higher prevalence of primary hypothyroidism. The prevalence of chronic kidney disease in India is 17.2% and its association with hypothyroidism. Chronic kidney disease causes uremia which affects peripheral metabolism and hypothalamus-pituitary-thyroid axis. Due to this effect there is disturbance in synthesis and secretion of adequate amount of T3 and T4.*
Methods: *Thyroid hormone was estimated and levels of thyroid hormone were studied in 50 chronic kidney disease patients verses 50 healthy controls. Serum T3, T4 and TSH was done by chemiluminiscence immunoassay technique (CLIA) on fully auto analyzer (Maglumi1000).*
Results: *We found both T3 and T4 were significantly reduced ($p<0.0001$) whereas TSH ($p<0.0001$) were significantly higher in patient group compared to healthy subjects.*
Conclusion: *In present study, we demonstrate that renal impairment may lead to thyroid hormone dysfunction. Thyroid function test is important in diagnosis, prognosis and medical management of Chronic Kidney Disease (CKD).*
Keywords: *Chronic kidney disease (CKD), Thyroid profile (T3, T4, TSH).*

Introduction

Chronic Kidney Disease (CKD) is a progressive loss of kidney functions due to progressive damage of kidney tissues and persistent, irreversible reduction in the overall renal functions[1]. CKD is a worldwide health problem. According to World Health Organization (WHO) Global Burden of Disease project, diseases of the kidney and urinary tract contribute to 8,30,000 deaths annually and 1,88,67000 disability adjusted

life years[2]. CKD is the 12th leading cause of death and 17th leading cause of disability[3]. The overall prevalence of chronic kidney disease in India is 17.2%[4]. The functions of thyroid and kidney are interrelated[5]. Kidney is involved in the metabolism and elimination of thyroid hormone therefore; the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism and elimination of thyroid hormones causing thyroid dysfunction. While, thyroid hormone is necessary for growth and development of the kidney and maintenance of water and electrolyte homeostasis[6]. So excretion of iodine is reduced in advanced renal failure. Impaired renal clearance of iodine leads to elevated serum levels of inorganic iodide that potentially blocks thyroid hormone production[7].

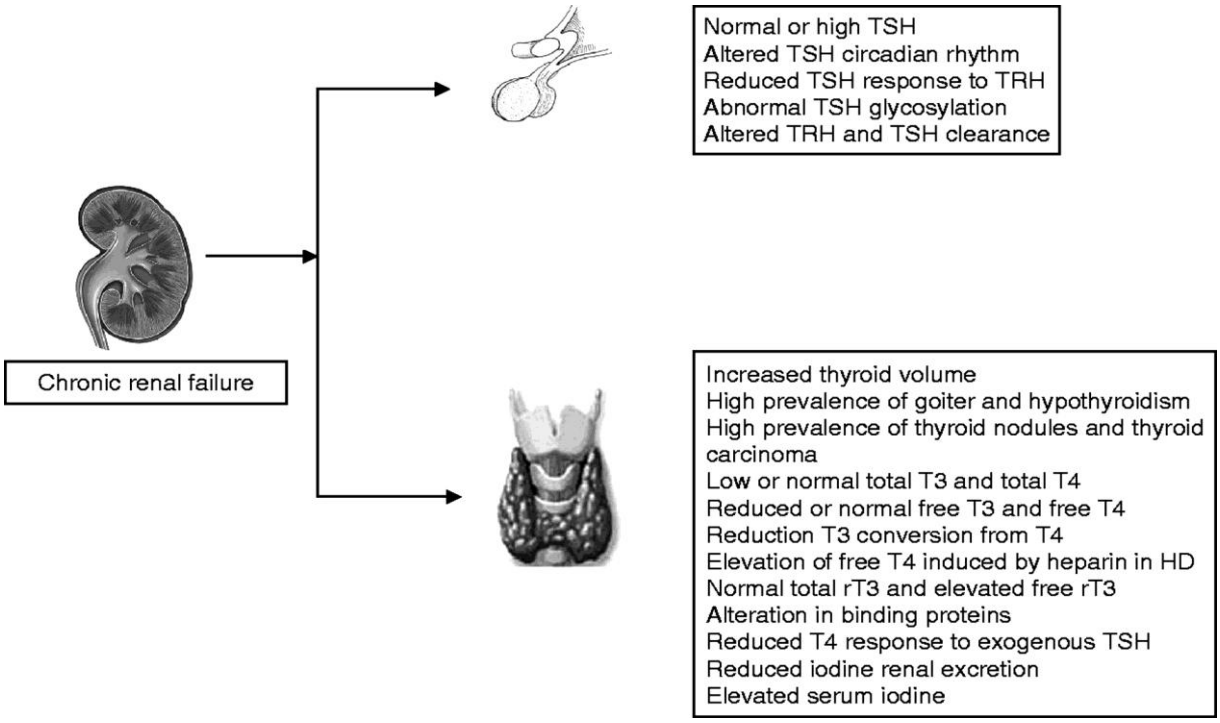

Figure-1: Effects of Chronic Renal Failure on Hypothalamus–Pituitary–Thyroid Axis[8]

Thyroid stimulating hormone (TSH) secreted by the anterior pituitary gland plays a pivotal role in control of the hypothalamus-pituitary-thyroid axis[9].Chronic kidney disease causes uremia which affects peripheral metabolism and hypothalamus-pituitary-thyroid axis. Due to this effect there is disturbance in synthesis and secretion of adequate amount of T3 andT4. Uremia influences the function and size of the thyroid gland. It increases the thyroid gland volume in chronic kidney disease patient[10].

In present study, we have determined the level of T3,T4 and TSH in chronic kidney disease patients and important parameters in diagnosis ,prognosis and management of chronic kidney disease (CKD) patients.

Material and Methods

Source of data: This study was designed to know the "Study of Thyroid hormone (T3, T4 and TSH) level in dialyzed Chronic Kidney Disease (CKD) Patients". The present study included 100 subjects of either sex among them 50 normal healthy controls without any clinical symptoms or disease and 50 chronic kidney disease (CKD). Chronic kidney disease patients were taken from Dialysis ward (Medicine) S.R.G hospital, Jhalawar Medical College, Jhalawar (Raj.). For diagnosis of chronic kidney disease, history and physical findings with supportive biochemical evidence were taken as criteria.

Ethical permission has been taken from Ethical committee, Jhalawar Medical College, Jhalawar (Raj.).

Study design: This case-control prospective study was conducted in the Department of Biochemistry, Jhalawar Medical College, Jhalawar (Raj.).

Subject Selection: Based on the following inclusion and exclusion criteria selection of subjects for the study was made on the basis of detailed history and proper clinical examination.

Inclusion criteria:

1) Patients with history and physical findings of kidney disease with no other major illness like diabetes mellitus, cancer.
2) Biochemical analysis suggestive of chronic kidney disease.
3) Both male and female with different age group.

Exclusion criteria:

1) Patients with diabetes mellitus, pregnant women.
2) History of anti-thyroid drugs.
3) Chronic use of medicine (eg: steroids, anticancer drugs)
4) Pregnancy
5) Any systemic disease: connective disorders, liver disease and Psychiatric disorders.

Collection of specimens: Around 5ml of venous blood samples was taken under aseptic conditions in sterile tubes from the normal healthy controls and from the patient of chronic kidney disease. Samples allowed to clot and centrifuged at 3000 rpm for 10 min and serum separated.T3, T4 and Thyroid stimulating hormone (TSH) was estimated on chemiluminiscence immunoassay technique (CLIA) by a Maglumi 1000 auto analyser in Clinical Biochemistry Laboratory, S.R.G. Hospital, Jhalawar Medical College, Jhalawar (Raj.)

Estimation of T3/T4/TSH hormone (Competitive immunoluminometric assay)

Principle: Use an anti-T3/T4/TSH monoclonal antibody to label ABEI {N-(4-Aminobutyl)-N-ethylisoluminol}, and use a purified T3/T4/TSH antigen to label FITC {Fluorescein isothiocyanate}. Sample, Calibrator, or Control, ABEI Label, FITC Label and Nano Magnetic Microbeads coated with sheep anti-FITC are mixed thoroughly and incubated at 37℃, forming complexes; after sediment in a magnetic field, decant the supernatant, then cycle washing for 1 time. Subsequently, the starter reagents are added and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU (Relative Light Unit) within 3 seconds and is proportional to the concentration of T3/T4/TSH present in controls or samples.

Table1: Reference Range (According to S.R.G. Hospital, Clinical Biochemistry Laboratory)

Parameters	Range
Total T3(Triiodothyronine)	0.69- 2.15 ng/ml
Total T4(Tetraiodothyronine)	52- 127 ng/ml
TSH(Thyroid stimulating hormone)	0.4-4.5 micro IU/ml

Results

In present study, we have estimated biochemical parameters (Serum TSH, Serum total T4 and Serum total T3) in chronic kidney disease patients (cases) and healthy patients (control) and analyzed through SPSS (Version 20.00) software using "Unpaired-t test".

The statistically data in our study was expressed as Mean ± SD, $p<0.05$ was considered as statistically significant. In present study, 50 cases of known chronic kidney disease and 50 healthy subjects were studied.

Table 2: Distribution of Age according to Controls and Cases Patients

Group	N	Mean ± S.D	P value
Control	50	34.56 ±14.68	0.24
Cases	50	38.00 ±14.39	

Table 2 shows statistically analyzed, mean age of healthy Controls and Cases of chronic kidney

disease (CKD). The Mean ± SD of age in Control was found 34.56 ± 14.68 years and Mean ± SD of age in Cases was found 38.00 ± 14.39 years which indicates no statistically significant difference of age between these two groups.

Table 3: Distribution of Gender according to Controls and Cases Patients

Gender	Group		Total
	Control	Cases	
Male	19 (38.0%)	30 (60.0%)	49 (49.0%)
Female	31 (62.0%)	20 (40.0%)	51 (51.0%)
Total	50 (100.0%)	50 (100.0%)	100 (100.0%)

Sex wise distribution in different group presented in Table 3. The present observation shows the percentage of male and female in Control were 38% and 62% respectively. The percentage of male and female in Cases were 60% and 40% respectively.

Table 4: Distribution of T3 (ng/ml) according to Controls and Cases Patients

Group	N	Mean ± S.D	P value
Control	50	1.37 ± 0.32	<0.0001
Cases	50	0.83 ± 0.40	

Serum total T3 levels were significantly lower in chronic kidney disease (CKD) patients (Mean 0.83& Std. Deviation 0.40) in comparison to healthy subjects (Mean 1.37& Std. Deviation 0.32) (p<0.0001).This difference was statistically significant.

Table 5: Distribution of T4 (ng/ml) according to Controls and Cases Patients

Group	N	Mean ± S.D	P value
Control	50	91.67± 13.84	<0.0001
Cases	50	74.38± 18.73	

Serum total T4 levels were significantly lower in chronic kidney disease (CKD) patients (Mean 74.38 & Std. Deviation 8.73) in comparison to healthy subjects (Mean 91.67& Std. Deviation 13.84) (p<0.0001).This difference was statistically significant.

Table 6: Distribution of TSH (micro IU/ml) according to Controls and Cases Patients

Group	N	Mean ± S.D	P value
Control	50	1.77 ±0.95	<0.0001
Cases	50	2.80 ±1.71	

Serum TSH levels were significantly higher in chronic kidney disease (CKD) patients (Mean 2.80 & Std. Deviation 1.71) in comparison to healthy subject (Mean 1.77 & Std. Deviation 0.95) (p<0.0001).This difference was statistically significant.

Discussion

The present study was conducted on 50 normal healthy subjects (Controls) and 50 patients of Chronic Kidney Disease (Cases) attended Dialysis (Medicine) ward and sample of both groups were collected to perform test at Clinical Biochemistry Laboratory of S.R.G. Hospital, Jhalawar Medical College, Jhalawar.

Table 2 shows statistically analyzed, mean age of healthy controls and cases of chronic kidney disease (CKD). The Mean ± SD of age in Control was found 34.56 ±14.68 years and Mean ± SD of age in Cases was found 38.00 ± 14.39 years which indicate no statistically significant difference of age between these two groups.

Sex wise distribution in different group presented in Table 3. The present observation shows the percentage of male and female in Control were 38% and 62% respectively. The percentage of male and female in Cases were 60% and 40% respectively.

Chronic kidney failure altering thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier proteins, possible reduction in tissue thyroid hormone content**,** Increased iodine store in thyroid gland[11].

In our study, found the Serum TSH level increased significantly (p<0.0001) in cases as compared to controls. While total T3 and total T4

decrease significantly in Chronic Kidney Disease patients (CKD) as compared to Controls ($p<0.0001$).

In the present study similar results were reported by others workers. They described that there was significantly decrease in the level total T3 and total T4 in CKD patients. Reduction in T3 concentration has been linked to a decrease in the peripheral synthesis of T3 from T4 and total T4 values in chronic renal failure patients may be primarily related to impaired T4 binding to serum carrier proteins[6,7,12]. Some researcher observed that the prevalence of hypothyroidism and abnormalities of thyroid gland in patients with chronic kidney disease at different levels of estimated glomerular filtration rate (e-GFR). Reduced glomerular filtration rate was associated with an increased prevalence of hypothyroidism, with many subclinical cases[13]. Some reports published in literature and described that low T3, T4 levels but high TSH levels in CKD patients when compared to controls due to TSH circadian rhythm and TSH glycosylation altered in Chronic Kidney Disease and low levels of both T3 and T4 could be due to defective release in response to TSH [8,14,15]. Study showed that lower level of T3 and T4 were higher risk for renal transplantation[16]. It has been reported that thyroid tumor prevalence in uremic subjects when compared with healthy subjects [10].

In present study evaluation of T3,T4 and TSH was important marker for progression, monitoring and medical management of chronic kidney disease subjects.

Conclusion

In our study we observed that, renal function was altered in chronic kidney disease patients that subsequently lead to thyroid hormone dysfunction and we concluded that monitoring of thyroid function may be beneficial to the chronic kidney disease (CKD) patients. However to avoid mistake in diagnosis, it's very important to know the effects of hypothyroidism and hyperthyroidism on renal function, as well as the changes in thyroid function tests induced by chronic kidney disease (CKD).The conclusion of our study was found to be that in chronic kidney disease patients, thyroid hormone derangement was important due to primary diagnosis of thyroid dysfunction and medical management of kidney disease as well as thyroid function.

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