Thyroid Profile and Its Correlation with Serum Creatinine in Chronic Kidney Disease Patients in Tertiary Care Hospital

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Abstract

Background: Chronic kidney disease (CKD) is defined as abnormalities in kidney structure or function present for > 3 months and have other health implications. Thyroid hormones are important for electrolyte homeostasis and also for the growth and development of the kidney. Study shows that hypothyroidism is commonly seen in later stages of CKD. This study was conducted to investigate thyroid hormone profile and its correlation with creatinine in CKD patients.

Materials and Methods: The present case control study was conducted at Dhiraj General Hospital, Piparia, Vadodara, Gujarat, India in which 100 subjects were enrolled, out of which 50 were cases of CKD patients and 50 were controls. The age group for the study was 18 to 70 years. Blood samples were drawn to measure blood urea, serum creatinine, thyroid profile. Interpretation of data was done using Medcalc software.

Conclusion: Serum TSH levels were high in cases compared to controls but results were not significant. Significant negative correlation was found between free thyroid hormones and serum creatinine. Correlation of creatinine with T3, T4 and TSH were not significant. Subclinical hypothyroidism is found in our population with undialyzed CKD. More studies involving large population size are required to ascertain these findings.

***Key words**: CKD, Serum Creatinine, Thyroid Hormones.*

Introduction

Chronic kidney disease is defined as abnormalities in kidney structure or function that are present for > 3 months and have other health implications. The disease is classified on the basis of cause and category of glomerular filtration rate (G1 - G5) and albuminuria (A1 – A3) KDIGO Classification of CKD is used for the diagnosis of Chronic Kidney Disease (CKD)[1]. It is a serious disease to human being. The incidence and prevalence of CKD increase with aging. In many cases, CKD leads to end stage renal disease and eventually it leads to death. Therefore, accurate evaluation of renal function is important for healthy individuals and CKD patients[2].

The thyroid gland regulates the most of the body's physiological actions. The interactions between kidney function and thyroid hormones are wildly studied. Thyroid hormones are important for water and electrolyte homeostasis and also for the growth and development of the kidney[3]. Metabolism, degradation and excretion of thyroid hormones are regulated by kidney; renal dysfunction affects thyroid hormone production, its distribution, and excretion. Data suggest that predialysis patients with chronic kidney disease have an increased risk of hypothyroidism and subclinical hypothyroidism[4].

Hypothyroidism is commonly seen in later stages of CKD[5]. Metabolism, degradation and excretion of thyroid hormones depend on kidney function. CKD

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affects the hypothalamus pituitary thyroid axis. CKD will lead to complications like thyroid dysfunction, lipid abnormalities and cardiovascular diseases. Thyroid gland related complications in CKD patients include decrease in circulating thyroid hormone levels, distorted peripheral hormone metabolism, inadequate binding to carrier proteins, condensed tissue thyroid hormone content and altered iodine storage in the thyroid gland. Thus, thyroid hormone metabolism is very much affected in CKD[6]. This study was conducted to investigate thyroid hormone profile and its correlation with creatinine in CKD patients.

Materials and Methods

The present case control study was conducted at Dhiraj General hospital, Piparia, Vadodara, Gujarat, India in which 100 subjects were enrolled, out of which 50 were cases of CKD patients and 50 were controls. Study was conducted from July 2019 to Dec 2019.

Case Groups: - Undialyzed cases of Chronic Kidney Disease

Controls:-Age and Sex matched Normal healthy Individual in and around the Dhiraj General Hospital is termed as controls.

Undialyzed CKD patients who are willing to participate, both male and female with the age group of 18-70 years were included in the study. Patients with known history of thyroid disorder, acute renal failure, patients on drugs which affects thyroid hormone levels, pregnant females, and previous history of dialysis and also patients who are not willing to participate were excluded from the study.

Sample Collection & Processing: -

Data were collected by personal interview, with every individual. Performa was available for the filling of biodata like age and gender, clinical examination findings and investigations. Participants were informed of the study purpose. We had taken 50 Undialyzed CKD patients as cases and 50 healthy individuals as controls within the age group of 18-70 years attending the medical outpatient department and inpatient department of Dhiraj General Hospital. Written Informed consents were taken in their respected languages and fasting blood was collected in plain vacutainer tubes. Then it was centrifuged for 15 min. at 3000 r/min. Serum was separated which was used for the estimation of blood urea, serum creatinine, total triiodothyronine (T3), total thyroxine (T4), free triiodothyronine (FT3), free thyroxine (FT4) and Thyroid stimulating hormone (TSH).

Methodology

Serum Creatinine was estimated by enzymatic method. Blood urea was estimated by urease method. Urea and creatinine were performed on EM-200 fully auto chemistry analyzer. Serum T3 and T4 were estimated by competitive chemiluminescence immunoassay. Serum FT3 and FT4 were estimated by CLIA(Chemiluminescence immunoassay). Serum TSH was estimated by sandwich chemiluminescence immunoassay. Serum T3, T4, FT3, FT4 and TSH were estimated on MAGLUMI fully auto chemiluminescence immunoassay analyzer.

Statistical Analysis

Data were presented as Mean and SD values. Comparisons between cases and controls were performed using the Independence student t- test. A p-value less than 0.05 ($p< 0.05$) was considered as statistical significant. Medcalc software was used for statistical analysis.

Results and Discussion

The age and sex distribution in cases and controls were comparable, and difference between groups was not statistically significant. Results in cases and control groups were given in Table 1 as mean±SD. The mean level of T3 was 0.87±0.52 in cases and 1.74±1.97 in controls, difference between them was statistically significant. The mean level of T4 was 5.09±1.19 in cases and 6.11±1.28 in controls, difference between them was statistically not significant. The mean level of FT3 was lesser in cases (1.35 ± 0.22) than controls (2.53 ± 0.82); the difference between them was statistically significant. The mean level of FT4 in cases was 0.77 ± 0.31, and in controls, it was 1.49 ± 0.32, and the significant difference was found between both the groups. There was higher mean serum TSH in cases (2.85 ± 0.94) as compared to controls (1.39 ± 0.66), and the insignificant difference was found between them. Significantly higher mean blood urea and mean serum creatinine were found in CKD cases compared to controls.

Table 2 shows correlation of creatinine with thyroid profile parameters among cases. A significant negative correlation was found between serum creatinine and serum FT3 ($r = -0.771$, $P < 0.01$) and between serum creatinine and FT4 ($r = -0.592$, $P < 0.01$). There were no significant correlations found between creatinine and T3, T4 and TSH.

Table 1: Mean distribution of biochemical parameters in CKD cases and controls.

Values are expressed as means ±SD.

Parameters	Cases (n=50)	Controls (n = 50)	P value
Age (yrs)	34.30 ± 7.37	32.72 ± 9.71	0.81
Blood Urea (mg/dl)	75.58 ± 30.67	27.17 ± 9.43	<0.001
Serum Creatinine (mg/dl)	9.62 ± 5.26	0.83 ± 0.21	<0.001
T3 (ng/ml)	0.87±0.52	1.74±1.97	<0.001
T4 (microg/ml)	5.09±1.19	6.11±1.28	0.17
FT3(pg/ml)	1.35 ± 0.22	2.53 ± 0.82	<0.001
FT4(ng/dl)	0.77 ± 0.31	1.49 ± 0.32	<0.001
TSH(mIU/ml)	2.85 ± 0.94	1.39 ± 0.66	0.11

$p < 0.05$ - significant, $p < 0.001$ - very significant, $p \geq 0.05$ - not significant

T3- triiodothyronine, T4 – thyroxine, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TSH: Thyroid stimulating hormone

Table 2: Correlation of serum creatinine with different variables and biochemical parameters among the cases.

Parameters		T3	T4	FT3	FT4	TSH
Serum creatinine	r value	0.228	0.012	-0.771	-0.592	0.188
	P value	0.071	0.88	<0.01	<0.01	0.323

$p < 0.05$ - significant, $p < 0.001$ - very significant, $p \geq 0.05$ - not significant

T3- triiodothyronine, T4 – thyroxine, FT3: Free tri-iodothyronine, FT4: Free thyroxine, TSH: Thyroid stimulating hormone

Abnormal thyroid hormone levels have been reported in association with chronic kidney disease patients. We have done a case–control study to correlate thyroid hormones status with serum creatinine between undialyzed CKD patients and healthy individuals. Studies showed that dialysis can affect the serum thyroid hormone levels in the CKD patients. Thyroid autoimmune diseases and subclinical primary hypothyroidism are highly seen in renal failure patients[4].

Possible ways by which CKD causes thyroid abnormalities include the following: 1.The blunting effect of uremia on TSH receptors in the hypothalamic–pituitary axis. 2. Declining glomerular filtration rate causing decreased clearance of cytokines such as tumor necrosis factor alpha and interleukin-1, which decrease the peripheral conversion of T4 to T3 as well as decreased clearance of iodine and other goitrogenic substances which causes hypothyroidis. The earliest thyroid hormone abnormality in CKD patients is decreased total T3 hormone level. This is due to chronic metabolic acidosis and chronic protein malnutrition which affect iodothyronine deiodination, protein binding of T3, decreasing the peripheral conversion of T4 to T3[7]. This explains low T3 levels in our study.

In our study, we found that serum levels of T3, FT3 and FT4 were low and serum creatinine and urea were high in cases as compared to controls, difference between them were statistically highly significant. TSH levels were insignificantly high in cases as compared to controls. There was significant inverse correlation found between the creatinine and serum FT3 and also between creatinine and FT4. Serum creatinine was positively correlated with T3, T4 and TSH, but correlation was not significant.

Our findings are coincides with study done by Okaka EI,et al which showed overt biochemical hypothyroidism and subclinical hypothyroidism were the predominant thyroid abnormalities found in nondialysis-dependent patients with CKD. Hypothyroidism was defined as the presence of elevated TSH and low T4 in a patient while SCH (subclinical hypothyroidism) was defined as the presence of elevated TSH values with normal T4 values[8]. In CKD patients who don't require chronic dialysis, subclinical hypothyroidism is more common. Michel chonchol et al showed this in their study[9]. Evaluation of total and free thyroid hormone levels in CKD patients was done by Mehta et al. They showed in their study that significant low levels of TT3, FT3, and FT4 were associated with increasing kidney damage[10]. Chandra A, et al observed in their study that the prevalence of hypothyroidism was more in patients with low GFR[11]. In one Study, a significant inverse correlation found between the renal parameters and FT3, FT4. There was no significant positive correlation found between the serum creatinine and TSH[12]. These findings are similar to our findings. TSH showed significant positive correlation with creatinine in overt hypothyroidism[13].

Cardiac dysfunctions seen in hypothyroidism include impaired systolic and diastolic function, impaired vasodilation at the endothelium, dyslipidemia and atherosclerosis. Some studies have shown new mechanisms for the increased mortality of CKD patients with hypothyroidism include increased vascular calcification and platelet reactivity leading to thromboembolic events[8]. So it is important to diagnose hypothyroidism in CKD patients for the prevention of further complications.

Conclusion

In our study, significant negative correlation was found between free thyroid hormones and creatinine. Correlation of creatinine with T3, T4 and TSH were not significant. Subclinical hypothyroidism is found in our population with undialyzed CKD. More studies involving large population size are required to ascertain these finding as our population size is small. Hypothyroidism can cause cardiovascular complications in CKD patients so it is important to screen CKD patients for thyroid gland dysfunction in order to prevent further cardiovascular complications.

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Conflict Of Interest: There is no conflict of interest.

References

1. Kettelar M, Block G A., et al. Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving Global Outcomes 2017 Clinical Practice Guideline Update. Clinical Guidelines, March 2018.
2. Xilian Qiu, Chunyong Liu, Yuqiu Ye, et al. The diagnostic value of serum creatinine and cystatin c in evaluating glomerular filtration rate in patients with chronic kidney disease: a systematic literature review and meta-analysis. Oncotarget 2017; 8(42): 72985–99.
3. P lglesias, J J Diez. Thyroid dysfunction and kidney disease. European Journal Of Endocrinology 2009;

160(4): 503-15.

4. Gupta UN, Jain A, Prakash P, et al. To study the prevalence of thyroid disorders in chronic renal disease patients. Journal of Integrative Nephrology and Andrology 2018; 5: 126-9.
5. Pan B., Du X, Zhang H, et al. Relationships of Chronic Kidney Disease and Thyroid Dysfunction in Non-Dialysis Patients: A Pilot Study. Kidney Blood Pressure Research Journal 2019; 44: 170–8.
6. Khatiwada S, Rajendra KC, Gautam S, et al. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. Endocrocrine Disorders 2015; 15: 65.
7. Basu G, Mohapatra A. Interactions between thyroid disorders and kidney disease. Indian Journal Endocrinology Metabolism 2012; 16: 204-13.
8. Okaka EI, Ayinbuomwan E. Thyroid profile in nondialysis-dependent patients with chronic kidney disease in a tertiary hospital in southern Nigeria. Journal of Medicine in the Tropics 2018; 20: 57-62.
9. Chonchol M, Lippi G, Salvagno G, et al. Prevalence of Subclinical Hypothyroidism in Patients with Chronic Kidney Disease. Clinical Journal of American Society of Nephrology 2008; 3(5) :1296-1300.
10. Mehta HJ, Joseph LJ, Desai KB, et al. Study to evaluate total and free thyroid hormone levels in chronic renal failure. Journal of Postgraduate Medicine 1991; 37:79-83.
11. Chandra A. Prevalence of hypothyroidism in patients with chronic kidney disease: a cross-sectional study from North India. Kidney Research and Clinical Practice 2016; 35(3): 165-8.
12. Srivastava S, Rajput J, Shrivastava M, et al. Correlation of thyroid hormone profile with biochemical markers of renal function in patients with undialyzed chronic kidney disease. Indian Journal Endocrinology Metabolism 2018; 22: 316-20.
13. Saini V, Yadav A, Kataria Arora M, et al. Correlation of creatinine with TSH levels in overt hypothyroidism — A requirement for monitoring of renal function in hypothyroid patients? Clinical Biochemistry 2012; 45(3): 212-4.