Evaluation of thyroid hormones in chronic kidney disease patients at tertiary care hospital- A comparative study

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Abstract

Introduction: The study is design to see the association between levels of thyroid hormones (Serum fT3, fT4 and TSH) and renal markers (serum urea, creatinine, and eGFR) in patients of chronic kidney disease (CKD). Hypothyroidism is associated with reduced eGFR while hyperthyroidism results in increased eGFR.

Aim and Objectives: To find out the association between levels of thyroid hormones and markers of renal function in chronic kidney disease (CKD) patients.

Materials and Method: A comparative study was carried out in 100 subjects, more than 18 years of age having chronic kidney disease and a group of 100 normal healthy individuals, age and gender matched from the same population served as controls. Serum urea, creatinine, fT3, fT4 and TSH were measured and glomerular filtration rate was calculated.

Results: In present study around 68% of patients were in stage 5, while 28% and 4% were in stage 4 and in stage 3 of CKD respectively. The most common thyroid hormone derangement observed was low fT3 (p=0.01) and high TSH (p=0.001) in the study group as compared to control group. Low free T3 level (p=0.001) correlated significantly in patients with low eGFR.

Conclusion: CKD is a progressive disease and these patients are more prone to develop thyroid dysfunction, therefore monitoring of thyroid function should be regularly advised to such patients in order to prevent adverse events in relation to kidney and thyroid function.

Keywords: Chronic kidney disease, Calculated Glomerular Filtration Rate, Thyroid function.

Introduction

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiological processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR <60 mL/min per 1.73 m^2) for 3 or more months, irrespective of etiology or by signs of kidney damage such as proteinuria including microalbuminuria, hematuria, abnormal imaging or biopsy findings.[1,2,3]

The overall prevalence of chronic kidney disease in India is 17.2% and prevalence of chronic kidney disease stages 1, 2, 3, 4 and 5 are 7%, 4.3%, 4.3%, 0.8% and 0.8%, respectively. [4]

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. Whereas thyroid hormone is necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis.[4,5,6]

The glomerular filtration rate (GFR) is reduced in hypothyroidism by decreased cardiac output, increased peripheral vascular resistance, intrarenal vasoconstriction, reduced renal response to vasodilators, and a reduced expression of renal vasodilators.[7,8] In addition, pathologic changes in the glomerular structure in hypothyroidism, such as glomerular basement membrane thickening and mesangial matrix expansion, may also contribute to reduced GFR.[9,10] The effects of hyperthyroidism on the kidney are usually opposite to the effects of hypothyroidism.[10,11] Among the pre-renal factors, thyroid hormones increase the cardiac output by positive chronotropic and inotropic effects as well as a reduction in systemic vascular resistance. It increases endothelial production of nitric oxide (NO) and causes the vasodilatation.[5,12,13]

Laura H et al. reported that disorders of thyroid function have also been linked to development of immune-mediated glomerular injury, and alterations in thyroid hormones and thyroid hormone testing occur in patients with kidney disease. [4,14,15]

Keeping in view of the different researcher's outcomes, the present study was designed to evaluate the pattern of thyroid hormones with calculated GFR in chronic kidney disease patients.

Materials and Methods

The present study was conducted at Department of Biochemistry, Government Medical College and Sir Takhtsinhji General Hospital, Bhavnagar. After obtaining clearance from institutional ethical committee for the research project, informed consents were taken from the participants. All participants were divided into two groups, Group-I and Group II. Group I was comprised of 100 normal healthy controls and Group-II was comprised of 100 chronic kidney disease patients as study group. They were primarily diagnosed by clinical examination & ultrasonographic findings and further evaluated by biochemical investigations. Patients with

H/O anti-thyroid drugs, on use of chronic medicine like steroids & anticancer drugs, pregnancy and patient with systemic diseases like connective tissue disorders, liver diseases and psychiatric disorders are excluded from the study. The healthy controls were selected from the working staff and people coming for their physical fitness and all patients were admitted to the Medicine ward.

They were instructed for sample collection. After ensuring 12 hours fasting venous blood sample was collected in plain vacutainer and assessed for serum urea, creatinine by UV kinetic on fully auto-analyzer I-Lab 650 and thyroid hormones (Serum fT3, fT4 and TSH) by Elisa immunoassay on I-Mark Micro plate Absorbance Reader (Elisa Reader).[16-20] The GFR was calculated by using Modification of diet in renal disease (MDRD) formula in order to understand the status of thyroid hormones in chronic kidney disease patients.

Statistical Methods

The results of the present study were analysed by using Graphpad instat version 3.0. In data analysis, comparison of all parameters between control and study group applying unpaired t-test. Values of serum urea, creatinine, fT3, fT4 and TSH were compared by using Mann Whitney U test (or Kruskal-Wallis) followed by Dunn's post hoc multiple comparisons. Interpretation of the test result was done according to p value ($p < 0.05$ – significant, $p < 0.001$ – highly significant and $p \geq 0.05$ – not significant).

Results

In the present study majority of study subjects were from 36 to 45 yrs of age group. The Mean ± SD of age in study group was 48.55 ±6.65 years as compared to 46.37 ± 5.86 in control group (Fig. 1). The male: female ratio in study group and control group were 1.7: 1 and 1.2:1 respectively (Fig. 2). In this study, there were higher numbers of male as compared to female in both these groups.

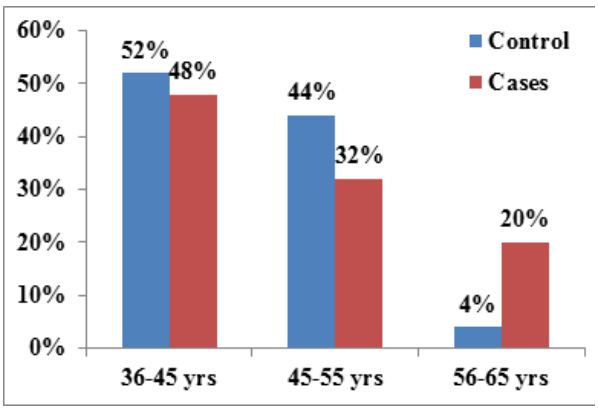

Fig. 1: Age distribution in CKD patients and healthy controls

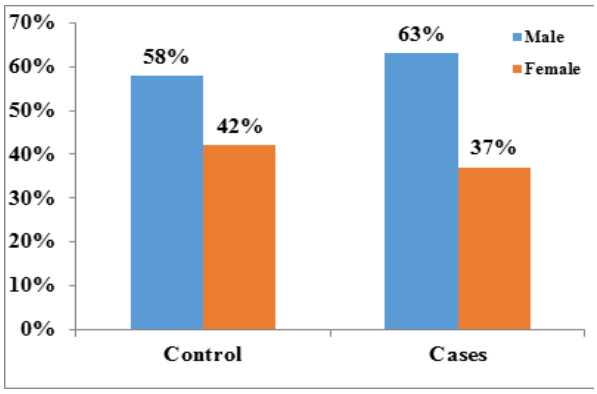

Fig. 2: Male and Female ratio in CKD patients and control

As per Table 1 Case group (N=100) shows serum urea, serum creatinine and serum TSH are significantly higher ($p<0.0001$) in the cases compared to the controls. While serum fT3 is significantly low ($p=0.01$) and serum fT4 value is not significant ($p=0.058$) in study group as compared to control group.

Table 2 shows that serum fT3 was positively correlated and serum creatinine, serum urea and serum fT4 were negatively correlated with calculated glomerular filtration rate.

Discussion

According to World Health Organization (WHO) Global Burden of Disease project, diseases of the kidney and urinary tract contribute to global burden with approximately 850,000 deaths every year and 115,010,107 disability adjusted life years. CKD is the 12th leading cause of death and 17th leading cause of disability.[21]

It is one of the most common chronic diseases worldwide, leading to greatest morbidity and mortality. CKD is a worldwide public health problem, both for the number of patients and cost of treatment involved. The kidney cannot regenerate new nephron, therefore with renal injury, disease, or normal aging, there is a gradual decrease in GFR and nephron number and there is a persistent and irreversible reduction in the overall renal function.[15,16,20]

Findings of the present study shows that the mean age of study Group was 48.55 ±6.65 years and control group was 46.37±5.86 without any significance difference between them (Fig. 1) while male: female ratio in study group and control group was 1.7:1 and 1.2:1 respectively. It suggests that the number of male patient is more than female in case group as compared to control group (Fig. 2).

In present study, there was highly statistically significant increase in serum creatinine, serum urea and serum TSH level in the study group as compared to control group ($p<0.001$). While, there was statistically significant decrease in fT3 level of the study group as compared to control group ($p<0.05$). There was no significant difference found in serum fT4 level between

both the groups (Table 1). Balaji Rajagopalan et al[23] study show that there were significantly decrease in the level of fT3 and fT4 in CKD patients. While Lim vs et al reported that despite decreased circulatory T3 and T4 level, TSH level is not elevated.

Table 1: Comparison of Biochemical Parameters between Group I and Group II

Parameter	Biological Reference Interval	Control Group (N=100)			Study Group (N=100)			Statistical Significance
		Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	
Creatinine (mg/dl)	0.7-1.2	0.76	0.84	0.8±0.19	4.64	5.35	5±1.79	t=23.33 p=0.0001
Urea (mg/dl)	15-40	19.99	22.38	21.19±6.03	122.11	138.23	130.17±40.56	t=26.57 p=0.0001
TSH (µIU/ml)	0.4-4.2	2.60	2.92	2.76±0.81	4.92	7.11	6.01±5.52	t=5.82 p=0.0001
fT3 (pg/ml)	2.5-5.8	3.46	3.80	3.63±0.84	2.84	3.61	3.10±2.049	t=2.35 p=0.01
fT4 (pg/ml)	10-21	14.32	15.40	14.86±2.72	12.71	15.12	13.91±6.06	t=1.43 p=0.15

Comparison of biological parameters and GFR in different stages of CKD in Case Group (N=100). Shows that serum fT3 was significantly decreased with decrease in GFR which was positively correlated with eGFR in study group. Serum creatinine, urea and fT4 were negatively correlated with calculated glomerular filtration rate. (Table 2)

Table 2. Comparison between different stages of CKD with Biochemical parameter

Stages of CKD	eGFR (ml/min/1.73 m^2)	Creatinine (0.7-1.2mg/dl)	Urea (15-40mg/dl)	TSH (0.4-4.2µIU/ml)	fT3 (2.5-5.8pg/ml)	fT4 (10-21pg/ml)
Stage- III (N=4)	32.5±1.73	2.17±0.09	109.5±28.57	6.66±6.23	3.47±3.02	13.07±8.38
Stage- IV (N=28)	18.39±2.94	3.35±0.68	122.46±34.75	7.03±5.88	2.4±1.28	13.58±5.57
Stage-V (N=68)	9.82±2.62	5.84±1.49	134.55±42.88	5.56±5.35	1.69±1.25	14.10±6.20
Statistical Significance	p<0.0001	p<0.0001	p<0.2194	p<0.3947	p<0.0001	p<0.9351

In the present study, it was observed that there was highly significant increase in serum creatinine, urea with increasing severity of CKD, whereas fT3 level decreased in the CKD patients with decreased GFR. There was no significant difference in serum fT4 levels in both the groups. So it is concluded that in CKD patients along with renal function, thyroid hormone function also get altered. Thus early monitoring of thyroid function will be beneficial to the CKD patients.

Conclusion

As CKD is a progressive disease and these patients are more prone to develop thyroid dysfunction, therefore monitoring of thyroid function should be regularly advised to such patients in order to prevent adverse events in relation to kidney and thyroid function.

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