ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 8, Issue – 1, January – 2023 , Page No. : 32 – 38

A study of thyroid profile in patients with chronic kidney disease

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Citation this Article: Dr. Ansh Rajput, Dr. Kushagra Tandon, Dr. Prakash Joshi, Dr. R. K. Jha, "A study of thyroid profile in patients with chronic kidney disease", IJMSIR- January - 2023, Vol – 8, Issue - 1, P. No. 32 – 38.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: There is limited data on thyroid dysfunction in CKD patients (CKD). Few study investigated thyroid hormones' effect on renal function deterioration. Undiagnosed thyroid dysfunction in CKD may worsen disease.

Methods: This case-control study was carried out in central India. 65 seemingly healthy control subjects and 60 non-dialysis CKD patients (stages 2-4) without thyroid disease were recruited for this study.

Results: Between the two study groups, there were no discernible differences in TSH levels. But FT3 and FT4 levels in CKD patients were considerably greater than in the control group. TSH levels did not differ significantly between CKD stages in study participants, while FT4 and FT3 levels did differ considerably across all CKD stages.

Conclusion: In patients with CKD, a reduction in eGFR is associated with higher levels of FT3 and FT4, but not TSH. Patients with CKD also have higher levels of FT3.

Introduction

A disease spectrum known as chronic kidney disease (CKD) is defined by a long-term decline of renal function. Reduced kidney function lasting longer than three months, as determined by measured or estimated glomerular filtration rate [1], is a symptom of the condition. The prevalence of CKD has been shown to be increasing globally, which has led to the recognition of CKD as a public health issue [2]. The proliferation and differentiation of cells are significantly influenced by thyroid hormones. Additionally, they influence crucial physiological processes in practically every human tissue [3]. Along with the incidence of thyroid dysfunction, which has been demonstrated to rise with the course of CKD, changes in thyroid hormone status have been seen in individuals with CKD [2,4]. No recommendations are available regarding the treatment of mild abnormalities of thyroid hormone levels in patients with CKD who do not require dialysis, despite improvements in the ability to

detect subtle changes in the status of thyroid hormones due to the variety of modern laboratory testing now available. These minor thyroid hormone abnormalities could be risk factors for negative health outcomes like cardiovascular disease and could complicate the progression of kidney disease [4]. An abnormality in lipoprotein metabolism may be a potential cause of renal disease, according to mounting data [5, 6]. Numerous research [5-7] have revealed that elevated TG levels and/or low levels of high-density lipoprotein cholesterol (HDL-c) are indicators of a higher risk of renal impairment. A number of comorbidities, such as dyslipidemia, thyroid dysfunction, and cardiovascular disease, have also been linked to the advancement of CKD [4]. Therefore, to increase patient quality of life and prolong survival, it is important to identify and treat CKD patients who are at risk for adverse cardiovascular events as soon as possible, especially in developing nations where resources for renal replacement therapy are scarce, expensive, or nonexistent [8]. An overall CKD prevalence of 46.9% was found in a multi-center screening research in Ghana to determine the prevalence of CKD among hypertensives in an out-patient context [9]. This was consistent with results of an earlier analysis of autopsy data [10]. We conducted this study to ascertain the thyroid hormone status in Indian patients with CKD and its correlation with altered thyroid function observed in CKD patients.

Methods

This case control study was carried out at the tertiary healthcare facility in the central India. 65 apparently healthy control subjects living in the nearby communities and 60 non-dialysis CKD patients with various CKD stages (stages 2-4) who had no prior history of thyroid dysfunction were recruited for this study. Thyroid function was evaluated in all newly recruited patients with stages 2-4 CKD who were not on dialysis.

Case definition As indicated by aberrant albumin excretion and quantified by an estimated glomerular filtration rate (eGFR) of less than 90 mL/min and proteinuria lasting more than three months, kidney damage or impaired kidney function are referred to as "chronic kidney disease" (CKD). The eGFR was calculated using the condensed Modification of Diet in Renal Disease (MDRD) research formula. Proteinuria was defined as a urine dipstick value of trace, 1+, or heavy (more than or equal to 2+). Stages 2-4 of non-dialysis-dependent CKD were defined by the American National Kidney Foundation as follows: The eGFR scale has four stages: stage 2, stage 3, and stage 4. Stage 4 is defined as 15-29 ml/min/1.73 m2.

Results

Table 1 shows Demographic and clinical information of 125 participants who met the inclusion criteria were recruited for this study. Clinical parameters and demographic data of the study population are presented in Table 1. There were significantly more females in the control group than in the CKD patient group. The mean age of the CKD patients was higher than that of the control group, but not significantly different between the two study groups. Body mass index was statistically different between the two study groups. Blood pressure was significantly higher in CKD patients when compared to the control group. The prevalence of hypertension in the CKD study group was 75%.

Table1:Demographic and clinical parameters of the study population

Parameter	CKD patients (N = 60)	Control (N=65)	95%CI Of mean diff	p-value
Age (yrs)	51.83±16.58	45.52±11.25	1.14-11.48	0.017*
Females	23%(47)	39%(60)		<0.05*[Y]
BMI (kg/m^2)	27.80± 4.86	26.13± 6.30	-0.48-3.81	0.127
SBP(mmHg)	136.94±23.29	117.51±15.58	12.21-26.65	<0.001*
DBP(mmHg)	83.00±14.41	75.86±12.63	2.09-12.15	0.006*
Hypertension (%)	75.0			

N=samplesize,CI=confidenceinterval,BMI=bodymassindex,SBP=systolicbloodpressure,DBP= diastolic blood pressure, D2M = type 2 diabetes mellitus.

Y=Z-scoresforproportioncomparison.Resultispresentedasmean±standarddeviation.*P-values less than 0.05 were considered statistically significant

Table 2 shows Biochemical parameters: Table 2 compares the biochemical parameters of CKD patients with those of the control group. The mean plasma FT3 and TSH concentrations were significantly higher in cases compared to controls (p= 0.000; p = 0.000 respectively), whereas there was no significant difference in the mean plasma FT4 concentrations between cases and controls (p = 0.999) (Table 2).

Table 2:Biochemical and thyroid hormones levels of the studied population

Parameter	CKD patients (N = 60)	Control (N=65)	95%CI Of mean diff	p-value
Serum Creat.(mmol/L)	189.84±111.42	78.06±20.59	83.81-139.73	<0.001*
Creat. Clear.(ml/min)	55.33±38.29	107.12±43.54	-67.29 -(-36.27)	<0.001*
GFR(ml/min/1.73m^2)	63.83±46.63	132.78±35.09	-84.12-(-53.80)	<0.001*
TSH(mIU/ml)	1.87±1.51	2.36±1.31	-1.02-0.03	0.064
FT3(pmol/L)	4.83±2.72	3.43±0.70	0.70-2.09	<0.001*
FT4(pmol/L)	14.32± 2.91	10.80± 2.71	2.47-4.57	<0.001*

N = Sample size, CI = Confidence Interval, CKD = Chronic Kidney Disease, Serum Creat = Serum Creatinine, Creat.Clear.=CreatinineClearance,GFR=GlomerularFiltrationRate,TC=TotalCholesterol,TG=Triglyceride, TSH = Thyroid stimulating hormone, FT3 = Free triiodothyronine, FT4 = Thyroxine Result is presented as mean ± standard deviation.

*P-valueslessthan0.05wereconsidered statistically significant.

Table 3 shows There were significant differences in the distributions of FT3-, FT4- and thyroid- status between cases and controls (p = 0.000; p = 0.012; p= 0.004 respectively) (Table 3). Thirteen (28.9%) cases had elevated FT3 while FT3 was not elevated in any control (Table 3). Whereas 1 (2.2%) and 7 (15.6%) cases had elevated and decreased FT4 respectively, there were none with elevated or decreased FT4 among controls (Table 3). Amongst the cases were 7 (15.6) sick euthyroid and 3

(6.7%) subclinical hypothyroidism whereas none was found among the controls (Table 3).

Table 3:Clinical,biochemical and thyroid hormonal status of chronic kidney disease stages

Parameter	Chronic kidney disease stages				p-value
	Stage1 (n=13)	Stage2 (n =7)	Stage3 (n =13)	Stage4 (n =16)	
Age(years)	41.61±17.03	45.57±14.73	58.69± 1.18	57.31±10.73	0.015*
Sr.Cr(mmol/L)	74.77±14.62	113.86±16.16	193.46±49.75	313.63±83.35	0.000*
Cr.Cl.(ml/min)	107.88±29.83	64.94±15.75	36.91± 7.22	23.42± 4.71	0.000*
eGFR (ml/min/1.73m^2)	129.20±33.22	75.01± 9.89	43.66± 8.27	22.20± 4.25	0.000*
TSH(mIU/ml)	1.08±0.76	2.03±1.36	1.65±0.77	2.60±0.88	0.354
FT3(pmol/L)	5.38±2.34	6.19±4.71	4.45±2.49	4.09±1.88	0.013*
FT4(pmol/L)	14.00± 3.51	15.51± 3.82	14.64± 0.98	13.80± 3.09	0.000*

n=sub-groupsize,CKDstagedefinition:Stage2 =60≤eGFR ≤89ml/min/1.73m^{2,} Stage3=30≤eGFR≤59ml/min/1.73m^{2,} Stage 4 = 15 ≤ eGFR ≤ 29 ml/min/1.73m$^{2.}$*P-values less than 0.05 were considered statistically significant

Thyroid function status: The results of our study groups' thyroid function status are displayed in Table 4. While 2% of CKD patients had subclinical hyperthyroidism, 3% of CKD patients had preclinical hypothyroidism, and 2% of CKD patients had subclinical hyperthyroidism.

Table 4:Thyroidhormonedysfunctionprevalenceinthestudiedpopulation

Group/Thyroid disorder	CKD patients (N = 49)	Non-CKD Control (N = 65)
Sub-clinical hypothyroidismn (%)	2(3.3)	3(4.6)
Primary hypothyroidismn (%)	0(0.0)	0(0.0)
Sub-clinical hyperthyroidismn (%)	2(3.3)	0(0.0)
Primary hyperthyroidismn (%)	0(0.0)	0(0.0)

TSHnormalrange:0.4-5.5mIU/ml,FT3normalrange:2.8-7.3pmol/L,FT4normal range: 8.5 - 22.5 pmol/L. Subclinical Hypothyroidism: when TSH is higher than 5.5 mIU/ml, FT3 and FT4 within normal range. Primary Hypothyroidism: when TSH is greater than 5.5mIU/ml, FT3 and FT4 less than normal. Subclinical Hyperthyroidism: when TSH is less than 0.3 mIU/ml, FT3 and FT4 within normal range.

Primary Hyperthyroidism:whenTSHislessthan0.3mIU/ml,FT3andFT4higherthannormal

Discussion

Due to the kidneys' participation in the metabolism, breakdown, and excretion of numerous chemicals, including thyroid hormones, thyroid dysfunction has an effect on renal function. As a result, it is anticipated that any decrease of renal function may affect thyroid physiology [2]. There is currently no information available on the thyroid state of clinically healthy euthyroid CKD patients in Ghana. In this investigation, we showed that TSH levels between CKD patients and clinically healthy people without CKD did not differ significantly. Although mean FT3 and FT4 values, as well as that of TSH, were all within the reference range, it was discovered that FT3 and FT4 levels were considerably greater in CKD patients than in the control group. Some investigations that focused on thyroid

function in end stage renal disease have found similarities in the TSH levels between the control group and CKD participants [12, 13]. Other research, primarily in Asian and Caucasian populations, has demonstrated that, in CKD patients with normal or low free and total T3 and T4 levels, serum TSH levels are typically normal or increased [14, 15]. Despite being at odds with studies that have identified low T3 and T4 levels as the most frequently observed thyroid alteration in CKD patients, our results—particularly for serum FT3 and FT4 levels in CKD patients—still contribute to the growing body of research showing that thyroid hormone alterations occur in people with CKD who do not need dialysis. The concurrent hypertension that our CKD individuals had may have caused the elevated FT3 and FT4 levels to be erroneous. There is evidence from numerous research that thyroid dysfunction and high blood pressure are related.

Elevated blood pressure is linked to both hyperthyroidism (overactive thyroid) and hypothyroidism (underactive thyroid) [16]. It has been proposed that milder forms of thyroid malfunction, such as subclinical hyper- and hypothyroidism, may also increase the risk of high blood pressure [17]. The relationship between thyroid hormones and renal function has been explained by a number of different potential processes. Overt hypothyroidism is characterised by decreased cardiac output and increased systemic vascular resistance, which reduce renal blood flow, decrease GFR and creatinine clearance, and raise serum creatinine levels [16, 17].

Contrarily, hyperthyroidism results in increased cardiac output and circulating blood volume, which enhance creatinine clearance and lower serum creatinine [16]. It is unknown how these mechanisms function in euthyroid people with low to normal thyroid function, despite the fact that they have been utilised to explain the connection between thyroid malfunction and hypertension [4]. Between CKD phases, we were unable to detect a significant rising or falling trend for TSH. Although FT3 and FT4 levels varied significantly between CKD stages 2-4, we were unable to determine whether there was an upward or downward trend for these thyroid hormones. Our results diverged from those of the 104,633 Korean participants in the Kangbuk Samsung Health Study (KSHS), with an average age of 38.0 years and baseline thyroid function that was normal. It was noted that higher risk of incident CKD, defined as eGFR 60 mL/min/1.73 m2, was associated with high-normal levels of TSH and low-normal FT3 levels but not FT4 levels [18]. This gap may be explained by the different criteria of CKD used in our investigation compared to the KSHS study, as well as the more older participants in our study. TSH receptor expression has also been documented in extra-thyroidal organs, such as the kidney. Therefore, it is conceivable that TSH may impact renal function without affecting FT4 or FT3 [17]. Only 2% and 3% of the CKD and control groups, respectively, had subclinical hyperthyroidism identified in their blood tests, while 2% of the CKD patient group did. It is significant to note that laboratory abnormalities—many of which are unrelated to obvious disease—are frequently used to demonstrate endocrine dysfunction. Our research has a few drawbacks. Our ability to identify severe thyroid dysfunction in the research population in the absence of clinical disease was constrained by the small sample size. Second, the quantity of anti-thyroid peroxidase antibodies was not assessed. The development of immune complexes containing thyroglobulin in glomeruli as a result of autoimmune thyroiditis may result in glomerular damage [19]. Future research may need to take into account other or alternate metrics for determining eGFR that are less biassed and more

accurate than the Modification of Diet in Renal Disease Study equation, particularly at higher GFR values [20].

Conclusion

We discovered that acute CKD and a reduction in eGFR were linked with greater levels of FT3 and FT4, but not low levels of TSH. It may be necessary to include more criteria for calculating eGFR and use bigger sample sizes for assessing thyroid hormone status in order to improve upon the biochemical criteria for diagnosing thyroid dysfunction.

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