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ORIGINAL RESEARCH

Association between Cystatin C, Vitamin D and Thyroid hormone in Chronic Kidney Disease Patients: A cross sectional study

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Abstract

Background: Chronic kidney disease (CKD) is a common health issue affecting 8% to 16% of the global population. This condition often co-occurs with other health complications, such as thyroid dysfunction, dyslipidemia, and cardiovascular diseases.

Aim: The objective of this study was to evaluate the potential association between cystatin C, vitamin D, and thyroid hormone levels in patients with CKD.

Materials and Methods: The study recruited a total of 250 patients diagnosed with CKD. Demographic information, biochemical data, and hormone levels of all the patients were collected and analyzed. The analytes measured included serum creatinine, cystatin C, vitamin D, free thyroxine (fT4), and thyroid stimulating hormone (TSH). Auto-analyzers were used for evaluating these variables, and all the results were recorded and analyzed using SPSS software.

Results: The mean serum creatinine level was 2.39 mg/dl, while the mean vitamin D and cystatin C levels were 37.5 ng/mL and 3.9 mg/L, respectively. The mean TSH level was 3.29 mU/L, and the mean free thyroxine level was 1.45ng/mL. The results showed that 16%, 24%, 24%, 20%, and 16% of the patients were classified as CKD stages I, II, III, IV, and V, respectively. The correlation between CKD grading and cystatin C levels was found to be significant.

Conclusion: The study suggests that most patients with chronic kidney disease have altered serum cystatin C levels that increase with disease progression. Cystatin C appears to be a sensitive biomarker for detecting early declines in renal function.

Key words: Chronic Kidney Disease, Vitamin D, Thyroid stimulating hormone, Cystatin C.

Introduction

Chronic kidney disease (CKD) affects between 8% and 16% of the population worldwide and is often under recognized by patients and clinicians. Defined by a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2, albuminuria of at least 30 mg per 24 hours, or markers of kidney damage persisting for more than 3 months, CKD is more prevalent in low- and middle-income than in high-income countries.[1- 3]

Effective identification and management are necessary in order to prevent CKD progression and cardiovascular events, reduce the risks associated with acute kidney injury (AKI), and

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improve patient safety and medicines management. Historically, it was considered that managing patients with CKD is the responsibility of nephrologists in secondary care settings, but improved understanding of the nature and implications of early stages of the condition mean that primary care clinicians have an essential role to play.[4- 6]

Cystatin C is freely filtered by the glomerulus and is largely resorbed and catabolised in the proximal tubules. Although its clearance cannot be measured because of this catabolism, its plasma or serum concentration is a good measure of GFR, with possible advantages over more established markers such as serum creatinine.[7]Vitamin D is labeled as the "sunshine vitamin," as it is produced in the skin on sun exposure. Vitamin D is required to maintain serum calcium concentration within the normal physiologic range for musculoskeletal health.[8]

Thyroid function tests are designed to distinguish hyperthyroidism and hypothyroidism from the euthyroid state. Direct measurements of the serum concentration of the two thyroid hormones—triiodothyronine (T3) and tetraiodothyronine (T4)—more commonly known as thyroxine, are extensively employed. The T3 resin uptake (T3RU) is used as an indirect measure of serum thyroid hormone binding capacity, and the Free T4 index (FT4I), derived from the T4 and T3RU, corrects estimates of T4 for serum binding abnormalities.[9- 11]Hence; the present study was conducted for evaluating Cystatin C, Vitamin D and Thyroid Function Test in patients with CKD.

Materials & methods

This cross-sectional study was conducted in the Department of Biochemistry, in collaboration with Department of Medicine and admitted patients in the Dialysis unit at Government Medical College and Associated Hospital, Rajouri (J&K). Total number of 250 patients was included in this study after fulfilling the inclusion criteria which included all the patients of Chronic Kidney Disease above 18 years of age. The CKD was diagnosed on the basis of history, examination, blood investigations and on NKF (National Kidney Foundation) criteria, CKD of 3 or more than 3 months duration were also included. Exclusion criteria included patients with family history of CKD, thyroid disorders, past history of any medication for CKD, thyroid disease, vitamin–D supplement and history of any surgery or any radiological intervention to both the kidneys and thyroid gland.An informed and written consent was taken from all the patients before their inclusion into the study. Demographic data, including age, gender, height, weight, marital status, and education level and employment status were collected. The data of CKD diagnosis, age, stage and cause of renal impairment at diagnosis as well as any comorbid conditions were ascertained from the patients themselves and/or confirmed by their relatives, medical records. This study did not focus on the cause of CKD but its presentation. Five (5) mL of blood samples were obtained from the patient by venipuncture from the ante-cubital fossa or another convenient site in a red top vials. Samples were allowed to clot for 30 min, separated by centrifugation at 3500 rpm for 5 min then the serum was aliquoted. Finally, biochemical analysis was done on it and serum creatinine, Cystatin C, Vitamin D, thyroid stimulating hormone (TSH) and free thyroxine (FT4) levels were estimated in CKD patients of all five stages. Diatron-Pictus 500 automatic clinical chemistry analyser (Tablas, Budapest, Hungary) was used for estimation of biochemistry variable and other variables (Cystatin C, Vitamin D, TSH and fT4) were estimated using chemiluminescence immunoassay (CLIA) by VITROS ECiQ immunodiagnostic system(Ortho Clinical Diagnostics, Rochester, NY, USA).Data was analysed with SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA). Results were expressed as mean ± SD. Pearson's correlation with taking 5% as level of significance was used to make statistical comparisons. A P-value < 0.05 was considered statistically significant.

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Results

Mean age of the patients was 43.8 years. Out of 250 patients, 58 percent were males while the remaining were females. Mean serum creatinine levels was 2.39mg/dL. Mean vitamin D levels were 37.5 ng/mL. mean cystatin C levels were found to be 3.9 mg/L. Mean TSH levels were found to be 3.29 mU/L while free thyroxine levels were found to be 1.45ng/mL.16 percent, 24 percent, 24 percent, 20 percent and 16 percent of the patients were of CKD stage I, II, III, IV and V respectively as shown in table no 1 &table no 2

Table 1: Variables

Variable	Mean	SD
Serum creatinine (mg/dL)	2.39	0.21
Vitamin D (ng/mL)	37.5	5.1
Cystatin C (mg/L)	3.9	0.8
TSH (mU/L)	3.29	0.68
Free thyroxine levels (ng/mL)	1.45	0.23

Table 2: Distribution of patients according to CKD grading

CKD Staging	Number	Percentage
Stage I	40	16
Stage II	60	24
Stage III	60	24
Stage IV	50	20
Stage V	40	16
Total	250	100

Table 3: Corelation of CKD grading and other variables

Variables	R value	p- value
Serum creatinine (µmol/L)	0.231	<0.05*
Vitamin D (ng/mL)	0.171	<0.05*
Cystatin C (mg/L)	0.353	<0.05*
TSH (mU/L)	0.168	0.245
Free thyroxine levels (ng/mL)	0.127	0.26

*: Significant

While correlating Cystatin C with CKD grading we got significant positive correlation with r value 0.353, we also got significant positive correlation when we compare between serum cretin and CKD grading with r value 0.231. On the hand we got insignificant positive correlation between Vitamin D, TSH and free thyroxine levels with CKD grading as shown in table number 3.

Discussion

Chronic kidney disease (CKD) is a significant health issue that is expected to continue to increase due to the aging population and rising numbers of patients with diabetes and hypertension. As the number of CKD patients increases, primary care practitioners will face the challenge of managing the complex medical problems unique to these patients.[10-12]Cystatin C is a valuable biomarker for evaluating renal function since it is not significantly affected by patient characteristics such as age, gender, body size and composition, and nutritional status.[11]

Vitamin D is essential for regulating calcium-phosphate homeostasis and proper functioning of the immune, musculoskeletal, cardiovascular, and nervous systems. However, changes in lifestyle and environment resulting from the technological revolution have significantly

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affected human life[12, 13]. Hence this study was conducted to evaluate Cystatin C, Vitamin D, and Thyroid Function Test in patients with CKD.

The study included 250 patients, with an average age of 43.8 years, of which 58% were males. The average serum creatinine levels were 2.39 mg/dL, average vitamin D levels were 37.5 ng/mL, average cystatin C levels were 3.9 mg/L, average TSH levels were 3.29 mU/L, and average free thyroxine levels were 1.45ng/mL. Ye Y et al found that TSH was negatively and linearly associated with Cr and eGFRCr (P<.001), and there were quadratic trends between TSH and cystatin C or eGFRCysC (P<.001). Compared with individuals with TSH of 2.01-3.00 mIU/L, the prevalence of CKDCysC was significantly higher in subjects with TSH<0.40 mIU/L, 3.01-4.00 mIU/L, and 4.01-7.00 mIU/L, while the prevalence of CKDCr was only significantly higher in subjects with TSH>7.0 mIU/L[12].

The study revealed that 16%, 24%, 24%, 20%, and 16% of the patients were classified as CKD stages I, II, III, IV, and V, respectively. Correlating CKD grading with cystatin C levels showed significant results. Tapper M et al found that 92.1% of CKD patients had elevated serum cystatin C levels, and there was a stepwise increase from stage 1-5. They also found a stepwise reduction in serum 25-OH-vitamin D levels from stage 2-5, with 22.1% having vitamin D insufficiency and 22.1% presenting with deficiency. One patient had overt hypothyroidism, and nine had subclinical hypothyroidism[13]. In a study by Chonchol M et al, the prevalence of subclinical hypothyroidism increased from 7% at an eGFR of 90 mL/min/1.73 m2 to 17.9% at an eGFR<60 mL/min/1.73 m2 in 3,089 unselected outpatient adults.[14]The effect of thyroid hormone replacement on renal function has not been widely investigated in hypothyroid CKD patients, especially in subclinical hypothyroidism. A recent study by Shin et al demonstrated that thyroid hormone treatment not only preserved renal function but was also an independent predictor of renal outcome.[15]

Conclusion

Serum cystatin C levels were found to be altered in the majority of patients with chronic kidney disease, and the levels increased progressively with disease progression in a stepwise manner. These findings suggest that serum cystatin C is a highly sensitive biomarker for detecting early decline in renal function.

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