ISSN 2664-4169 (Print) & ISSN 2664-7923 (Online)
South Asian Research Journal of Biology and Applied Biosciences
Abbreviated Key Title: South Asian Res J Bio Appl Biosci

| Volume-6 | Issue-5 | Sep-Oct -2024 | **DOI: https://doi.org/10.36346/sarjbab.2024.v06i05.001**

Original Research Article

Evaluation of Thyroid Hormone, Fibroblast Growth Factor 23 and Cystatin C Concentrations in Patients with Chronic Kidney Disease

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Article History
Received: 27.07.2024
Accepted: 05.09.2024
Published: 07.09.2024

Abstract: The age of 20-≤71years old. Also, in the current study, 30 healthy people were taken as a control group. Findings of the current study revealed substantial variations between chronic kidney disease (CKD) levels. The results of the current study demonstrated significant differences in s. urea between studied groups. Whereas, s. urea levels in CKD patients (107.42±8.52), were demonstrated a significant (P≤0.05) elevated in compared to a control (19.35± 2.16). while, creatinine levels in CKD patients (6.81± 0.55) demonstrated a significant (P≤0.05) elevated in compared to a control (0.84± 0.19). T3 levels in the end stage (5.17± 0.14) indicated a significant (P≤0.05) reduced than in other CDK stages and control group (6.34±0.28). T4 levels in the end stage (7.17±0.14) were significantly lower (P≤0.05) than in other CDK stages and control group (10.44±0.31). Thyroid-stimulating hormone (TSH) levels in the end stage (2.83±0.12) increased significantly (P≤0.05) compared to other CDK stages and control group (1.52±0.24). In contrast, fibroblast growth factor 23 (FGF-23) levels in the end stage (184.03±17.31) increased significantly (P≤0.05) as compared to other CDK stages and control group (5.16±0.45). Cystatin C level in CKD patients (17.11±1.94) was demonstrated a significant (P≤0.05) elevated in compared to a control (8.04±0.37). It is concluded from the study that CKD patients suffer from hypothyroidism based on hormone concentrations. The study also revealed a negative correlation between FGF-23 and Cystatin C levels with eGFR in CKD patients.

Keywords: CKD; FGF-23, Cystatin C, thyroid, hypothyroidism.

INTRODUCTION

End-stage kidney disease (ESKD) is a complicated and multidimensional illness that causes renal failure. Disease-related complications raise the likelihood of cardiovascular-related morbidities and accelerated the course of chronic kidney disease (CKD) [1, 2]. Global health issues include CKD. Approximately 13.4% of people worldwide have CKD, according to a meta-analysis of observational research estimating CKD prevalence [3]. The majority, 79%, had advanced kidney disease (CKD) at stages 3-5. Nevertheless, as early renal disease is clinically silent, the true number of individuals with CKD (stages 1 or 2) is probably significantly higher [4]. Being responsible for regulating most physiological processes in the body, the thyroid gland plays one of the most crucial roles in human health. The thyroid gland secretes two hormones, T3 and T4, which are involved in metabolism, growth and development, the production of proteins, and the control of numerous other vital hormones [5, 6]. Thyroid hormones are essential for kidney growth and the upkeep of the body's internal environment [7]. Thyroid hormone production and renal function are correlated [8]. The kidney plays a crucial role I n the activity of thyroid hormones in addition to being involved in their metabolism and excretion. Patients with CKD experience disruptions in thyroid hormone secretion due to effects on the hypothalamus pituitary thyroid axis [9]. As an alternative, thyroid disruption modifies renal architecture, renal blood flow, tubular function, GFR, water and electrolyte balance, and kidney architecture [10, 11]. Numerous investigations have shown that as CKD progresses, circulating FGF23 levels rise [12]. When the body absorbs phosphate from the diet, osteoblasts and osteocytes secrete FGF23. Then, by inhibiting phosphate reabsorption at renal tubules, FGF23 operates on the kidney to enhance urine phosphate excretion [13], preserving the phosphate balance. It is possible that as CKD progresses, the progressive rise in circulating FGF23 levels makes up for the increasing decline in the number of functioning nephrons, maintaining phosphate homeostasis,

because FGF23 raises phosphate elimination per nephron [14]. So, the aim of current study was detecting the concentrations of thyroid hormones, fibroblast growth factor 23, and cystatin C in patients with CKD.

MATERIALS & METHODS

Study Population

110 Patients with CKD, of both sexes, who visit Azadi Teaching Hospital and Kirkuk Teaching Hospital in Kirkuk, Iraq, from January to July 2024, ranging in age between 20 and ≤71 years, are the target group. Hemodialysis was administered to each patient with end-stage renal failure for four hours, twice or three times a week. Also, in the current study, 30 healthy people were taken as a control group.

Blood Samples

Every patient had a blood sample taken by skilled nurses. Five milliliters of venous blood were donated by each patient, and they were split between a 4.0 ml vacutainer plain tube and a 1.0 ml EDTA tube. After centrifuging for ten minutes at 4000 rpm, the serum was extracted. After being separated, the serum was put into tubes and kept cold until it was time for analysis.

Glomerular Filtration Rate (GFR)

The serum creatinine methodology used in this test is dependent on the manufacturer's instructions. The concentration was determined using the CKD-Epidemiology (CKD-EPI) equation.

$$eGFR = 141\ x\ (SCr/k)\ a\ x0.993Agex\ [1.018\ if\ Female]\ x\ [1.159\ if\ Black]$$

Measurements

Regarding the measurements related to the current study, urea and creatinine were measured by using standard methods with reagents from BioMaghreb Company – Tunisia. Thyroid hormones ELISA kits are a solid phase direct sandwich method. The assay was performed according to the steps described by the manufacturer (SUNLONG, China). Fibroblast growth factor-23 and cystatin C ELISA kits are a solid phase direct sandwich method. The assay was performed according to the steps described by the manufacturer (SUNLONG, China).

Statistical Analysis

Version 18 of the SPSS application was utilized to code and enter the results onto a computer for data analysis. Each data point was grouped by frequency. A p-value of <0.05 was considered significant.

RESULTS & DISCUSSION

Estimated Glomerular Filtration Rate (eGFR)

The results of the current study showed that the percentage of healthy people in the current study was 30 (21.4%), while the number of patients with kidney failure was 93(66.4%), while other stages of kidney disease were reported, the third stage included 7(5%) patients while. The fourth stage included 10(7.1%) patients. The eGFR levels at end stage of kidney failure were 11.52±1.42, as shown in Table (1).

Table 1: Glomerular filtration rate levels in different stages of CKD

Gender / Stages	Mean ± SD	Male	Female	Total
Stage 1 (control)	139.84±9.29 a	17(56.7%)	13(43.3%)	30 (21.4%)
Stage 2	———	———	———	———
Stage 3	35.16±6.51 b	3(42.9%)	4(57.1%)	7(5%)
Stage 4	20.42±3.14 c	4(40.0%)	6(60.0%)	10(7.1%)	
Stage 5	11.52±1.42 d	55(59.1%)	38(40.9%)	93(66.4%)
Total	———	**79(57.04%)**	**61(42.96%)**	**140(100.0%)**

The current study supports the findings of Salih *et al*., [15], who found a significant (p≤0.01) reduce in CKD patients compared to the control group. The decrease in eGFR represents irreversible nephron loss, and this parameter dictates even the early asymptomatic phases of CKD. It reflects the rate at which exogenous chemicals are cleared from the plasma into the urine. Creatinine is the most essential measure of GFR since it is removed through glomerular filtration. eGFR decreases due to tubular excretion [16].

Kidney Function

Table (2) show the levels of urea and creatinine in CKD patients and healthy volunteers, S. urea levels in CKD patients (107.42±8.52), were demonstrated a significant (P≤0.05) elevated in compared to a control (19.35± 2.16). while,

creatinine levels in CKD patients (6.81± 0.55) demonstrated a significant (P≤0.05) elevated in compared to a control (0.84± 0.19).

Table 2: The levels of urea and creatinine

Groups / Parameter	Control (30)	Patients (110)	P-Value
Urea (mg/dl)	19.35± 2.16	107.42±8.52*	0.001
Creatinine (mg/dl)	0.84± 0.19	6.81± 0.55*	0.001

The blood level of urea increased in patients, which is consistent with a study that found that higher BUN levels were related with poorer renal outcomes in those with moderate to severe CKD, regardless of eGFR [17]. This greater level suggested that there was some blockage in excreting urea in kidney failure individuals, in addition to an impairment in the function of the kidneys, which could be due to a reduced eGFR that interfered with urinary excretion [18]. Urea nitrogen levels in the blood are directly related to the kidney's excretory activity. During CKD, the kidneys are unable to eliminate urea, which accumulates in the bloodstream [19]. The inability to excrete urea is caused by injury to the kidney, which results in tubular necrosis and lack of filtering function. Medications may potentially cause kidney injury. Dehydration caused by CKD can also boost urea levels due to the slow rate of excretion of renal [20]. Renal excretion, tubular secretion, and creatinine degradation are reduced in patients, causing creatinine levels to rise. Additionally, meat consumption and protein supplementation cause an elevated in creatinine. Another cause of high creatinine levels is the use of drugs that limit tubular creatinine release and reduce creatinase breakdown in the gut [21].

Thyroid Function

Table (3) show the concentrations of T3, T4 and TSH in CKD patients and healthy volunteers, T3 concentration in the end stage (5.17± 0.14) indicated a significant (P≤0.05) reduced than in other CDK stages and control group (6.34±0.28). T4 concentration in the end stage (7.17±0.14) were significantly lower (P≤0.05) than in other CDK stages and control group (10.44±0.31). Thyroid-stimulating hormone (TSH) concentration in the end stage (2.83±0.12) increased significantly (P≤0.05) compared to other CDK stages and control group (1.52±0.24).

Table 3: The levels of urea and creatinine

Groups / Parameter	Control (30)	Patients (110)	P-Value
T3 (nmol\l)	6.34±0.28	5.17± 0.14*	0.001
T4 (nmol\l)	10.44±0.31	7.17±0.14*	0.001
TSH (µIU\ml)	1.52±0.24	2.83±0.12*	0.001

Chronic kidney disease affects the pituitary-thyroid axis, which is responsible for thyroid hormone regulation and metabolism. Primary hypothyroidism is frequent among CKD patients with declining estimated eGFR. Low T3 syndrome is the most frequent thyroid issue among CKD patients. However, T4 levels are also altered due to poor T4 protein binding [22]. T3 reduction in CKD patients is linked to a number of parameters, including systemic acidosis, endothelium damage indicators, and inflammation. The enzyme 1 5′-deiodinase converts T4 into T3 during inflammation. Some cytokines, including tumor necrosis factor (TNF) and interleukin (IL)-1 [23], suppress the production of this enzyme. Low T3 levels are prevalent in CKD patients because peripheral deiodinase converts T4 to T3. This impact results from metabolic acidosis and protein deficiency, both of which are present in CKD [24]. In response to feedback inhibiting T3 and T4, the pituitary gland releases TSH. People with chronic kidney illness have lower levels of TSH because of reduced renal clearance of TSH, weaker TRH response, and blunted TSH response. Non-thyroidal illness (NTI), which resolves with the resolution of CKD, can also cause this [25]. In CKD patients, thyroid hormone levels decrease in both sexes and all age groups. The impact of clinical hypothyroidism on physical function in patients with CKD are influenced by a variety of factors, such as anomalies in iodine metabolism and autoimmune thyroiditis [26]. Studies on persons with chronic renal disease and subclinical hypothyroidism showed a significant reduction in eGFR rates among those who did not take thyroid hormone. Because thyroid hormone therapy reduces the rate at which eGFR declines in kidney failure patients with subclinical hypothyroidism, it may postpone the onset of end-stage renal disease [27, 28].

Fibroblast Growth Factor 23 (FGF-23) and Cystatin C

Table (4) show the concentrations of fibroblast growth factor 23 (FGF-23) and cystatin C in CKD patients and healthy volunteers, FGF-23 levels in the end stage (184.03±17.31) increased significantly (P≤0.05) as compared to other CDK stages and control group (5.16±0.45). Cystatin C level in CKD patients (17.11±1.94) was demonstrated a significant (P≤0.05) elevated in compared to a control (8.04±0.37).

Table 4: The levels of fibroblast growth factor 23 (FGF-23) and cystatin C

Groups / Parameter	Control (30)	Patients (110)	P-Value
FGF-23 (pg/ml)	5.16±0.45	184.03±17.31*	0.001
Cystatin C (pg/ml)	8.04±0.37	17.11±1.94*	0.001

The current study's findings showed a considerable variation in CKD stages. Conversely, compared to earlier phases of CDK, the FGF-23 level at the end stage shown a significant (P≤0.05) rise. There was a dose-response correlation between FGF23 and the probability of dying or developing end-stage renal disease (ESRD) [29]. 32.5% of the 419 CKD children aged 1 to 16 who were followed for a median of 5.5 years attained the progression end goal, meaning they required dialysis, had a kidney transplant, or had an eGFR drop of more than 50%. This information comes from a recent study. FGF23 was found to be independently linked to an increased risk of reaching the progression end point [30]. Also, Liu *et al*., [31], reported significant negative correlation between FGF23 and eGFR. This investigation found that serum cystatin C levels were considerably higher in the sick group compared to the healthy control group; these findings were consistent with [32-34]. Serum cystatin C has been suggested as a suitable endogenous eGFR measurement. The body produces Cystatin C steadily; it is not impacted by elevated protein catabolism, altered renal function, or changes in diet. Moreover, unlike creatinine, it is not affected by age or muscle mass. Because of its biochemical characteristics, cyclostatin C can freely filter in the renal glomerulus before being metabolized and reabsorbable by the proximal tubule [35, 36]. Consequently, some investigations have discovered that blood cystatin C levels might be considerably impacted by both overt and subclinical thyroid dysfunctions [37, 38].

CONCLUSIONS

It is concluded from the study that CKD patients suffer from hypothyroidism based on hormone concentrations. The study also revealed a negative correlation between FGF-23 and Cystatin C levels with eGFR in CKD patients.

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