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Original Research Article

The Mutual Relationship between Thyroid Hormones, Kidney Function, and Vitamin D_3 Deficiency

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Abstract: Thyroid hormones and renal function known to interact. To understand the role of thyroid hormones, play in the onset of chronic kidney disease (CKD) to management of individuals with both thyroid and renal dysfunction. This connection still causes confusion and debate because some things about it are still unknown. The aims of this work study the correlation between thyroid hormone disruptions and renal function CKD and hypothyroidism patient and their effect in Vitamin D3, parathyroid hormone (PTH) level and calcium level. In this research, there are 60 participants (20-45 years old) with both gender; 40 patients that divided in two group, the first group 20 patient has CKD and 20 patient has hypothyroidism. A control group with 20 healthy participants where included in this study. The blood sample (5ML) drawn from each participant then centrifuged to obtain the serum that used to determine the level of thyroid hormone level (TSH, T3 and T4), PTH, Albumin and vitamin D3. In addition, determined uric acid, blood urea and creatinine. The results show there is significantly increase in the TSH level in hypothyroidism patient and CKD group. While T3 and T4 group decrease significantly in hypothyroidism and CKD patient. The level of creatinine was significantly increase in CKD and hypothyroidism patients also the level of blood urea was significantly increase in CKD patient. In addition, there is no different in the level of uric acid and albumin among these two group. The level of PTH increase significantly, while the level of Ca significantly decrease in CKD patient group and D3 was significantly decrease in both patient group. It is possible to conclude that individuals with chronic kidney disease (CKD) are more likely to experience hypothyroidism; also, hypothyroidism can increase the risk of chronic kidney disease.

Keywords: Thyroid hormones, chronic kidney disease, renal dysfunction, Vitamins D3, calcium and parathyroid hormone.

INTRODUCTION

It is general known that there is a complex relationship between thyroid and renal function. In the twenty first century, chronic kidney disease (CKD) is the one of the leading causes of death and sickness globally [1]. A high burden of comorbidities, including obese, diabetes, hypertension and cardiovascular disease, is linked to chronic kidney disease (CKD) (2). The most common causes of CKD diabetes, hypertension and some genetic disorders but there is some proportion of causes remain unclear [1]. Patient with chronic kidney disease (CKD) are more likely than the general population to have hypothyroidism. This is because thyroid hormones have both direct and indirect effects on the kidney [3]. Thyroid hormones are responsible of regulated cell biology including growth, differentiation and energy generation. The kidney, however, maintains the body's internal balance. Even though they have different targets of action one at the cellular level, the other at the extracellular level [4]. Water and electrolytes in our bodies are impacts by thyroid hormones. The growth and development of the kidneys are facilitate by thyroid hormones, which makes them crucial to kidney function [5].

Thyroid hormones may affect renal function, and kidney failure may exacerbate thyroid disruption, according to certain research findings demonstrated that

thyroid hormones might impact renal function and kidney failure may exacerbate thyroid disruption. Reduces renal function is 1.64 times more common in people with thyroid impairment of any kind than in people with normal thyroid function [6]. Drop in T4 hormone causes reduced glomerular filtration rate, modified tubular reabsorption resulting in reduced water secretion, and reduced blood supply to the kidneys [7]. In contrast, increase T4 hormone may result in polyuria after improvement in tubular re-absorption and glomerular filtration [8]. However, the thyroid hormones metabolism, excretion from our bodies, and specific effects are all facilities by the kidney. Consequently, alterations in thyroid hormone levels are linking to impaired renal function [9].

Chronic kidney disease (CKD) prevalence has been report to range from less than 1% to 13% in the past. As of right now, data from the kidney disease center of international society of nephrology indicated a prevalence of 17 % [10]. Research has shown that acute or chronic renal disease affects the hypothalamus-pituitary-thyroid axis. Hypothyroidism impairs renal function through lowering cardiac output, producing vasoconstriction in the kidneys, and upsetting the renin-angiotensin-aldosterone system (RAAS), which in turn alters renal blood flow (3). The main part of thyroid hormones is in the case of blood-related protein, which may affected in CKD. Patients with CKD have inhibitors that prevent thyroid hormones from attaching to proteins (1).As well as structural modifications such as shortened tubular mass, changed glomerular architecture, and a lower kidney to body weight ratio [11]. Another area of recent attention is how thyroid function is impacts by inflammation in people with chronic kidney disease [9]. Since the kidney is in charge of iodine clearance and the breakdown and excretion of thyroid hormones, it makes sense that renal disease would affect thyroid hormones level. However, dialysis has been linked to a higher risk of thyroid cancer and nodules [12]. However there have been few studies on the connection between CKD and thyroid hormone levels that are within normal ranges. Our goal in this study was to determine the intricate relationship that exists between thyroid dysfunction, thyroid hormones, and chronic kidney disease.

MATERIAL AND METHODS

Study Population

In this study, we recruited 60 participant 40 patient who visited the Yarmouk hospital. This patient divided in two group the first suffering from chronic kidney disease (CKD) n=20.The second group who diagnostic with hypothyroidism n=20. The other 20 participant was healthy control subjects. The age of groups was range from 20-45 years old of both gender. The data for final analysis was collect from all participant in period from Jun 2024 to September 2024.

Study Protocol

Five milliliters of Venous blood that drawn from each subject, patient and control group by venipuncture. This blood put in a gel activator tube than allowed to coagulate for 15 minutes at 40 C. After that centrifuged at 3000 rpm for 10 minutes to separate the serum. This serum used to determine the following:-

1. Thyroid hormones concentration including Thyroid-Stimulating Hormone (TSH), Triiodothyronine Hormone (T3), Thyroxine Hormone (T4). In addition Vitamin D3 and parathyroid hormone (PTH). By using a kit from Bio Merieux – France Company.
2. Blood urea, Uric acid, serum creatinine, calcium and albumin by using A German-made Cobas 6000 analyzer (c501).

Statistical Analysis

Results are expressedas mean ± standard error (M±SE). Data were analyzed by one-way analysis of variance, followed by Fisher's test for multiple comparisons, using Statview version 5.0. Differences were considered significant when $p<0.05$.

RESULTS

In the Figure 1:

Show the level of thyroid hormones in CKD, hypothyroidism and control group. The level of TSH was significantly increase in hypothyroidism patient and CKD patient in compared to control group. In addition, the level of T4 was significantly decrease in hypothyroidism and CKD patient when compared to control and it was lower in hypothyroidism than CKD group. In addition there is significantly decrease in the level of T3 in two patient groups when compared to control group.

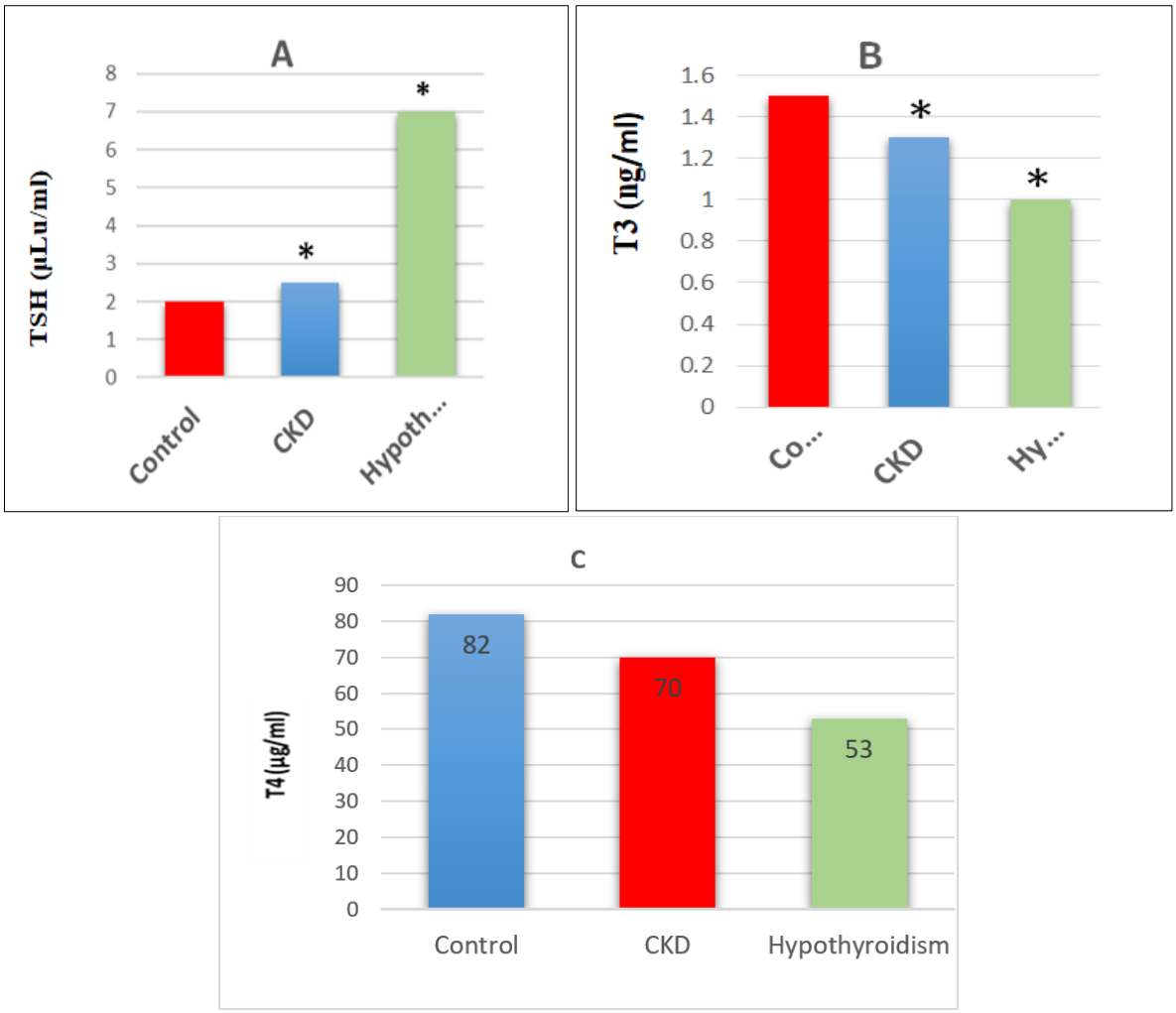

Figure 1: The level of TSH, T3 and T4 in CKD and hypothyroidism in comparison with control group

In figure 2show the alteration of creatinine and blood urea in CKD, hypothyroidism and control group. Serum creatinine level was significantly increase in the CKD and hypothyroidism patients when compared to control with higher significantly increase in CKD patient than hypothyroidism group. While the level of serum urea was significantly higher in CKD in compare with control and hypothyroidism.

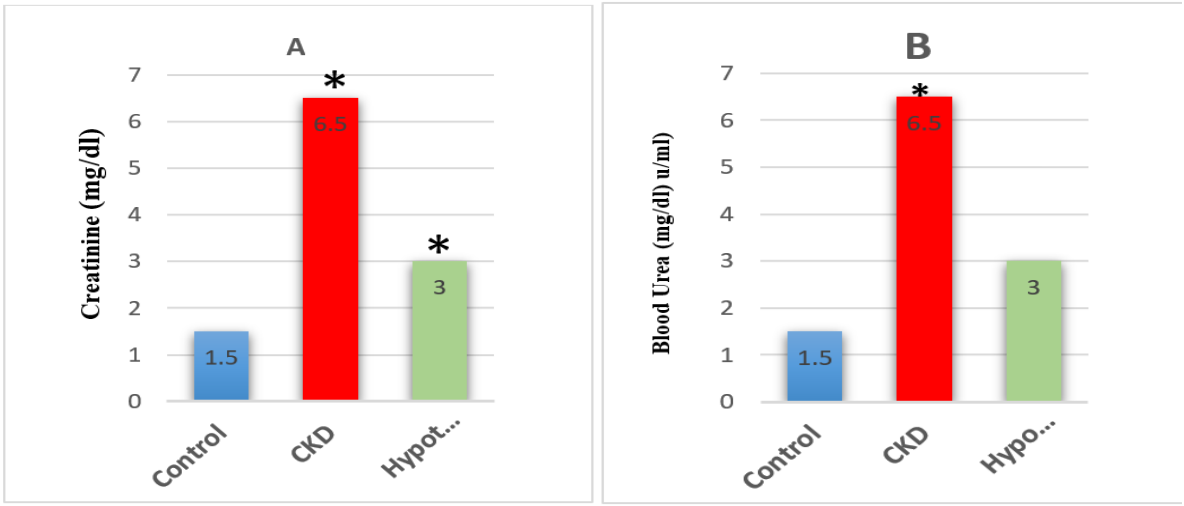

Figure 2: The level of creatinine and blood Urea in CKD and hypothyroidism in comparison with control

In figure 3 show there was no significant different in the uric acid and albumin level in the CKD, hypothyroidism and control group.

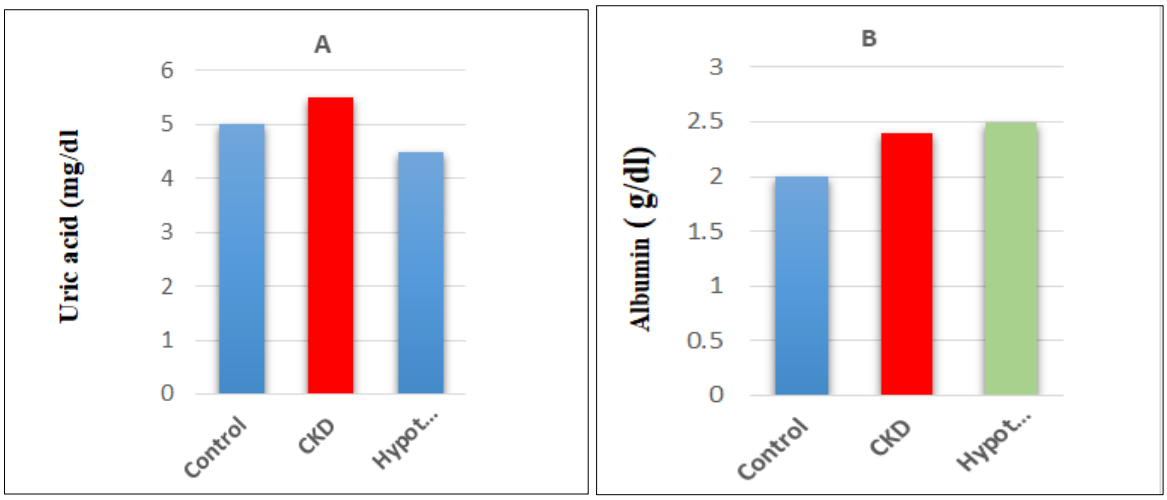

Figure 3: The level of Uric acid and Albumin in CKD and hypothyroidism in comparison with control

In Figure 4:

Show there is a significantly decrease in the level of calcium level in CKD in compere to hypothyroidism and control group. While there is significant increase in the parathyroid hormone in CKD patient when compare to control and hypothyroidism group. While the level of Vitamin D3 level was significantly lower in CKD and hypothyroidism when compare to control.

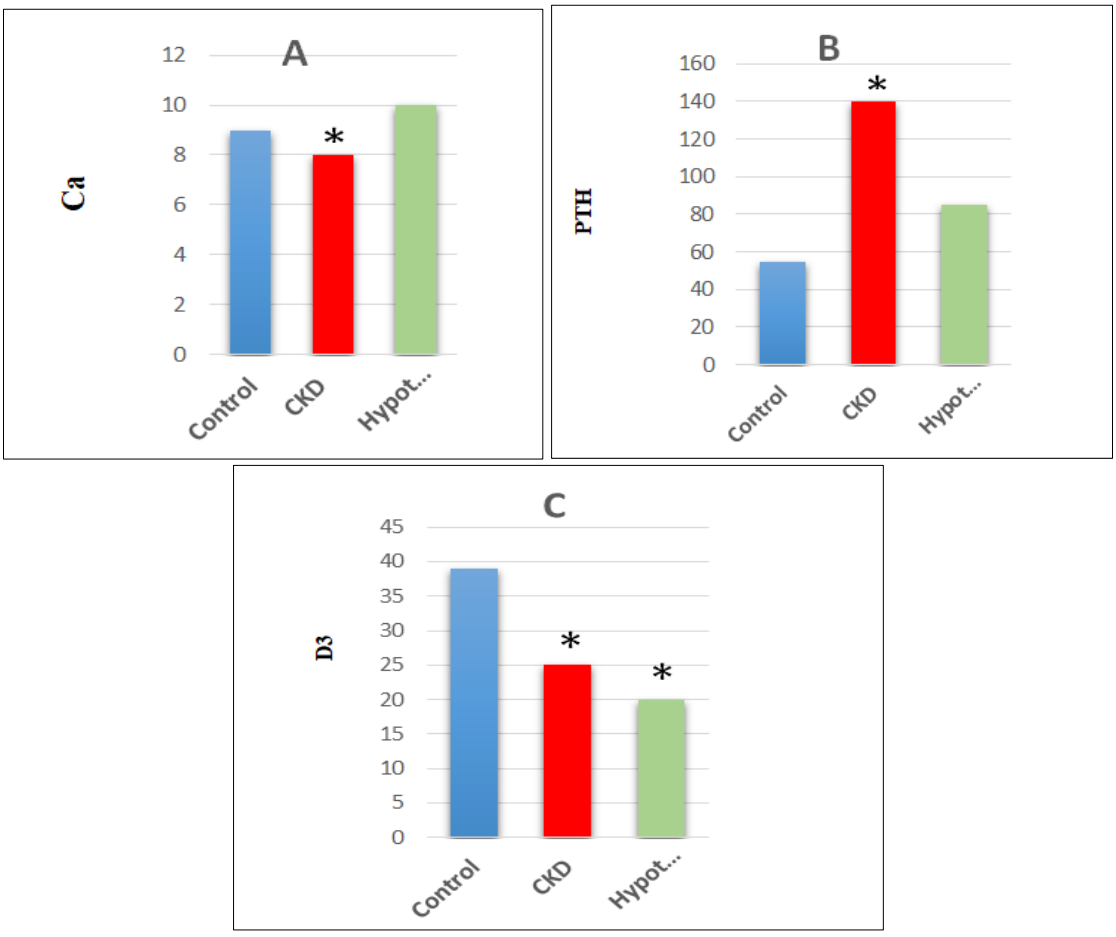

Figure 4: The level of Calcium, PTH and vitamin D3 in CKD and hypothyroidism in comparison with control

DISCUSSION

The connection between kidney function and Thyroid hormone has been known for several years as they have a two-way relationship as they can causes one another. The kidney influencing the production, secretion, metabolism and excretion of thyroid hormones. As well as the growth, development and electrolytic balance of the kidneys are affect by thyroid hormones [13]. Thyroid dysfunction increase the risk of incident chronic kidney disease (CKD) and its development. It is also associated with a higher overall mortality rate among CKD patient [4]. All levels of the hormones that make up the hypothalamic-pituitary-thyroid axis may also be affected, including changes in hormone production, disruption and secretion. Before starting dialysis, individual with CKD are more likely to develop hypothyroidism [10].

Previous studies demonstrated that there is a significantly increase in TSH level in hypothyroidism and CKD group when compared to control group [10-15], which agreed with our result that there is significantly increase in the level of TSH in hypothyroidism and CKD groups when compare to control group. The increase of the TSH it unrelated linked to a decline of renal function as well as thyroid dysfunction has been shown in experiments to impact renal blood flow, electrolyte balance, and nephron shape and function(15).In our finding there was significantly decrease in the level of T3 and T4 in CKD and hypothyroidism group. In more recent study that agreement with our result that demonstrated there is decrease in the levels of T3 and T4 [16]. Thyroxine (T4), the main hormone secreted by the thyroid gland, which mostly transformed to tri-iodothyronine (T3), which is more active. In the kidney deiodinases T4 locally, resulting in the generation of T3 by isoform D1 of the enzyme T4- 5′-deiodinase leads to generation of the T3 hormones. In CKD there was decrease in the remove the inflammatory cytokines that play role in decrease in T4-5′-deiodinase this causes decrease in peripheral conversion of T4 to T3 this is again lead to low T3 levels [10]. Among the impacts of the hypothyroidism are the metabolic effects. The physiology of the kidney, including blood vessel resistance, renal salt management and renal blood flow is known to affects by hypothyroidism [17].

Many investigation have shown that the hypothyroidism causes highly serum creatinine which similar to our finding [17, 18], this as a result of decrease blood flow and tubular function that caused by hypothyroidism in tissue. The production of creatinine from its precursors is little impacted by thyroid [18]. When rats received pharmacologically induced hypothyroidism, their kidney size and creatinine clearance were decreased, which in turn decreased their glomerular filtration rate (GFR). We may conclude from the data that alterations in renal excretion are the cause of the elevated creatinine levels in the hypothyroidism and CKD groups [19]. According to our research, blood urea, albumin, and uric acid levels were all normal in hypothyroidism patients, indicating that there is not any acute kidney damage in these individuals. Study conduct 40 France participant demonstrated that there is significantly increase in blood urea in-patient with CKD this finding agreement with our finding [20].

In current study there is significantly decrease in the level of calcium concentration in CKD patient when compare hypothyroidism and control group this finding confirms earlier studies' that demonstrated the low level of calcium in CKD patient [21]. Also in our study, there is significantly decrease in vitamin D3 level in CKD patient and this finding agreement with more recent study that show there is decrease in the level of D3 in-patient with CKD [22]. In healthy kidney the vitamin D3 that absorb from food or from sun light can be converted to active form that help in absorbed the calcium. However, the kidneys' capacity to produce active vitamin D is diminished in chronic kidney disease this causes decrease in the calcium level in blood [23]. It is commonly known that when chronic kidney disease progress, intestinal calcium absorption increases and depends more on the positive gradient due to the possibility of calcium absorption and loss throughout the digestive system. The shortage of calcium can induce hyperparathyroidism and severe bone loss. The decrease in calcium level causes the parathyroid gland to secreted PTH, which increases calcium reabsorption in the collecting duct, distal convoluted tube, and Henley's ascending loop (24). Additionally, the PTH causes the kidneys to secrete more vitamin D3, which promotes the intestinal absorption of calcium [25]. In this study there is no significantly different in the level of calcium in hypothyroidism and control group a study this finding was agreed with Borzuei [26].

In current study the level of PTH was a significantly increase in the CKD patient than the hypothyroidism and control group. The disruption of activation D3 that accrue in the renal due to chronic kidney disease can causes hypocalcemia and hyperphosphatemia resulting in an increase secretion of parathyroid hormone by parathyroid cellularity and as well as secondary hyperparathyroidism [27]. Our results showed that only vita D3 levels was significantly decreased while PTH and Ca levels didn’t change in the hypothyroidism compared to control. There are two possible explanations for the decreased vitamin D3 levels in hypothyroidism, the first Malabsorption of vitamin D from the gastrointestinal tract; second inadequate body activation of vitamin D.Most notably, steroid hormone receptors are bound by thyroid hormone and vitamin D [28].

It is known that certain investigators have looked on the incidence of vitamin D insufficiency within the Iraqi populace. However, our study was one of the few that looked at the relationship between PTH,

calcium, and vitamin D levels and hypothyroidism in Iraq, particularly in Baghdad. Thus, the purpose of this study was to compare the levels of vitamin D3, calcium, and PTH in CKD, hypothyroidism patients to those in healthy controls who did not experience any thyroid disease symptoms.

CONCLUSION

CKD patents have an elevated risk of hypothyroidism while hypothyroidism patents have an increased chance of CKD.We conclude that our data pointed to the possibility that thyroid hormone levels are a significantly altered by CKD. Furthermore, vitamin D3 levels decrease in people with CKD and hypothyroidism. This could be due to malabsorption of the vitamin from the GUT or a failure on the part of the body to activate it. As well as increase level of PTH in CKD patient can causes reduce in active vitamin D3 and thus lead to reduce absorption of calcium by kidney. More research evaluating the clinical significance of thyroid hormone status in CKD patients would improve our knowledge on the subject.

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