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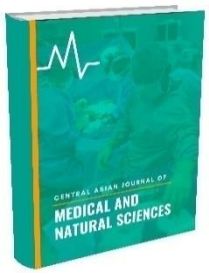

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The Interplay of Thyroid Hormones, Body Mass Index, and Kidney Function in Wasit City: Implications for Metabolic Health

1. **Aseel Shakir Ghlaim Al_Jaree**
2. **Hussein ghalib salman, Raghad Qahtan Mahdi**
3. **Jumana Ali Hassan**
4. **enas abaas hasaan**
5. **Faws Kareem Tohma**

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[1] Ministry Of Health –Wasit , Iraq
[2] College of Biotechnology, Alqasim Qreen University – Babylon, Iraq
[3] College of Physics, Al-Mustansiriyah University - Bagdad, Iraq
[4] Alkut- Private Boy Secondary School - Wasit , Iraq
[5] college of science, biology department, wasit university - Wasit , Iraq

Abstract: The research discusses the challenges in assessing obesity in patients with Chronic Kidney Disease (CKD) and the limitations of using Body Mass Index (BMI) for this purpose. It also touches on the potential connection between BMI, particularly underweight, and kidney disease , use of urea and creatinine concentrations to evaluate renal function and mentions the common clinical presentations of kidney disease. Lastly, it notes the impact of CKD on thyroid hormone levels. To assess thyroid hormones (FT3, FT4 and TSH) in chronic renal failure (CRF) patients it included 50 patients, 29 were males and 21 were females and their age range from 20 to 60 years. The patient was diagnosed as having renal failure for both sex based on the history and clinical examination. The control groups were 30; they were collected from medical staff and relatives who were free from signs and symptoms of renal disease, lipid disorders, and thyroid hormones disorders. 20 were males and 10 were females, and their ages range from22 to 66 years. BMI has a positive significant correlation with gender , and it has a negative significant relationship with T4.TSH showed a significant negative correlation with T3 and T4 and a significant positive relationship with kidney failure Serum urea and creatinine concentrations in chronic renal failure (CRF) patients were found to be significantly high compared with control group (P<0.001).Serum FT3, FT4

and TSH concentrations in CRF patients were found to be no significantly lower compared with control group.

Key words: body mass index, Thyroid gland, kidney function, glomerular filtration.

The thyroid gland produces and releases triiodothyronine (T3) and thyroxine (T4), the only iodine-containing hormones in vertebrates (1). T3 is the biologically active thyroid hormone, essential for tissue growth, development, and normal function (2). Thyroid hormones regulate the basal metabolic rate of cells, including hepatocytes, and modulate liver function. Normal circulating levels of thyroid hormone are required for normal liver circulation and bilirubin metabolism (3). Thyroid dysfunction can impair liver function and vice versa. Thyroid hormones are crucial for kidney development and physiology, affecting the cardiovascular system by influencing renal blood flow and metabolism. (4) Kidney disease status can affect thyroid hormones, as kidneys are responsible for thyroid hormone metabolism and excretion A persistent decline in kidney function known as chronic kidney disease (CKD) causes abnormally high levels of metabolic lesions, mineral bone abnormalities, dyslipidemia, and dysfunction. Thyroid hormones are processed, destroyed, and eliminated by the kidney, which can be impacted by chronic kidney disease (CKD). Different forms of thyroid dysfunction can appear, such as thyroid hypertrophy, a lack of or an excess of thyroid hormone, or subtle or overt disorders. According to epidemiological research, CKD patients had much greater rates of thyroid function abnormalities than the general population, especially hypothyroidism. Reduced glomerular filtration, hyponatremia, and alterations in water disposal can all be results of thyroid dysfunction, which can also produce major changes in glomerulus tubes, electrolyte hemostasis, and water yield. Thyroid function significantly changes as a result of renal illness.(5,6)

Thyroid hormones directly affect the kidney, influencing renal growth, development, GFR, transport systems, and homeostasis(7). Hypothyroidism and hyperthyroidism are accompanied by significant alterations in renal function. Kidney is involved in TH physiology, and treatments like dialysis and kidney transplantation can affect circulating TH levels(8,9). Recent investigations have focused on kidney and thyroid pathologies, with a special emphasis on thyroid function tests and cardiovascular morbidity(10). Thyroid hormone contributes to renal development and physiology, and its effects are mediated by the cardiovascular system, renin-angiotensin system, and renal blood flow(11).

Calcium balance is a complex concept that involves calculating whole-body calcium retention or deficit by subtracting total body calcium losses from total calcium inputs(12). It is particularly challenging in chronic kidney disease (CKD) patients due to the physiological processes controlling calcium balance. Calcium balance studies require subjects to be in steady state, with a tightly controlled and stable dietary intake starting at least one week before measurements.(13) The fecal

calcium:PEG excretion ratio can be used to determine when subjects have equilibrated to a new controlled dietary calcium intake level.(14) This is particularly important for patients on dialysis, as dialysis disrupts calcium balance and may promote fluxes in soft tissue and bone mineral content.(15) Diets must provide consistent amounts of calcium and other nutrients, and registered dietitians are often required for sophisticated diet design Calcium balance studies require controlled diets with consistent amounts of calcium and other nutrients like phosphorus, sodium, and magnesium. Nutrient databases are used, but errors can occur.(16.17) Registered dietitians design sophisticated diets, ensuring duplicate meals are prepared and analyzed. Subjects must eat all study meals, and uneaten food should be weighed back and accounted for. Calcium intake from supplements and medications must also be stable and controlled . (14) Hyperkalemia is rare when GFR is above 60ml/min/1.73m2 and increases with lower GFR. In individuals with preserved GFR, hyperkalemia is less prevalent and associated with pseudohyperkalemia, cell shift increases, and drug-induced potassium excretion impairment. Homeostasis occurs due to adaptive potassium secretion in remaining nephrons, similar to normal individuals. Chronic potassium loading increases renal potassium excretion, leading to structural changes and increased sodium reabsorption.(20,21) Dietary potassium bioavailability is influenced by other nutrients, including vitamins, antioxidants, carbohydrates, and fiber. High-potassium fruits and vegetables promote potassium entry and excretion through dietary fiber.(22) Salt-substitutes, food additives, and preservatives are hidden sources of potassium, contributing to daily intake. Potassium chloride (KCl) is being used in salt substitution due to public health campaigns, but safety in advanced stages of CKD requires further investigation(23)

MATERIALS & METHODS

Control Groups:

A Total number of 50 patients of chronic kidney disease and 50 controls were selected for the present study from AL KRAMMA hospital & Al Zahraa hospital

Patients:

A total of 50 chronic kidney patients admitted to Al Zahraa and Al kramma hospital and The patient was diagnosed as renal failure for both sexes based on the history, clinical

examination and taking thyroid test and electrolyte test and kidney function test. Subject was fasting 12-14 hr. at the time of blood withdrawal. Their age range between 18-60 years where

included in this study throughout the period between January –march 2023.

Full history and general physical examination were obtained from the patients file.

Sample Collection:

Each patient who was fasting had five milliliters of venous blood taken from them. Using a tourniquet and slowly aspirating a sample of venous blood with a syringe to prevent hemolysis 15 cm above the cubital fossa, applicable. The samples that had been severely hemolyzed were all disregarded in favor of other samples. After placing the samples into clean, disposable tubes, they were centrifuged for 20 minutes at 5000 revolutions per minute after being left at room temperature for 30 minutes to allow for clot formation. The serum was divided into two parts, the first of which was kept in an Eppendrof tube meant to assess liver function and maintained at a temperature between 2 and 8 degrees Celsius. The second 1ml of serum was kept in the Eppendr of tube. Using Cobbase e411

and 111, the storage serum was used to determine the results of all biochemical analyses employed in the study.

Table (1): Hormone levels changes in chronic kidney patients and control groups.

Biochemical parameters	Control Mean N= 30	Patients Mean N= 50	pv	c.s
body mass index	23.83± 5.54	27.91± 5.44	P< 0.001	Hs
Urea	165.24 ± 34.66	32.16 ± 5.74	P< 0.001	Hs
Creatinine	7.95 ± 2.44	0.64 ± 0.14	P< 0.001	Hs
FT3	2.36 ± 0.72	2.47 ± 1.13	P> 0.05	Ns
FT4	0.96 ± 0.22	1.02 ± 0.21	P> 0.05	Ns
TSH	2.49 ± 1.82	2.64 ± 2.73	P> 0.05	Ns

The best measure of obesity in patients with CKD is not known, and BMI is commonly used to assess obesity. However, it does not differentiate between elevated BMI due to muscle mass and adipose tissues. Studies suggest that increased BMI increases the risk for CKD and ESRD, but ethnicity and sex may modify these associations. Some studies have indicated that patients within the lowest BMI category (underweight) have an increased risk of kidney disease. Malnutrition is a feature of uremia, and a reverse epidemiology has been described.(23) Because the classifications of underweight, overweight, and obesity vary across studies, findings from various studies regarding the association between underweight BMI and kidney disease may be affected, and thus more data is required.(24) The results show significant (P< 0.001) increase in urea and creatinine concentration in chronic renal failure patients when compared with those of the control group. (25,26) Most doctors use the plasma concentrations of the waste substances of creatinine and urea to determine renal function. These measures are adequate to determine whether a patient is suffering from kidney disease. Patients with kidney disease may have a variety of different clinical presentations.(27) Some have symptoms that are directly referable to the kidney (gross hematuria, flank pain) or to extra renal symptoms (edema, hypertension, signs of uremia).(28) Many patients, however, are asymptomatic and are noted on routine examination to have an elevated serum creatinine concentration or an abnormal urinalysis. These tests can help measure how well the kidneys are filtering the blood.(29,30) As the kidney function gets worse, the amount of nitrogen (shown by the BUN test) and creatinine in the blood increases. The level of creatinine in the blood is used to find out the glomerular filtration rate (GFR). (31)The GFR is used to show how much kidney function the patient still have. The GFR is also used to find out the stage of the kidney disease and to guide decisions about treatmentFree and total T3 and T4 concentrations are usually normal or low in patients with CKD [32]. The reduction in T3 levels (low T3 syndrome) is The most common change in the thyroid gland is observed in these patients.

This decrease in T3 concentrations has been linked to a decrease in peripheral synthesis of T3 from T4. Chronic metabolic acidosis associated with chronic kidney disease may contribute to this effect. Although free and total T4 concentrations may be normal or slightly low, sometimes they may be elevated due to the effect of heparin used for anticoagulation during hemodialysis (HD), which prevents the binding of T4 to its bound proteins (33,34).

Serum TSH concentrations are usually normal or elevated in chronic kidney disease (CKD), but its response to its releasing hormone (TRH) is generally low [35]. These findings suggest the presence of intrathyroidal and pituitary disturbances associated with uremia [36]. Also, both TSH circadian rhythms as TSH glycosylation are altered in CKD(37). The latter may compromise TSH bioactivity. From a clinical practical perspective, in patients with kidney disease it is usually sufficient the use of thyroid function tests commonly used in the clinic. However, to avoid mistakes in diagnosis, it is important to know the effects of hypothyroidism and hypothyroidism on renal function, as well as the changes in thyroid function tests induced by acute and chronic kidney diseases. Drugs used in the treatment of thyroid and kidney diseases may induce changes in renal and thyroid physiology, respectively(38,39). A relationship between T3 levels and mortality has been proven in uremic patients; however, the relationship between TSH and survival, well established in other population groups, has not been reported in patients with different degrees of kidney insufficiency. Further investigation in this field will provide new insights in our understanding of the biological significance of thyroid hormone changes in patients with kidney disease.(40)

Conclusion

The study found a positive link between obesity and gender in patients with Chronic Kidney Disease (CKD). It also revealed that as BMI increased, T4 levels decreased, indicating an influence of obesity on thyroid hormones. There was a significant correlation between TSH and T3 and T4, indicating disruptions in thyroid hormone regulation. However, no significant differences in thyroid hormone levels were found between CKD patients and the control group. Further research is needed to understand these relationships.

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