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THYROID DISORDER ASPECT IN SECTION OF PATIENTS WITH CHRONIC KIDNEY DISEASE BEFORE AND AFTER HEMODIALYSIS

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Abstract : It is well established that there is interaction between thyroid and kidney. Many studies reviewed the interaction between thyroids disorder and renal statues while the opposite situation, the interaction between renal diseasesand thyroid hormones, need more study to understand it. The aim of this research were to compare the biochemical variables such as blood urea and serum creatinine in patients with chronic kidney disease (CKD) between before and after hemodialysis and their affect on thyroid hormones (T3, T4), calsitonin (CT), and thyroid stimulation hormone (TSH).Blood samples were collected from 25 patients with renal failure on hemodialysis, who visited Yarmok hospital in Baghdad/ Iraq, after and before dialysis and 25 healthy as control. Their ages were between 20 to 80 years old. Blood urea,serum creatinine, TSH, and CT levels were significant higher in the patients before dialysis which went back down after dialysis but this levels remained significant higher than in control while T3 and T4 levels were significant lower in patients group whether before or after daiylsis compared to control groups. T3 and T4 have negative correlation with blood urea but not with serum creatinine while TSH and CT have significant positive correlation with both blood urea and serum creatinine. It could be concluded that the renal diseases could be caused thyroid disorders and may be also parathyroid disorder due to the closed interaction between CT and parathyroid hormone (PTH) which need more works to prove it.

Key words : Blood urea, serum creatinine, T4, T3, TSH

INTRODUCTION

The definition and classification of chronic kidney disease (CKD) has evolved over time, but now, the international guidelines determine this condition as a decrease in renal function due to eitherdegrease glomerular filtration rate (GFR) less than 60 ml / min per 1 x 73 m^2, Kidney damage, or both, for at least 3 months (Webster A C *et al*, 2017) CKD is usually an irreversible progressive condition and is the 8th leading cause of death (Mohamedali M *et al*, 2014). It affects more than 1500/ million people in high prevalence countries. Nearly two-thirds of CKD patients receive haemo dialysis, one quarter have kidney transplants, and one tenth receive peritoneal dialysis (Abbasi M A *et al*, 2010). CKD have many Risk factors include hypertension, hyperlipidemia, diabetes, and thyroid disorders (Mohamedali M *et al*, 2014).

The interaction between the functions of kidney and thyroid is known for many years (Kaptein E M, 1986). Physiology and development of kidney affect by thyroid dysfunction (Braunlich H *et al*, 1984; Vargas F *et al*, 2006 and Kumar J *et al*, 2009), whereas kidney disease can lead to thyroid disorder (Mori T and Cowley A W, 2004 and Kaynar K *et al*, 2007). Thyroid and kidney disorders may co-exist with common triggers. Furthermore, treatment of on disease could be affecting other organs (Yu F *et al*, 2007 and Wang L C *et al*, 2003).

In CKD patients, commonly observed the functional disorder of thyroid (Rhee C M *et al*, 2015). Hypothyroidism, which is usually determined by biochemical tests included increased TSH in conjunction with a reduced (overt) or normal thyroxine (subclinical hypothyroidism) (Ladenson P W 2013), is more prevalent in patients with impaired renal function compared to others have normal renal function (Lo J C *et al*, 2005). Furthermore,thyroid dysfunction is often observed in CKD patient due to changes in thyroid hormons synthesis, metabolism and regulation (Rhee C M *et al*, 2015; Ladenson P W 2013; Lo J C *et al*, 2005 and Kaptein E M, 1996). These need more study to understand it, so the aim of this research were to compare the biochemical variables such as urea and creatinine in patients with chronic kidney disease (CKD) between before and after

hemodialysis and their affect on thyroid hormones (T3, T4), calsitonin (CT), and thyroid stimulation hormone (TSH).

MATERIALS AND METHODS

In this study, 25 patients visited the Yarmok hospital in Iraq, who were previously diagnosed with chronic kidney disease onheamodialysis, as well as 25 healthy students and employees were randomly selected from the Department of Biology/ College of Science/ Mustansiriyah University/ Baghdad/Iraq as control volunteer subjects, the age of groups was ranged from 20 to 80 years of both gander were included.

From patient (immediately before and after dialysis) and control subjects, 5 ml of venous blood was collected from antecubital vein by disposable syringe in a sterilized test tube. The blood samples were centrifuged for 15 min at 3000 rpm. The serums were used to estimate the level of:

1. T4 and T3 by a competitive enzyme liked assay method using a kit supplied by Human T4 and T3, Germany.
2. TSH bya direct enzyme liked assay method using a kit supplied by Human TSH, Germany.
3. CT byanindirect enzyme liked assay method using a kit supplied by Human CT, Germany.
4. Blood urea and serum creatinine using C4000 from ABBOT, USA

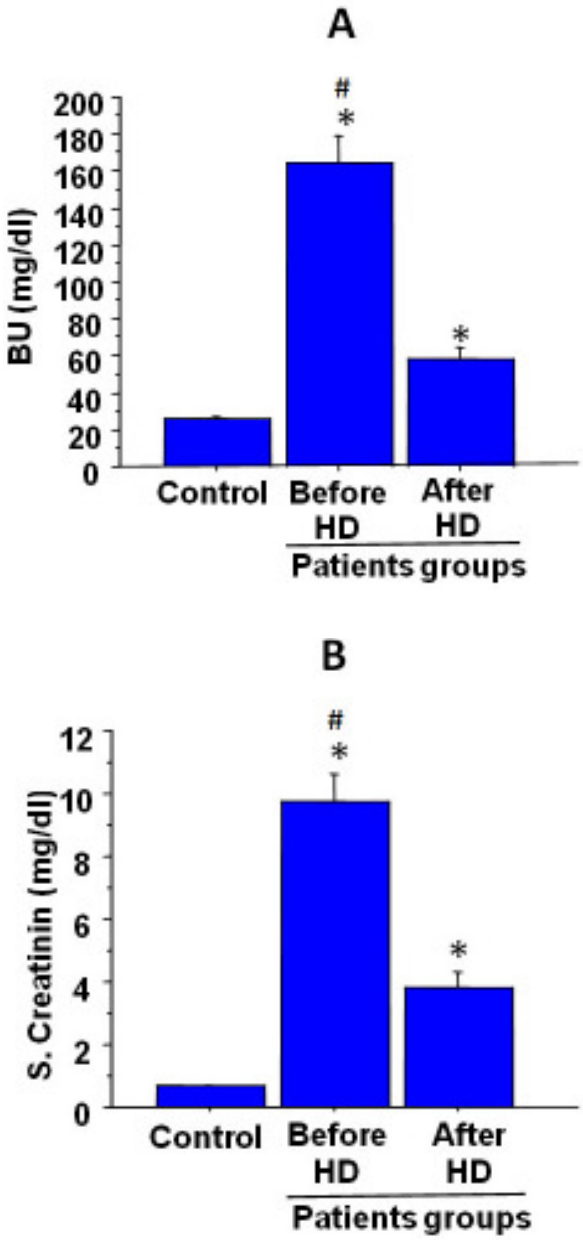
Results are expressed as mean ± standard error (M±SE). Data were analyzed by one-way analysis of variance (ANOVA) followed by Fisher's test for multiple comparisons, using Statview version 5.0. Differences were considered significant when $p<0.05$. Regression analysis was performed by analysis of covariance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

RESULTS AND DISCUSSION

Fig. 1 shows significant higher blood urea and serum creatinine levels in the patient groups compared to control. These levels recorded its highest values in patient group before hemodialysis (HD) and go back down after hemodialysis, but still high compared to control.

T3 and T4 levels are significant lower while TSH and CT levels are significant higher in patients group whether before or after hemodailysis compared to control group (figure-2).

Essential the same differences in blood urea and serum creatinine levels were observed in TSH and CT levels, These levels recorded its highest values in patient group before hemodialysis (HD) and go back down after hemodialysis, but still higher compared to control (figure-2C&D).

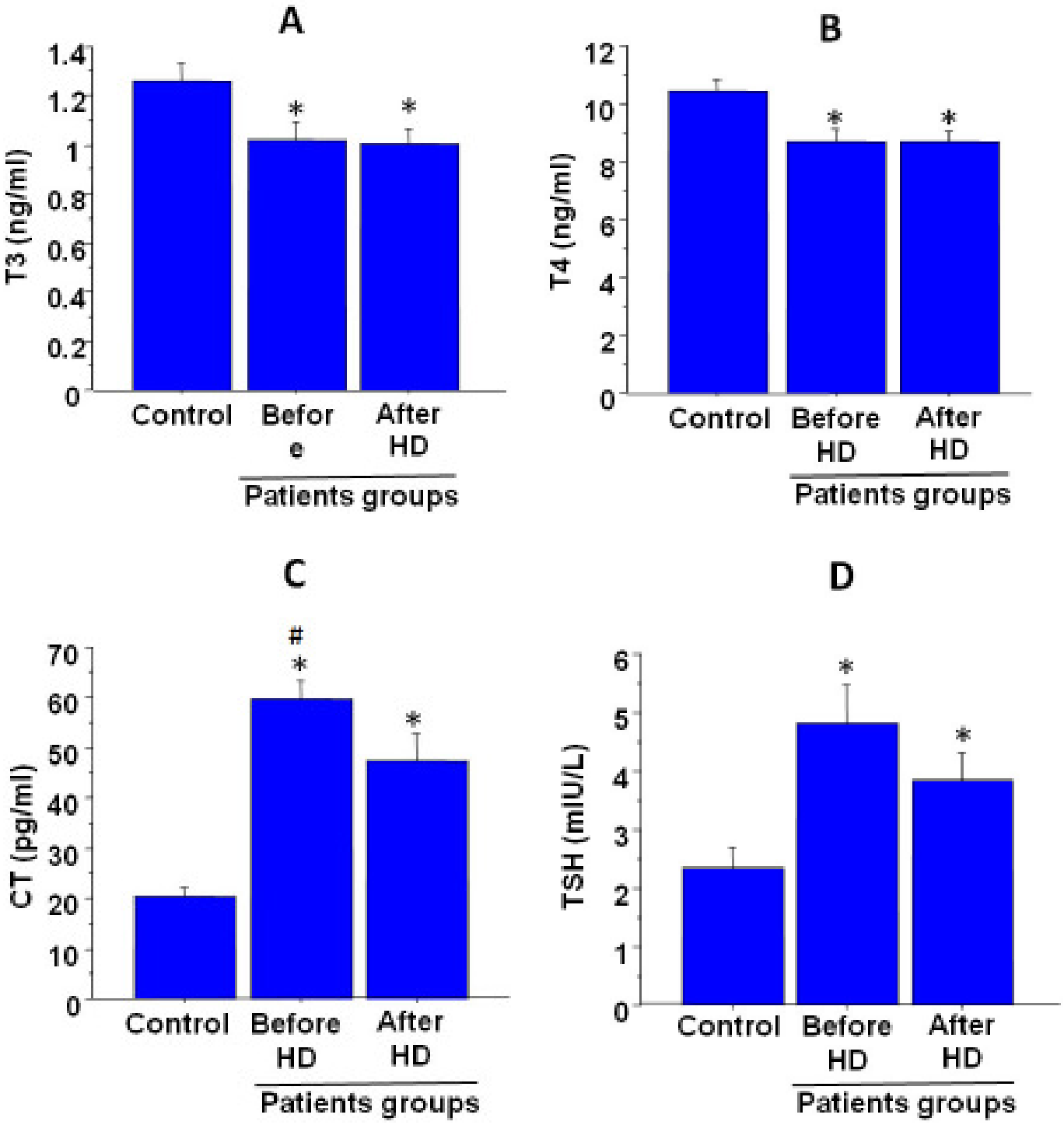


* Significant differences in patients groups vs. control, # significant differences in patient before hemodialysis vs. after hemodialysis

Figure 1 : Blood urea (A) and serum creatinine (B) levels in serum of control, before, and after hemodialysis groups.

At atime when serum creatinine hasn't any correlation whether with T3 (figure-3B) or T4 (figure-3D), Blood urea hasnegative correlations, significantly with T3 (R^2=0.0032, figure-3A) and non-significantly with T4 (R^2=0.078, figure-3C) while blood urea and serum creatinine have significant positive correlations with TSH (R^2=0.073 and 0.058, respectively, figure-3E&F), and CT(R^2=0.141 and 0.188, respectively, figure-3G&H),

The function of kidney is usually estimated using s. creatinin and blood urea concentrations(Rehberg P B,



* Significant differences in patients groups vs. control, # significant differences in patient before hemodialysis vs. after hemodialysis

Figure 2 : T3 (A), T4 (B), CT (C), and TSH (D) levels in serum of control, before, and after hemodialysis groups

1926).S. creatinine is a chemical waste, by-product of normal muscle function, in the blood that passes through the kidneys to be filtered and eliminated in the urine(Colls P C, 1896). It is filtered freely but not metabolized or reabsorbed (Stevens L A *et al*, 2006). The fact that small changes in S.Creatinine translate significant changes in kidney function has led to the consolidation ofs. creatinine determinations in all clinical laboratories.

B. urea is the main nitrogen waste product generated from protein breakdown.It is removed from the body almost exclusively by the kidneys in the urine, measuring its concentration, first in the urine and then in the blood, it has been clinically applied in evaluating renal function for more than 150 years. The highest levels occur

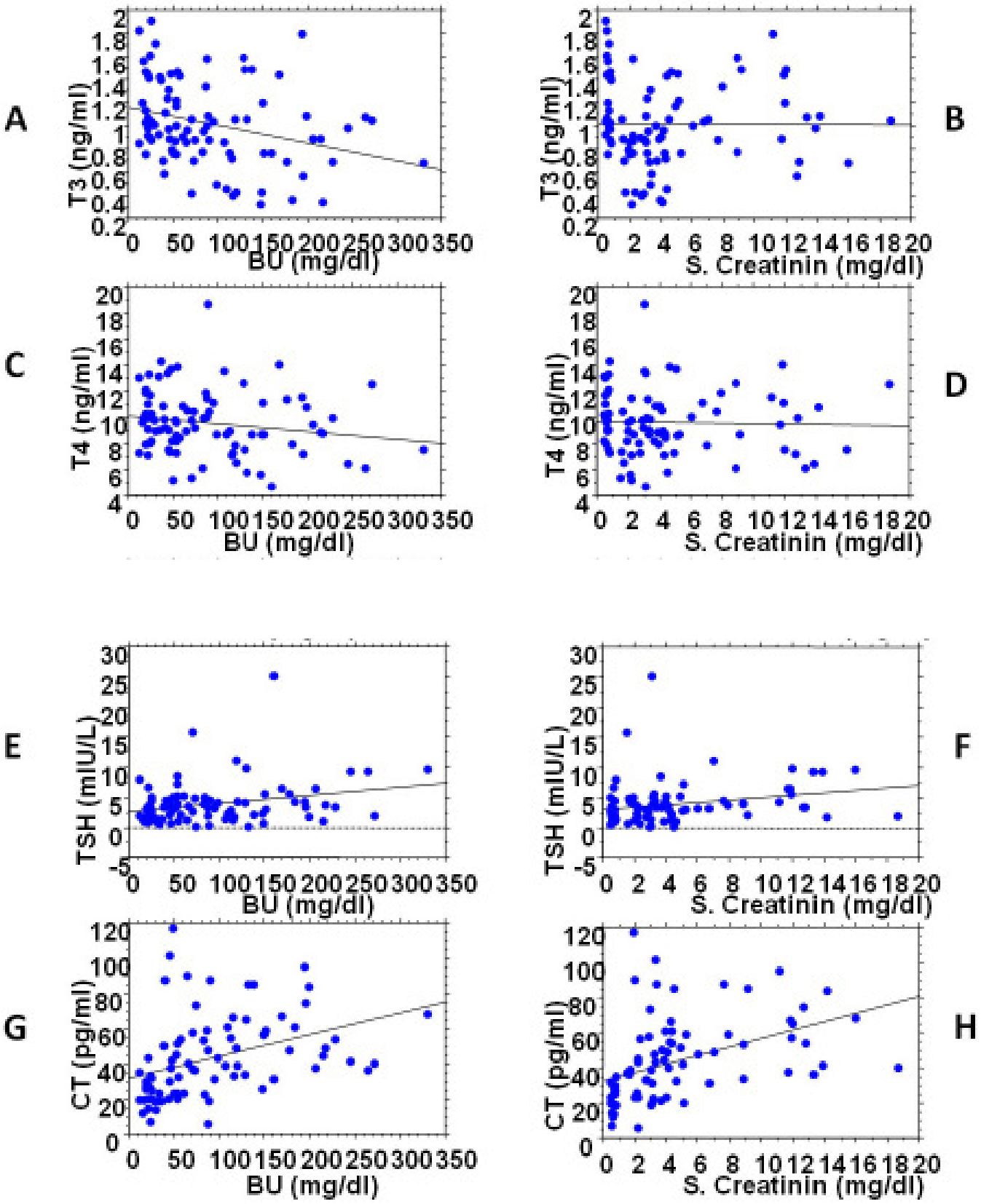


Figure 3 : Correlation results between the biochemical and hormonal levels. Left panel: Blood urea correlations with T3 (A), T4 (C), TSH (E), and CT (G); right panel: serum creatinine correlations with T3 (B), T4 (D), TSH (F), and CT (H).

significantly in the context of reducing urinary removal due to CKD and the significant reduction associated with glomerular filtration rate (GFR). B. urea is less valuable than S. creatinine because the rate of urea production is unstable and increases with tissue breakdown or a rich protein diet such as muscle trauma, steroids or bleeding. On the other hand, a low-protein diet or liver failure can reduce urea without affecting the GFR (Lopez-Giacoman S and Madero M, 2015).In hemodialysis, excess water and wastes are removed by using a dialyzer, an external filter contains a semipermeable membrane. The basic principle of dialysis is the diffusion or movementof dissolved particles across a semipermeable membrane down the concentration gradient from the circulation to the dialysate (Vadakedath S and Kandi V, 2017).these evidences can explain the elevation in the levels of S.craetinine and B. urea in patient group before hemodialysis which go down after dialysis in our results.

Not surprisingly, impaired kidney function leads to thyroid dysfunction since the kidney plays an important role in the metabolism, degradation and secretion of many thyroid hormones (Schultheiss U T *et al*, 2017 and Alsaran K *et al*, 2011). Alsaran et al suggested that the anomalies in thyroid function tests often occur in uremia as a result to changes in production, distribution, and excretion of several thyroid hormones which may be including all levels of the hypothalamic-pituitary-thyroid axis (Alsaran K *et al*, 2011).

Primarily through glomerular filtration, the kidney usually contributes to the removal of iodide. Thus, iodide secretion in advanced renal failure is diminished, leading sequentially to the high concentration of plasma inorganic iodide and an initial increase in thyroid absorption of iodide.The significant increase in the iodide basin within the thyroid gland leads to reduced radio-iodide absorption of thyroid in patients with uremia(Ramirez G *et al*, 1973) which can mask the production of thyroid hormones (the Wolff-Chaikoff effect)(Kaptein E M, 1996) andmay worsen protein malnutrition (Lim V S, 2001). Zoccali *et al* reported that the low levels of serum thyroid hormones are frequently recorded in inflammatory diseases, and patients with CKD since thyroid hormones are severely suppressed in CKD during inflammatory processes (Alsaran K *et al*, 2011; Zoccali C *et al*, 2005). The low levels of T3 and T4 increase TSH levels from the anterior pituitary by negative feedback mechanism (Pirahanchi Y and Jialal I, 2018).

Since kidneys are the primary site of CT metabolism (Kanis J A *et al*, 1982 and Simmons R E *et al*, 1988), it expected with reduced the metabolism of CT in CKD, CT level can be increased (Messa P *et al*, 1995; Schneider R *et al*, 1977).

All these evidences could explain the reducingvalue of T3 and T4, and elevating value of TSH and Ct in patient groups with CKD compared to controlabserved in pour results.

Rodrigues et al reported that the changes in thyroid hormones influx and efflux in erythrocytesof uremic patients on HD could act as a compensatory mechanism that normalized thyroid hormones levels in order to maintain the euthyroid state (Rodrigues M C *et al*, 2004) and also lower morbidity and mortality (Wiederkehr M R *et al*, 2004) which could explain the reducing TSH and CT levels immediately after hemodailysis were found in our results. These changes could normalize the levels of T3 and T4 later after hemodialysis.

As conclusion, CKD results to abnormalities in thyroid hormones (T3, T4, CT, and TSH), causes thyroid disorders and may be also parathyroid disorder due to the closed interaction between CT and parathyroid hormone (PTH) which need more works to prove it. These levels could be normalizing after hemodialysis to lower morbidity and mortality.

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