Thyroid Dysfunction of Chronic Kidney Disease Patients at Nephrology & Urology Minia University Hospital

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Article History: Received: 02.06.2023 **Revised:** 05.07.2023 **Accepted:** 08.07.2023

Abstract

Background: Chronic kidney disease (CKD) has a major burden on worldwide health. CKD patients commonly manifested with a disorder of the thyroid hormones; though, the relationship is unclearly identified. ***Objective:*** assessment of the thyroid dysfunction among pre- dialysis CKD patients at Minia University Hospital. **Methods:** We analyzed data from the outpatient clinic of Nephrology & Urology at Minia University Hospital. 180 patients aged ≥ 18 years who had CKD at different stages except end- stage renal disease were included in this study and assessed for their renal and thyroid function. **Results:** There were significant differences in free thyroxine levels (FT3, FT4) and thyroid-stimulating hormone (TSH) among different stages of CKD (p=0.032, 0.037, 0.007 respectively). The percentage of stage IV CKD patients showed significant increase from (26.2%) euthyroidism to (54.2%) subclinical hypothyroidism (SCH) to reach (60%) overt hypothyroidism (p<0.004).There was a significant positive correlation between FT3 and FT4 with e GFR (P-value <0.0001, 0.003 respectively).While a significant negative correlation of TSH with eGFR (P-value <0.0001).

Conclusion: that thyroid dysfunctions especially SCH and overt hypothyroidism were closely associated with pre-dialysis CKD patients.

Keywords: euthyroidism, Sub clinical Hypothyroidism, pre-dialysis patients

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Introduction

CKD is a multifactorial disease that usually progress to end-stage renal disease. CKD cause morbidity and mortality and is considered an important risk factor for cardiovascular disease (CVD) so, it represents a major burden on global health [1]. The prevalence of CKD has augmented over the past few decades due to the increasing percentage of hypertension, diabetes, and obesity in all age groups **[2–5].** Thus, early recognition and management of these risk factors is very essential. The kidneys play a role in the metabolism and removal of thyroid hormones that are essential for the development of the kidneys and the maintenance of electrolyte and water balance **[6].**Some studies didn't found association between thyroid dysfunction and CKD **[7–10]** while other studies established this relationship **[11–14].** Data on CKD and thyroid dysfunction are inadequate so, more researches are needed to recognize the possible influence of thyroid dysfunction on the kidneys.

Methods: in this cross-sectional study; 180 patients were recruited from the outpatient clinic of the Nephrology unit at Nephrology and Urology MINIA University Hospital for 6- month duration from March 2022 to August 2022. critically ill patients, aged >60, end- stage renal disease, known to have any frank thyroid disease ,use of medication such as antithyroid drug ,and/or thyroid hormones ,or pregnant women were excluded(2-6). Physical examinations including weight and height to calculate Body mass index (BMI) by dividing the weight (kilogram) by the height in squared meters (m2)**[15]**. BMI was categorized according to the World Health Organization for Asian standards into four classes which are underweight (<18.5 kg/m2), normal weight (18.5–22.9 kg/m2), overweight (23-24.9 kg/m2), and obese (≥25 kg/m2) **[16].** Laboratory tests were performed on all patients as free thyroxine (FT3&FT4), TSH, and Serum creatinine & urea levels. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation **[17]**: serum creatinine level >0.7 mg/dL, eGFR=144 × (Serum creatinine /0.7)-1.209×(0.993)Age for women and serum creatinine level>0.9 mg/dL, eGFR= 141 × (Serum creatinine/0.9)-1.209×(0.993)Age for men. Definition of CKD is an eGFR <60 mL/min/1.73m2 and/or ACR≥30 mg/g **[18]**. Euthyroidism was defined as a serum TSH and FT4 within the laboratory reference ranges of 0.62–6.68 mIU/L and 0.89–1.76 ng/dL respectively) **[19]**. Subclinical hyperthyroidism was defined as normal FT4 while TSH level <0.62 mIU/L , and SCH was

defined as normal FT4 and TSH levels>6.68 mIU/L.

Statistical analysis

Data were conveyed as mean ± standard deviation (SD) for quantitative variables and. number and percentage for qualitative one . Data were compared using a general linear model and the chi-square test for quantitative and qualitative variables respectively. All statistical analyses were performed using SPSS Statistics version 25. Results was considered statistically significant if a p- value <0.05.

Results

The demographic and laboratory data of the 180 participants are presented in Table (1).58.9% of participants were males, with a mean age of 50.4 ± (7.05) years.

Table (1): Statistical distribution of the Patient's studied sample according to their Socio-demographic & laboratory data.

		Studied cases (N=180)
Age (years)	**Range** **Mean ± SD**	18-60 years 50.4 ± 7.0
Gender	**Male (N, percent)** **Female (N, percent)**	106 (59%) 74 (41%)
BMI	**Mean ± SD**	25.3 ± 4.2
Creatinine	**Mean ± SD**	2.01 ±0.71
Urea	**Mean ± SD**	53.59 ± 15.62
eGFR	**Mean ± SD**	36.27 ± 17.02
FreeT3	**Mean ± SD**	5.01 ± 1.29
FreeT4	**Mean ± SD**	15.44 ± 3.26
TSH	**Mean ± SD**	3.44 ± 2.36

Table (2): Socio-demographic data and laboratory data according to thyroid state among studied cases.

Characteristic	**Normal thyroid function (n =126)**	**sub-clinical hypothyroidism (n =48)**	**overt hypothyroidism (n =5)**	**overt hyperthyroidism (n =1)**	**p-value**
Age (years) **Mean ± SD**	48.85±7.12	55.50±4.13	50.40±7.40	53.00	<0.0001*
Gender Male Female	 80(63.5%) 46(36.5%)	 25(52.1%) 23(47.9%)	 1(20.0%) 4(80.0%)	 0(0.0%) 1(100.0%)	0.059
BMI **Mean ± SD**	24.61±4.22	27.14±3.48	28.16±2.21	18.30	<0.0001*
Creatinine **Mean ± SD**	1.89±0.69	2.30±0.67	2.30±0.65	1.10	0.002*
Urea **Mean ± SD**	50.92±14.92	60.19±14.95	61.80±19.49	32.00	0.001*
eGFR **Mean ± SD**	43.09±17.57	30.08±11.15	27.52±11.05	57.50	<0.0001*
15-29	33(26.2%)	24(52.2%)	3(60.0%)	0.0(0.0%)	0.004*
>30	93(73.8%)	22(47.8%)	2(40.0%)	1(100.0%)	
FreeT3 **Mean ± SD**	5.32±1.16	4.14±0.68	2.52±0.59	9.00	<0.0001*
FreeT4 **Mean ± SD**	15.76±2.88	14.47±2.69	7.76±1.35	27.50	<0.0001*
TSH **Mean ± SD**	2.38±1.06	5.80±1.09	10.52±4.90	0.15	<0.0001*

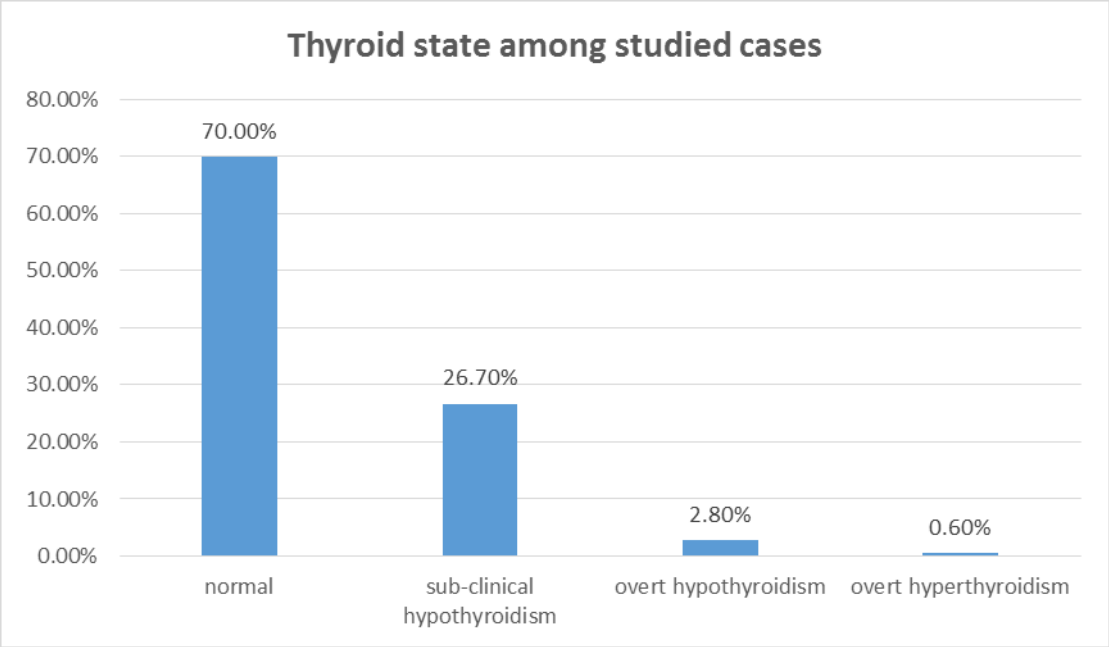

Figure (1): Thyroid state among studied cases.

We found a large percentage of patients with SCH (26.7%), while a small percentage of overt hypothyroidism (2.8%) and 1patient had overt hyperthyroidism incidentally discovered during our study so, we sub-divided the patients into 4 groups according to their thyroid states. there wasn't significant sex difference (p-value: 0.059). mean BMI showed a significant increase with the deterioration of thyroid functions from normal thyroid function to SCH and then to overt hypothyroidism (p-value<0.0001).there were significant increases in mean s.creatinine &Mean b.urea in SCH & overt hypothyroidism group with a p-value of (0.002&0.001respectively).Mean eGFR showed significant decline in the SCH& overt hypothyroidism group with a p-value of (<0.0001). Thyroid hormonal profile showed a significant differences in different thyroid state groups with a P-value (<0.0001). The percentage of stage IV CKD patients showed significant increase from (26.2%) euthyroidism, (54.2%) SCH to (60%) overt hypothyroidism (p=0.004). There were significant differences in FT3, FT4 and TSH among different stages of CKD (p=0.032, 0.037, 0.007 respectively) There was a weak positive linear correlation between FT3, FT4 with eGFR (r 0.271,0.218)While a weak negative linear correlation of TSH with eGFR (r -0.277).

Table (3): Thyroid parameters according to Stage of chronic kidney failure among studied cases.

Characteristic	I (n=3)	II (n=18)	III a (n=37)	III b (n=60)	IV (n=62)	p-value
FreeT3 Mean ± SD	6.43±0.61	5.14±1.09	5.29±1.29	4.90±1.25	4.66±1.27	0.032*
FreeT4 Mean ± SD	17.70± 1.11	16.11±3.09	15.82±3.42	15.54±3.37	14.28±2.91	0.037*
TSH Mean ± SD	2.23±1.12	2.29±1.31	2.92±1.47	3.53±2.19	4.21±2.85	0.007*

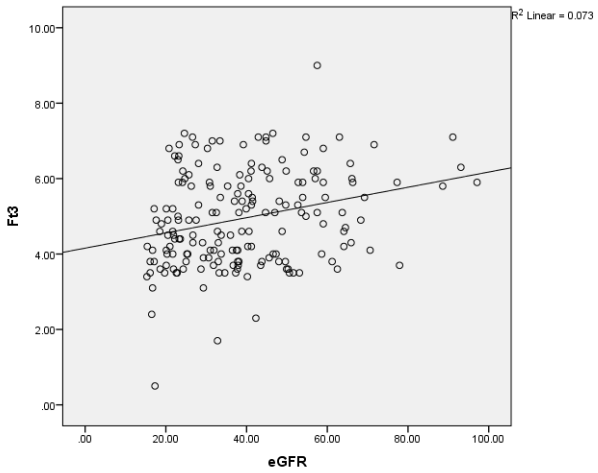

Figure (2): Correlation between FT3 and severity of eGFR among studied cases.

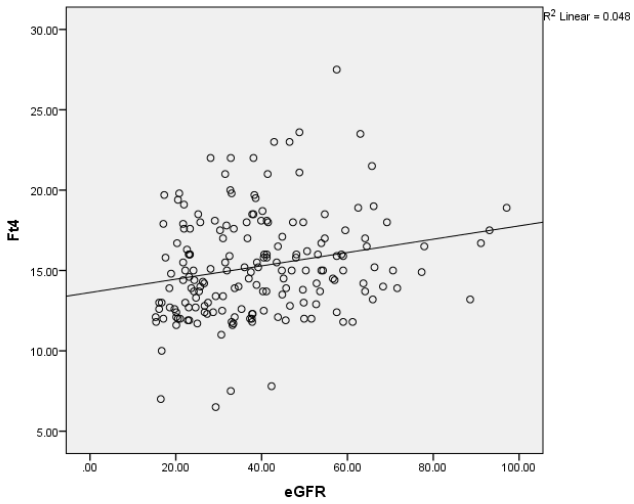

Figure (3): Correlation between FT4 and eGFR among studied cases.

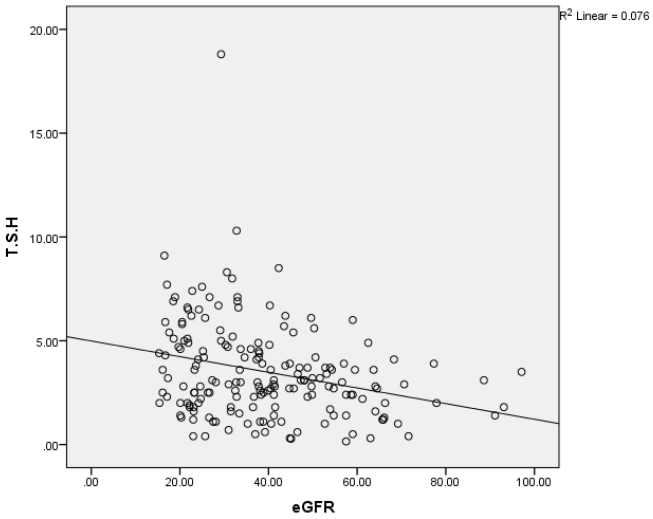

Figure (4): Correlation between TSH and eGFR among studied cases.

Discussion

It has been reported that the kidneys and the thyroid gland had a close relationship **[20-22].** Thyroid hormones are vital for the kidney maturation and metabolism indirectly by their effect renal blood flow, and directly by affecting glomerular filtration rate, tubular secretion, absorptive function, and electrolyte balance **[23, 24].** So, any form of thyroid dysfunction may lead to electrolyte, water and lipid imbalance. In our study, a positive linear relationship was shown between eGFR each FT3 and FT4 which was in agreement with the study of Pan et al **(25)** in FT3 But it showed that free and total T4 concentrations may be slightly decreased or even normal what explained as FT4 binding to its binding proteins was inhibited by anticoagulation effect of the heparin used during hemodialysis[**26]** in contrast our study as we didn't share the hemodialysis patients .Some studies **[2, 3]** predicted that CKD may lead to a higher prevalence of SCH which was Similar to our study. Several studies have reported an association between SCH and CKD in the general population **[7–14]** which support our results. Our study showed that there was increase in TSH level and was negatively correlated with eGFR which was reinforced by Norwegian and Chinese studies **[8, 11].** An Australian study showed that no significant association was observed between SCH and CKD In contrast to this study **[7]**. Our study found an association between most of thyroid dysfunction forms especially SCH &overt hypothyroidism and risk of CKD However, other studies found an association between SCH only and risk of CKD as Brazilian and other studies **[11-14]** which was unsupported by other studies **(7-10)**. These varying results among studies may be due to alterations in the characteristics of the population such as age, sex, region, etc. Additionally, when we divided CKD patients into stages according to their thyroid state we found a statistically significant difference in eGFR among groups ($p<0.0001$) in contrast to the study of Kim *et al* **(27)** who found significant difference between groups in albuminuria only . Although eGFR and renal blood flow are known to increase with hyperthyroidism **[6],** our study as previous studies **[7–11]** revealed no significant association between hyperthyroidism and CKD. Our study has some limitations due to numerous possible confusing factors as social and medical conditions, cross-sectional design, and single- center experience. Transient variation of thyroid and renal function usually occur so, repeated measures of thyroid and renal functions should be made through a longitudinal study to provide more dependable results in this matter and avoid the enrollment of these temporary changes with the results.

Conclusion:

Our findings verified that thyroid dysfunctions especially SCH and overt hypothyroidism were closely associated with pre-dialysis CKD patients**.**

Recommendations:

Some patients with SCH and overt hypothyroidism with CKD may get benefit from the replacement therapy after further longitudinal studies on thyroid dysfunction and CKD be made.

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