ORIGINAL ARTICLE

Evaluation of Thyroid Functions in Patients with Chronic Kidney Disease and its Relation to the Disease Severity

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Abstract

Background: ***Chronic kidney disease (CKD) constitutes a significant public health concern. The prevalence of CKD in the general populations of different nations varies from ten percent to twelve percent.***

Aim: ***To evaluate the thyroid functions in cases with CKD and to clarify its relation to the disease severity.***

Patients and methods: ***This was a case-control research that performed on 90 Egyptian subjects above 18 years old.***

Results: ***There was highly significant reduction in FT3 level in group Ithan group II. Also, the level of FT4 showed a statistically highly significant decrease in group I than group II, while the level of TSH also showed a statistically highly significant increase in group I than group II. There was a significant negative correlation between FT3 levels and FBS, PPBS, and creatinine levels in patients of group I. FT4 levels were negatively correlated with creatinine and positively associated with eGFR levels. TSH levels were positively correlated with creatinine and HDL levels, but negatively associated with eGFR levels.***

Conclusion: ***Hypothyroidism is more prevalent in CKD patients, with free T3 and free T4 levels decreasing as CKD stage increases. Subclinical Hypothyroidism also increases in individuals with a decline in GFR. Monitoring thyroid functions is crucial for improving the quality of life in patients with advanced renal impairment.***

Keywords: Thyroid Functions; Chronic Kidney Disease; Disease Severity

1. Introduction

An epidemic of chronic kidney disease has spread throughout the globe. One major problem with public health is CKD. General populations in different nations have an incidence of CKD that varies from ten to twelve percent.[1]

CKD is defined as kidney damage or an estimated Glomerular Filtration Rate (eGFR) under 60 ml/min/1.73 m2 that has persisted for three months or more, irrespective of the cause. The condition is characterized by an ongoing decrease in kidney function that, in the end, necessitates some form of Renal Replacement Therapy (RRT), such as dialysis or a kidney transplant.[2]

The kidney is generally involved in the breakdown, elimination, and metabolism of thyroid hormones. In thyroid hormone metabolism, the kidneys play a role by converting T4 to T3, the active metabolite.[3]

The stage of CKD is significantly correlated with the incidence of thyroid dysfunction. As renal insufficiency increases, the incidence of thyroid hormone abnormalities also increases. As renal failure progresses, the thyroid profile, which includes T3, T4, and TSH, decreases while TSH increases.[4]

Patients suffering from chronic renal illness may show abnormal results when testing their thyroid function. A number of thyroid activities are impacted by CKD. These include decreased concentrations of thyroid hormone in the blood, changes in peripheral hormone metabolism, disruptions in binding to carrier proteins, and potential decreases in thyroid content in tissues, in addition to increased iodine reserves in the thyroid glands.[5]

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This research aimed to assess the thyroid functions in cases with CKD and to clarify its relation to the disease severity.

2. Patients and methods

This was a case-control trial performed on 90 Egyptian subjects above 18 years old. They were separated into 2 groups as follows: Group 1 [Patients group]: 60 CKD cases, subdivided into: 1a) 30 individuals with CKD stages (2, 3, 4) and 1b) 30 individuals with End Stage Renal Disease (Stage 5), while Group 2 [Control group]: 30 healthy control subjects age and sex matched with the patients.

Inclusion Criteria: CKD Patients who are more than 18 years old and of both sexes.

Exclusion Criteria: Any patient who had been diagnosed to be having thyroid disorder, individuals receiving thyroid hormone replacement or drugs altering thyroid functions such as (Amiodarone, Steroids, Estrogen pills, Phenytoin, Dopamine, Iodide containing drugs), cases known to have thyroid surgery either total or partial thyroidectomy and Patients having autoimmune disease affecting thyroid functions or Collagen disorders.

Methods

All patients were subjected to the following:

Full History taking, full Clinical examination, including thyroid examination. Laboratory investigations involving: Complete Blood Count (CBC): (2ml) blood sample was collected into an EDTA-containing tube for CBC. Cell Dyne Ruby, a cell counter based in Germany, used Abbott, another German company, to calculate the CBC. Thyroid function tests (FreeT3, FreeT4, TSH): Kits were supplied by SunRed Biotechnology Company, China. Test principle: The thyroid profile uses a blood sample to evaluate the function of the thyroid gland. A thyroid profile can help diagnose and monitor the treatment of thyroid disorders. Test procedure: (2ml) whole blood samples were withdrawn from subjects, separated into serum, and stored at -20°C until assay. Free T3, Free T4, and TSH were assayed utilizing Electro ChemiLuminescence on a Cobas e411 immunoassay device. The serum was then used for measurements of kidney functions, serum sodium, potassium, total calcium, phosphorus, uric acid, serum cholesterol, triglycerides, HDL, and LDL. Tests were performed using Cobase C311 and Roche kits. All tests were conducted using Cobase C311 and Roche kits. Fasting and Post Prandial Blood Sugar (FBS & PPBS): For FBS, A venous sample was taken after at least 8 h fasting and for PPBS, A venous blood sample was taken after 2 h of eating a meal without doing any exercise. Estimated Glomerular Filtration Rate (eGFR): Using the Cockcroft and Gault formula: $CCr=\{((140-age) \times weight)/(72 \times SCr)\} \times 0.85$ (if female)

Abbreviations/ Units: CCr (creatinine clearance) = mL/minute, Age = years, Weight = kg and SCr (serum creatinine) = mg/dL

Statistical Analysis

An analysis was performed utilizing the Statistical Package for the Social Sciences (IBM SPSS) version 27, which involved revising and coding the data obtained from the history, clinical examination, laboratory investigations, and outcome measures. When the data was parametric, it was shown as the mean plus or minus the standard deviation (SD) and ranges; when it was non-parametric, it was shown as the median and inter-quartile range (IQR). Counts and percentages were used to depict the qualitative data.

The following statistical tests are available: chi-square, Fisher's exact, independent t-test, Mann-Whitney, post hoc, Spearman correlation coefficients, Kruskal-Wallis, and receiver operating characteristic (ROC) curve. A 95% confidence interval and a 5% margin of error were both approved. The following constitutes the significance level of the probability (P-value): The results were categorized as non-significant (NS) if the P-value was above 0.05, significant (S) if the P-value was under 0.05, and highly significant (HS) if the P-value was below 0.01.

Ethical Considerations

The research objectives and tools were explained to the participants. The Research Ethics Committee of Al-Azhar University, Cairo, Egypt had approved the protocol before progressing into the study.

3. Results

Regarding systolic and diastolic blood pressure, diabetes, hypertension, and IHDs, there was a highly significant distinction among the groups that were evaluated. However, there was no significant variation when it came to age, gender distribution, BMI, or smoking. (Table 1)

Table 1. Comparison among group I and group II concerning demographic data and characteristics

		GROUP I	GROUP II	TEST VALUE	P-VALUE	SIG.
		No.= 60	No.= 30			
AGE	Mean ± SD	58.05 ± 10.73	59.43 ± 16.31	-0.482•	0.631	NS
	Range	30 – 81	31 – 70			
GENDER	Female	19 (31.7%)	14 (46.7%)	1.938*	0.164	NS
	Male	41 (68.3%)	16 (53.3%)			
BMI	Mean ± SD	28.75 ± 4.34	29.69 ± 5.91	-0.860•	0.392	NS

	Range	19.9 – 41.7	18.9 – 46.7			
SMOKING	Negative	49 (81.7%)	21 (70%)	1.575*	0.209	NS
	Positive	11 (18.3%)	9 (30%)			
SBP	Mean ± SD	131.5 ± 20.49	116.17 ± 4.68	-4.036•	0.000	HS
	Range	90 – 180	110 – 120			
DBP	Mean ± SD	79.33 ± 12.19	73.67 ± 4.14	-2.469•	0.015	S
	Range	40 – 100	70 – 80			
DM	Negative	33 (55%)	30 (100.0%)	19.286*	0.000	HS
	Positive	27 (45%)	0 (0.0%)			
HTN	Negative	13 (21.7%)	30 (100.0%)	49.186*	0.000	HS
	Positive	47 (78.3%)	0 (0.0%)			
IHDS	Negative	34 (56.7%)	30 (100.0%)	18.281*	0.000	HS
	Positive	26 (43.3%)	0 (0.0%)			

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant *: Chi-square test; •: Independent t-test

There was significant variance among examined groups regarding Hb, Urea, Creat, Na, K, eGFR, Ca+2 and Po4 p<0.05, while no significant variance concerning TLC, PLT & U.A p>0.05. (Table 2)

Table 2. Comparison between group I and group II regarding laboratory parameters

		GROUP I	GROUP II	TEST VALUE	P-VALUE	SIG.
		No.= 60	No.= 30			
HB	Mean ± SD	9.54 ± 1.5	12.09 ± 2.28	-6.350•	0.000	HS
	Range	6.6 – 15.1	8.2 – 17.5			
TLC	Mean ± SD	8.12 ± 3.92	8.33 ± 3.88	-0.239•	0.812	NS
	Range	1.2 – 20.1	2.9 – 22.3			
PLT	Mean ± SD	257.3 ± 94.57	258.53 ± 104.15	-0.056•	0.955	NS
	Range	34 – 584	129 – 544			
UREA	Mean ± SD	127.83 ± 56.41	38.13 ± 9.21	8.628•	0.000	HS
	Range	36 – 278	23 – 50			
CREAT	Median (IQR)	5.1 (2.75 - 7.15)	0.8 (0.7 - 0.9)	-7.647	0.000	HS
	Range	0.9 – 17.4	0.55 – 1.1			
NA	Mean ± SD	136.43 ± 5.2	139.1 ± 3.04	-2.592•	0.011	S
	Range	124 – 148	131 – 145			
K	Mean ± SD	4.65 ± 0.79	4.21 ± 0.44	2.816•	0.006	HS
	Range	3.3 – 6.3	3.3 – 5.5			
U.A	Mean ± SD	7.29 ± 3.08	6.09 ± 1.7	1.984•	0.050	NS
	Range	2.3 – 15.6	2.6 – 10			
EGFR	Median (IQR)	16.05 (10.7 - 33)	102.65 (93.7 - 122.6)	-7.703	0.000	HS
	Range	6.5 – 71.1	90.1 – 227.9			
CA+2	Mean ± SD	8.49 ± 0.96	9.65 ± 0.78	-5.721•	0.000	HS
	Range	5.4 – 10.1	8.3 – 11.8			
PO4	Mean ± SD	5.05 ± 1.86	3.47 ± 0.73	4.487•	0.000	HS
	Range	2.7 – 10.5	1.7 – 5.8			

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test

There was highly significant reduction in FT3 level in group Ithan group II with p-value <0.01. Also, the level of FT4 showed highly significant decrease in group I than group II with p-value <0.01 while the level of TSH also showed highly significant increase in group I than group II with p-value <0.01. (Table 3)

Table 3. Comparison among group I and group II concerning thyroid functions

		GROUP I	GROUP II	TEST VALUE	P-VALUE	SIG.
		No.= 60	No.= 30			
FT3	Mean ± SD	1.26 ± 0.31	2.3 ± 0.73	-9.488•	0.000	HS
	Range	0.8 – 2.21	1.15 – 4.1			
FT4	Mean ± SD	0.76 ± 0.34	1.31 ± 0.26	-7.722•	0.000	HS
	Range	0.15 – 1.8	0.84 – 1.71			
TSH	Mean ± SD	4.76 ± 1.28	3.54 ± 1.05	4.489•	0.000	HS
	Range	0.07 – 6.8	1.05 – 4.83			

The best cut off point for FT3 to differentiate between group I and group II was ≤ 1.72 with sensitivity of 95.0%, specificity of 80.0% and area under curve (AUC) of 0.916 while the best cut off point for FT4 to differentiate between group I and group II was ≤ 0.92 with sensitivity of 86.67%, specificity of 93.33% and AUC of 0.901. Also, the best cut off point for TSH to differentiate among group I and group II was > 4.83 with sensitivity of 66.67%, specificity of 100.0% and AUC of 0.832. (Table 4)

Table 4. Receiver operating characteristic curve (ROC) for thyroid profile among group I and group II

	CUT OFF POINT	AUC	SENSITIVITY	SPECIFICITY	PPV	NPV
FT3	≤1.72	0.916	95	80	90.5	88.9
FT4	≤0.92	0.901	86.67	93.33	96.3	77.8
TSH	>4.83	0.832	66.67	100	100	60

There was significant negative correlation among the level of FT3 and FBS, PPBS and creatinine level among patients of group I. FT4 level was negatively associated with creatinine level and positively correlated with eGFR level. There was statistically significant positive correlation between TSH level and creatinine and HDL levels among patients of group I. There was statistically significant negative correlation among TSH level and eGFR level among patients of group I. (Table 5)

Table 5. Correlation of thyroid profile with the other examined parameters among cases of group I.

GROUP I	FT3		FT4		TSH	
	r	p-value	r	p-value	r	p-value
AGE	-0.067	0.613	0.041	0.756	0.089	0.501
BMI	-0.128	0.329	0.074	0.575	-0.126	0.336
SBP	-0.009	0.946	-0.098	0.455	0.075	0.570
DBP	-0.088	0.504	0.007	0.955	0.029	0.823
HB	0.178	0.174	0.211	0.106	-0.138	0.292
TLC	0.069	0.599	0.040	0.764	0.108	0.413
PLT	0.219	0.093	0.056	0.668	0.015	0.911
UREA	-0.065	0.624	-0.208	0.111	0.054	0.679
CREAT	-0.074*	0.014	-.349**	0.006	0.101*	0.011
NA	0.027	0.838	0.223	0.087	-0.070	0.594
K	0.069	0.601	-0.130	0.321	0.123	0.349
U.A	-0.103	0.434	-0.215	0.099	0.234	0.072
EGFR	0.049	0.708	.326*	0.011	-0.198**	0.009
CA+2	0.064	0.628	-0.015	0.911	-0.038	0.771
PO4	0.165	0.209	-0.090	0.493	-0.094	0.475
FBS	-.307*	0.017	-0.103	0.432	0.070	0.595
PPBS	-.303*	0.019	-0.094	0.477	0.119	0.366
CHOLEST	0.003	0.984	-0.052	0.695	-0.062	0.637
TGS	0.111	0.397	-0.006	0.961	-0.103	0.433
HDL	-0.050	0.707	-0.140	0.285	.255*	0.050
LDL	-0.132	0.314	-0.253	0.051	0.046	0.724

4. Discussion

The kidney typically functions significantly in the metabolism, degradation, and excretion of several thyroid hormones. Consequently, it is unsurprising that renal impairment disrupts thyroid physiology, potentially affecting all components of the hypothalamic-pituitary-thyroid axis, including modifications in hormone synthesis, transport, and excretion. Epidemiological research indicates that predialysis individuals with chronic renal disease exhibit a heightened incidence of Hypothyroidism, with numerous instances being subclinical.[6]

Our current investigation revealed a highly statistically significant distinction between Group I and Group II concerning FBS, PPBS, systolic and diastolic blood pressure, diabetes mellitus, hypertension, and ischemic heart disease. No significant distinction was observed between Group I and Group II for age, gender, BMI & smoking status.

Our results came in agreement with Tannor & E.K.,[7] Individuals with hypertension (HTN), hypertension (HTN + DM), or diabetes mellitus (DM) alone were the subjects of a cross-sectional investigation conducted in five Ghanaian health institutions as part of the Ghana Access and Affordability Program (GAAP). Demographic information, medical history, and results of the clinical assessment were gathered using a standardized questionnaire. Laboratory tests were performed to measure serum creatinine, proteinuria, and estimated glomerular filtration rate. A multivariable logistic regression model was used to identify variables associated with chronic kidney disease (CKD). There was available data on serum creatinine and proteinuria for 2781 out of 3294 participants (84.4%). Patients with DM and HTN had a frequency of 242 (28.5%), patients with HTN had a prevalence of 417 (26.3%), and patients with DM alone had a prevalence of 56 (16.1%). Instances of chronic kidney disease were associated with diabetes mellitus and high systolic blood pressure. Chronic kidney disease is prevalent among individuals with diabetes mellitus and hypertension in Ghana.

The current investigation revealed a highly significant disparity among the two groups in terms of hemoglobin, serum urea, serum creatinine, sodium, potassium, estimated glomerular filtration rate, calcium, as well as phosphorus.

Our result is consistent with Khatri et al.,[8] who showed elevated serum urea and creatinine and lower eGFR in end stage renal disease group individuals in contrast to the control group with mean blood urea 146.3 mg/dl, mean creatinine 9.8 mg/dl and mean eGFR of 7.47 ml/min among chronic kidney disease patients.

Also, our results came in agreement with Badura.,[9] who showed that the results of the basic laboratory examinations for the individuals with CKD (either end-stage renal disease (ESRD) individuals on hemodialysis or individuals with CKD receiving conservative therapy) revealed anemia, in contrast to the control group whose haemoglobin levels were within the normal range, obviously due to uremia.

In our present study, we found that there was high significant variance among the examined group I and group II as regard thyroid profile. and there was no significant variation among group Ia and group Ib as regard thyroid profile.

Our results came in line with Malik,[10] who showed that in comparison to the control group, all CKD patients who were receiving conservative treatment and undergoing regular hemodialysis exhibited a significant reduction in their FT3 and FT4 levels. Nevertheless, there were no significant variations in the TSH level. It was determined that (68.75%) and (62.25%) of the H.D. individuals have FT3 as well as FT4 levels below the normal range, correspondingly, while (54.55%) as well as (72.72%) of the conservatively treated group have FT3 in addition to FT4 levels below the normal range. In contrast, there were no significant variations in FT3 and FT4 among those on conservative management and those on hemodialysis.

Our result came in disagreement with Khatri et al.,[8] whose results showed that the most prevalent thyroid dysfunction observed in individuals with end-stage renal disease was minimal FT3. In twenty-four individuals, the serum TSH level was altered. Twenty of the twenty-four patients exhibited elevated levels of TSH, while four exhibited low levels. The low level of FT3 may be attributed to the inhibited

peripheral conversion of T4 into T3. Additionally, other factors, such as metabolic acidosis, the loss of bound and free T4 in urine, and the Malnutrition-Inflammation syndrome in patients undergoing hemodialysis, may contribute to the same outcome.

In our research, we found that Hypothyroidism was highly significantly more frequent in the CKD group (I), compared with the control group (II).

Our result also came in agreement with Rhee,[11] who showed that Individuals with severe chronic kidney disease had approximately five times the frequency of Hypothyroidism compared to those without renal disease.

Our current investigation revealed a negative association between FT3 and FT4 levels and creatinine levels, whereas a positive correlation was seen between FT3 and FT4 levels and eGFR levels. Additionally, a positive association was seen between TSH levels and creatinine levels, whereas a negative correlation was noted with eGFR levels.

Our result came in agreement with Falhi et al.,[12] who examined 50 CKD individuals aged 20 to 50 years and demonstrated a statistically significant reduction ($P < 0.01$) in T3 and T4 levels, and an elevation in TSH levels, contrasted with controls.

4. Conclusion

We concluded that Hypothyroidism is more common in CKD individuals in contrast to the control group, with free T3 and free T4 levels decreasing as CKD stage increases. Subclinical Hypothyroidism also increases in individuals with a decline in GFR. Monitoring thyroid functions is crucial for patients with advanced renal impairment to improve quality of life. The incidence of thyroid dysfunction correlates with the stage of CKD, with higher renal insufficiency leading to thyroid hormone abnormalities.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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