Thyroid Dysfunction and Kidney Dysfunction: Parallel Disorders

Intisar Al Fahdi[1], Issa Al Salmi[1,2*], Fatma Al Rahbi[2], Faisal Shaheen[3], and Suad Hannawi[4]

[1]Oman Medical Specialty Board, Azaiba, Muscat, Oman

[2]The Renal Medicine Department, the Royal Hospital, Muscat, Oman

[3]DSFH, Riyadh, Saudi Arabia

[4]The Medicine Department, MOHAP, Dubai, UAE, PO Box 6552

Received: 26 May 2021

Accepted: 31 October 2021

***Corresponding author:** isa@ausdoctors.net*

DOI 10.5001/omj.2022.55

Abstract:

Rationale & Objective: Chronic kidney disease (CKD) is rising worldwide with an increasing incidence and prevalence throughout the globe. It is becoming more common in the developing world with increasing impact of non-communicable disease in these countries. Also, the autoimmune disorders including thyroid dysfunction is more common and may worsen the clinical status of patients with CKD. Hence, the aim of this study is to determine the thyroid status in patients with CKD, and to explore the clinical, biochemical, immunological, and hematological parameters that can be affected by thyroid dysfunction among CKD patients.

Method: this is a cross-sectional observational study conducted at the Royal Hospital (RH), Muscat. The data was progressively collected for all the newly diagnosed CKD patients with no known past history of thyroid disease during the period from January 2018 to December 2019.

Exposure(s): Thyroid hormones; assessment of thyroid status at their initial clinical encounter with diagnosis of CKD.

Outcome(s): Kidney function and various laboratory measurements

Analytical Approach: Data are presented as number and percentages. Continuous data are presented as mean and standard deviation (mean ± SD). Student t-test is used to compare the means of the two groups.

Results: during the study period, 121 females (40%) and 179 males (60%) were diagnosed with CKD with no prior thyroid diseases. The mean age (SD) for female and male were 53.6 (16.6) and 49.6 (16.5) year, respectively. There were 35 patients with thyroid dysfunction with prevalence of 11.7 %, out of which 21 patients (60 %) had subclinical hypothyroidism and 12 patients (34.3%) had subclinical hyperthyroidism. Two more patients (5.7%) had clinical thyroid dysfunction; one hypo and the other one hyperthyroidism. Total cholesterol (TC) and Low-density lipoprotein (LDL) were higher in hypothyroid patients. Urea was higher in hyperthyroid patients with CKD and hemoglobin level was significantly lower.

Conclusion: Thyroid dysfunction was not uncommon among CKD patients, with subclinical hypothyroidism was more common than subclinical hyperthyroidism. Thyroid dysfunctions coexisted with kidney dysfunction were these hormonal axis dysfunctions may not be apparent at first presentation and therefore may require a close clinical and laboratory evaluations.

Keywords: Chronic kidney disease (CKD); thyroid dysfunction; subclinical hypothyroidism; subclinical hyperthyroidism; glomerular filtration rate.

Introduction:

The interactions between kidney function and thyroid hormonal status have been investigated by researchers for years. For example, the hormonal activity of the thyroid gland influences the prenatal kidney and post-natal growth and functionAlso, the metabolism and elimination of thyroid hormone is controlled by the maintenance of a good kidney function (1, 2). In addition to the alteration of the hypothalamic-pituitary-thyroid hormone, Lim etal. reported that end stage kidney disease (ESKD) alters the peripheral thyroid hormone metabolism (2, 3).

The body water and various electrolyte equilibrium on different compartments of the body are influenced by the thyroid hormonal balance. In a review paper, Mariani and Berns stated that the kidney is an important end-organ target for thyroid hormonal action and it plays part on the control of metabolic rate and abolition of thyroid hormones (4). The decrease in the action of thyroid hormones is escorted by an incapability to get ride off an oral fluid overload. This effect is not due to an incomplete suppression of vasopressin production, or a decrease in the re-absorptive capacity in the tubule-dilutor segment of the kidney, but rather to a drop in the glomerular filtration rate (GFR) (1).

Among patients with chronic kidney disease(CKD), the identification of hypothyroidism can be easily missed, because of the overlap in the symptoms of CKD and hypothyroidism (5). Well-timed diagnosis and management of hypothyroidism may avoid deterioration of patient condition and extend survival.

There are several factors that may lead to thyroid abnormalities among CKD patients. The circulating and tissues active forms of triiodothyronine-T3 – were found to be low secondary to the deiodinase activity diminution (2, 3). Because of diminished kidney secretion, inorganic iodide

generated by residual deiodinase activity accumulates in stage 4 and 5 of CKD, which in turn dampens hormonal synthesis in the thyroid gland (6). On the other-hand, among CKD patients, accumulation of uremic poisonous solutes changes the vital (hypothalamic) control of the pituitary gland, and the thyroid stimulating hormone (TSH) response to thyrotropin-releasing hormone is abnormally low (2, 3). However, the feed-back loop mechanism of the thyroid–pituitary remains intact, because steady-state plasma TSH remains substantially normal and TSH undergoes the expected rise after thyroidectomy. Also, the toxic uremia poisonous solutes inhibit the capability of protein binding of thyroxin (7). Furthermore, researchers in the last decade found that in general inflammation and systemic metabolic acidosis produced by patients with CKD, might alter the various thyroid function (8-10).

The kidney contributes, as well, to the metabolism and clearance of the iodine primarily through GFR alterations. Among patients with CKD, serum iodine concentrations are elevated. However, this high level is not parallel to the degree of deterioration of GFR and CKD stages (5, 7). The Wolff–Chaikoff effect is an auto-monitoring trends of the creation of hormones of the thyroid inside its follicles, and the discharge of its hormones to the circulation is hindered by the high iodine level in the blood. Among CKD, the high prevalence of thyroid abnormalities, such as goiter and hypothyroidism, has been suggested to be due to excess iodine level (2, 3, 5).

A few researchers found that limiting the amount of iodine in the food can abolish the development of hypothyroidism and hence avoid the requirement for replacement therapy with thyroxine among patients with CKD on hemodialysis (11, 12). Researchers found that in patients with subclinical hypothyroidism in CKD, thyroxine supplementation may reduce the progression of CKD towards ESKD and hence improve GFR (13).

We have more than two thousand and five hundred patients on hemodialysis therapy and 250 patients on peritoneal dialysis. In addition, it was reported that 1% of the population aged 40 years and over have severe kidney disease, 9% have moderate kidney disease and 29% have mild kidney disease (14-16). Hence, there is a need to assess presence of thyroid dysfunction and its relation to kidney function at first encounter of diagnosis with kidney dysfunction. This study evaluated the thyroid function tests and various clinical, and laboratory findings among patients with CKD at initial clinical encounter.

Methods:

The study was approved by the Scientific Research Committee at the Royal Hospital, Muscat, Oman, Ministry of health, MOH/CSR/18/9073, and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments ethical standards. This cross-sectional observational clinical study was conducted at the Royal Hospital (RH), Muscat, Oman. The RH has an excellent medical record and IT system where everything is computerized and had received a well-recognized international certificate of excellence for its achievement in its electronic medical file system called Al Shifa. The RH has the central laboratory tests for all hormone studies, including thyroid hormones, for all patients from all over the country. All data including clinical, laboratory and radiological data were collected prospectively in the Al-Shifa. We recruited 300 newly CKD patients with no past history of thyroid disease, who attend the adult nephrology out-patient clinic from 2018 to 2019 was included in this study for assessment of thyroid status at their initial clinical encounter with diagnosis with CKD.

The following data were collected: age (years), body-weight (kg), height (cm), BMI (kg/m2), diabetes mellitus, hypertension, TSH, Thyroxine (Free T4), serum creatinine, blood urea, e-GFR

(ml/min/m2), serum albumin, hemoglobin level, white cell count (WCC), plasma glucose level, glycosylated hemoglobin (HbA1c), total cholesterol, LDL, high-density lipoprotein (HDL), triglyceride (TG), urinary protein / creatinine ratio (UPCR), total amount of the red blood cells in the urine, complement level of C3 and C4, anti-nuclear antibody (ANA), anti-neutrophil cytoplasmic antibodies (ANCA), immunoglobulin-A (IgA level), virology screen, bone profile, parathyroid hormone (PTH) and Dual-energy X-ray absorptiometry (DEXA) study. The hypothyroidism defines as TSH is higher than normal range and the Free T4 is low, subclinical hypothyroidism when TSH is high but Free T4 still within normal values range.

We used immunoassay on Siemens Atelica System, Germany. Both TSH and T4 were concurrently measured at the same time and in the same laboratory. Hyperthyroidisms was defined as low TSH and high Free T4. Subclinical hyperthyroidism was defined as a low TSH but normal Free T4. The normal range for TSH was 0.2 – 4.5 mIU/L and it was 8 – 24 pmol/L for Free T4.

Statistical analysis: Data were presented as number and percentages. Continuous data were presented as mean and standard deviation (mean ± SD). Student t-test was used to compare the means of the two groups. One-way analysis of variance test was performed for the comparison of parameters between groups. The relationship between parameters was evaluated by Pearson correlation analysis. P value of <0.05 was considered statistically significant. All the Patients were classified by gender, into male and female. Then they were classified into the normal thyroid patient and those with thyroid dysfunction. All statistical analysis carried out using STATA software.

Results:

As shown in Table 1; 300 newly diagnosed CKD patients at initial visit at the OPD clinics. The mean (SD) of age for females was 53.6 (16.6) years and for males was 49.6 (16.5) years with p=0.038. The mean (SD) for BMI was 27.5 (8.0) Kg/m^2 and 28.7 (7.4) Kg/m^2 for females and males respectively, p=0.34. Hypertension was present in 70% and diabetes in 49% of patients. Among females, diabetes was present in 59 and hypertension in 93 patients. Among males, hypertension was present in 88 and diabetes in 116 patients. The prevalence of thyroid dysfunction was 11.67 % and it was more prevalent in females than males with a P-value of 0.004.

Table 2 showed the comparison of biochemical parameters of male and females. The e-GFR level were significantly lower in females with P-value of 0.003 although the creatinine level showed no statistical difference. Moreover, the urine protein creatinine ratio (PCR) was higher in the females compared to male with a P-value of 0.04. In addition, the albumin and HDL level were both significantly lower in the female group with a P-value of <0.001 and 0.04, respectively. Other biochemical parameters like TSH, T4, total cholesterol, LDL, TG, calcium, phosphate, alkaline phosphatase (ALP), PTH, urea and creatinine did not show any statistical difference between male and female groups.

Hematological parameters showed that the hemoglobin was significantly lower in the females with P-value of <0.001. However, the platelets and WCC levels showed no statistical difference.

Immunological and virology parameters presented in table 3. It showed that low levels of complement C4 was significantly more frequent in the females compared to males with P-value of 0.006. Also, the virology status was looked at especially for hepatitis B, Hepatitis C and human immunodeficiency syndrome (HIV) and all of those showed no significant difference.

Table 4 shows radiological investigations. DEXA scan was done and 39.13% showed normal results, 42.0% showed osteopenia and 18.8% had osteoporosis. The US abdomen results revealed more CKD changes in females than males with a P-value of 0.001.

There were 35 patients with thyroid dysfunction with a prevalence of 11.7 %. In those who had thyroid dysfunction; there were 22 patients (60%) who had subclinical hypothyroidism and 13 patients (34.3%) who had subclinical hyperthyroidism. Thyroid dysfunction group had higher mean age of 56.82 (17.89) years compared to 50.48 (16.55) years in those who had normal thyroid function with a P-value of 0.03. BMI, diabetes mellitus and hypertension status were similar in both groups.

Table 5 showed the various laboratory parameters comparison between patients with normal thyroid function and those with dysfunction. Urea was significantly higher in the thyroid dysfunction group with a P-value of 0.03 and GFR was significantly lower in this group with a P-value of 0.04. Both albumin and hemoglobin were significantly lower in the thyroid dysfunction group with a P-value of 0.01 and 0.004 respectively. White cell counts and LDL were both higher in thyroid dysfunction group with a P-value of 0.01 and 0.03 respectively. Other biochemical, hematological, immunological parameters and virology status did not show any statically significant difference between the normal thyroid patient and those with thyroid dysfunction.

Table 6 showed the comparison of various laboratory parameters between hypothyroid and normal thyroid function patients. Biochemical parameters showed that TSH was significantly higher in hypothyroid group with a P-value of 0.0000 and free T4 was significantly lower with a P-value of 0.044. Kidney parameters including serum creatinine, GFR, urea, hematuria and proteinuria was similar in both hypothyroid and normal thyroid groups. WCC, Total cholesterol and LDL were

higher in hypothyroid patient compared with normal thyroid patient with a P-value of 0.02, 0.03, and 0.01, respectively.

Other parameters including immunological, virology status, CKD findings in the abdominal ultrasound (US) and Osteoporosis in DEXA scan did not show any significant difference between hypothyroid and normal thyroid groups.

Table 7 showed the comparison of various laboratory parameters between hyperthyroidism and normal thyroid function patients. It showed that TSH was significantly lower in hyperthyroid group with a mean of 0.095 miu/L (P-value <0.001) and free T4 was significantly higher with a mean of 16.66 pmol/L (P-value =.023). Kidney parameters showed that GFR is significantly lower in hyperthyroid group with a P-value of 0.023. However, creatinine was not showing any statistical difference between the two groups. Also, it was found that urea is higher in hyperthyroid compared to normal thyroid group with a mean of 23.64 mmol/L and a P-value of <0.001. Other parameters like hematuria and proteinuria were similar between the groups. Moreover, it was noted that hemoglobin level was significantly lower in hyperthyroid group with a mean of 9.63 g/dl and a P-value of 0.001. Other biochemical and hematological parameters was similar in both groups. Immunological parameters, virology status, CKD findings in US abdomen and Osteoporosis in DEXA scan did not show any significant difference between hyperthyroid and normal thyroid groups.

Discussion:

This cross-sectional study examined the relationship between thyroid functional test results and various clinical parameters in CKD patients. Thyroid dysfunctions existed in parallel along with

kidney dysfunction. These hormonal axis dysfunctions may not be apparent at first presentation and may require a close clinical and laboratory evaluations. There are several interesting findings, including 1) the high prevalence of thyroid dysfunction (12%), 2) high cholesterol and LDL levels in hypothyroid patients, and 3) higher levels of urea in hyperthyroid patients (suggesting greater catabolism).

Thyroid hormone abnormalities have been reported among clinically euthyroid patients with ESKD, including reduced total and free T3 and T4 levels (2-4, 8, 9, 11). The background for these abnormalities is unclear, however it has been postulated to be due to adaptive response to chronic non-thyroidal illness, uremia and protein malnutrition (5, 17). The present study showed that even among newly diagnosed patients with CKD, thyroid dysfunction was present in almost 12% of the studied population.

Hypothyroidism was almost present in two third and hyperthyroidism was representing one third of thyroid dysfunction among CKD population. One study by Aljabri et al. form Kingdom of Saudi Arabia (KSA), has similar results. It was found that hypothyroidism is highly prevalent in Saudi patient with long term CKD and Type 2 diabetes mellitus with prevalence of 26% (18). A study from The United States showed that subclinical primary hypothyroidism is relatively a common condition (~18%) among person with chronic kidney disease, who were not requiring chronic dialysis and it is independently associated with progressively lower estimated GFR in large cohort of unselected outpatient adults (19). In addition, a study showed a considerably high prevalence of subclinical hypothyroidism in CKD patients on hemodialysis especially among females (20). However, in the present study, we showed that even at early stage of CKD, thyroid abnormalities present among CKD population. This may get worse with time and, contributes to the deterioration of CKD towards ESKD. Therefore, early intervention may ameliorate the progression to end stage.

This study showed that urea was significantly higher in the hyperthyroid group however it demonstrated that creatinine level did not show statistical difference. Mariani etal stated that hyperthyroidism is characterized by an increase in renal plasma flow and GFR resulting in a reduction of serum creatinine level (4). The reduction in serum creatinine has also been reported in subclinical hyperthyroidism (21). Researchers have shown that in hyperthyroidism, the cardiac output is increased, and the serum creatine is increased as well. Thus, serum creatinine concentration was suppressed due to a decrease in creatinine synthesis and an increase in renal creatinine excretion. Blood urea nitrogen (BUN) was high, primarily due to an increase in urea nitrogen production secondary to excessive protein catabolism together with insufficient excretion of UN (22-24).

The present study showed a similar result regarding the increased serum urea level, however there was some discrepancy compared to international studies regarding serum creatinine level. In a study by Shirota T, et al. it showed that serum urea is increased, creatinine is decreased, and GFR was increased in hyperthyroidism (23). Moreover, a regional study form Sudan showed that hyperthyroidism decreases serum creatinine levels slightly and increases serum urea (25). The reason of this discrepancy between our study and other studies could be due to the difference of characteristic of the study group as all of our patient are actually CKD patient with low mean GFR 37.9 (SD 27.86) and the other studies was not done in CKD patient it was selected randomly.

The undiagnosed and untreated hypothyroidism is posing a danger upon CKD patients in many ways. One of the most important factors is that ESKD patients have a well-recognized increased risk of cardiovascular disease that begins early in the course of CKD and results in 10-fold or higher cardiovascular mortality rates after the start of kidney replacement therapy (KRT) (26-28). Hypothyroidism itself is also a risk factor for cardiovascular disease, thus adding to the existing

risks (29). However, hypothyroidism is a modifiable risk factor, hence should be recognized and treated on time. In addition, hypothyroidism impairs myocardial function (30). In CKD patients, cardiac function can be already challenged by fluid overload, overt hypertension, anemia, etc., leading to cardiac failure and hypothyroidism can worsen the situation.

Many studies showed that hypothyroidism is risk factor for atherogenic lipid profile, in which they clearly showed that total cholesterol and LDL were higher in hypothyroid patient compared to euthyroid patients. One study by Biondi B, et al. showed that the mean total cholesterol and LDL cholesterol levels of subjects with TSH value between 5.1 and 10 mlU/L were significantly greater than the corresponding mean lipid level in euthyroid subjects (29). However, there is controversy whether subclinical hypothyroidism can lead to alteration of lipid profile. One meta-analysis done by Xiao-Li Liu, et al. suggested that the serum TC, LDL and total triglyceride level were significantly increased in patient with subclinical hypothyroidism compared to with euthyroid individual; the WMD (weighted mean difference) were 12.17mg/dl, 7.01 mg/dl and 13.19 mg/dl respectively. No significant difference was observed for serum HDL, however, they mentioned that there are limitations with the included studies mainly in the control of potential confounding factors (31). One study done regionally in Iraq by Sheymaa G. regarding the effect of thyroid hormone in serum cholesterol and albumin; showed significant increase in in the rate of cholesterol compared to control group (32).

Similarly, our study revealed that total cholesterol and LDL were significantly higher in hypothyroid patient compared to euthyroid patients, and to be noted that our patients in this group are all having subclinical hypothyroid except one patient with clinical hypothyroidism.

Certainly, hypothyroidism is associated with anemia, approximately 20-60% of patients with hypothyroidism are also diagnosed with anemia. It can have various etiologies, and can manifest

as normocytic, microcytic or macrocytic anemia (33, 34). In patients on maintenance hemodialysis, erythropoietin resistance is a common problem, and hypothyroidism should be also ruled out together with the other well-known causes (24). Hyperthyroidism contributes to anemia in CKD patient as well. Kaynar et al. showed that hyperthyroidism is considered one of the causes of anemia with resistance to human recombinant human erythropoietin (EPO) (35). Our study showed that hemoglobin level was significantly lower in hyperthyroid group. It also showed that WCC was higher in hypothyroid patient compared with normal thyroid patient, although literature showed that thyroid hormone deficiency results in a decrease in total blood counts including WCC (36). The reason for this could be other confounding factor in our study like presence of infection at time of testing.

Thyroid hormone is known to promote albumin catabolism thus albumin degradation is reduced in hypothyroidism (37). One study done by Mee Kyoung Kim, et al. showed that glycated albumin is spuriously high in non-diabetic patient with overt hypothyroidism (38). Another study done regionally in Iraq regarding the effect of thyroid hormone in serum cholesterol and albumin; showed that albumin level did not have significant difference between hypothyroid group and the control group (32). In contrary to the above studies, our study showed that serum albumin was significantly lower in the hypothyroid group. Our finding is supported by a study of Gilles R et al., which concluded that patients with proteinuria have higher TSH levels, consistent with urinary loss of thyroid hormones (39). However, our patients have no significant difference in proteinuria between the compared groups. Another study done by Shantha et al. demonstrated similar results to our study; that albumin was significantly lower in the hypothyroid group and concluded that decreased level of serum albumin is a risk factor for subclinical hypothyroidism in patient with ESKD (40).

Limitations

This is a single centre study, but it covers the entire country. Also, the study is performed at a single point in time at initial clinical encounter with CKD diagnosis and did not examine progress over time between different stages of CKD.

In addition, this study did not compare between normal and abnormal structural thyroid abnormalities but only examined the hormonal abnormalities. Furthermore, we did not obtain similar data in a healthy control group.

Conclusion:

The present study found that thyroid dysfunction is not uncommon in patient with early CKD and that most encountered abnormality is subclinical hypothyroidism. Hence, a proper clinical evaluation of thyroid disorders among CKD patients is important. However, more researches are needed especially intervention studies to ascertain that proper management of thyroid status may ameliorate CKD progression towards end stage.

Compliance with Ethical Standards:

Disclosure of potential conflicts of interest:

The study was approved by the Scientific Research Committee at the Royal Hospital, Muscat, Oman, Ministry of health, MOH/CSR/18/9073, and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments ethical standards. https://mohcsr.gov.om/my-researches.

Informed consent: each participant was freely given, informed consent to undergo biopsy and laboratory investigations.

Availability of data and material: Data of this paper is not available publicly but can be requested from the corresponding author in a reasonable time.

Funding: no funding available for both authors.

Conflict of Interest: authors declare no conflict of interest.

Acknowledgment: we would like to thank our patients and all the staff responsible for the delivery of patients' care**.**

Tables:

Table 1: Shows the clinical parameters of the 300 chronic kidney disease patients

Parameters	Male (Mean +/- SD)	Female(Mean +/- SD)		95% CI	P-value
Age (years)	49.57 +/- 16.59	53.66 +/- 16.59		49.31 – 53.13	0.038
BMI (kg/m^2)	28.71 +/- 7.41	27.54 +/- 7.99		26.97 – 29.37	0.336
Parameters	Male (N)	Female (N)	Total	Percentage	P-value
Hypertension	116	93	209	70.13 %	0.036
Diabetes mellitus	88	59	147	49.33 %	0.871
thyroid dysfunction	13	22	35	11.67 %	0.004

Table 2: Shows the biochemical and hematological parameters of the 300 chronic kidney disease patients

Parameters	Male (Mean - SD)	Female (Mean- SD)	95% CI	P-value
TSH (miu/l))	2.379 +/- 7.45	2.272 +/- 3.32	1.63 – 3.03	0.882
T4 (pmol/l)	12.42 +/- 3.70	13.83 +/- 4.18	12.01 – 14.51	0.270
Urea (mmol/l)	13.90 +/- 9.95	15.14 +/- 11.02	13.22 – 15.58	0.311
Creatinine (umol/l)	321.60 +/- 323.58	300.05 +/- 235.72	279.83 – 345.98	0.530
GFR (ml/min/1.73 m^2)	41.83 +/- 28.42	32.24 +/- 26.11	34.80 – 41.13	0.003
Urine PCR (mg/mmol)	312.98 +/- 601.93	466.33 +/- 581.30	299.66 – 445.90	0.043
Hematuria (RBC/H.P. field)	47.83 +/- 79.28	118.14 +/- 541.41	30.96 – 116.70	0.119
Albumin (g/l)	35.43 +/- 6.25	32.63 +/- 6.23	33.57 – 35.02	0.0002
ALP (iu/l)	108.59 +/- 89.77	132.52 +/- 191.44	102.32 – 137.17	0.147
Calcium (mmol/l)	2.37 +/- 0.15	2.39 +/- 0.20	2.36 – 2.40	0.349
Phosphate (mmol/l)	2.16 +/- 7.76	1.38 +/- 0.43	1.16 – 2.53	0.266
PTH (pmol/l)	22.00 +/- 26.02	27.57 +/- 34.97	20.6 – 28.12	0.150
HB (g/dl)	12.42 +/- 2.58	10.86 +/- 2.05	11.50 – 12.07	0.0000
WCC (x10^9/l)	7.13 +/- 2.48	7.46 +/- 3.23	6.94 – 7.58	0.318
PLT (x10^9/l)	259.13 +/- 78.78	275.47 +/- 109.37	255.21 – 276.23	0.133
HBA1c %	6.60 +/- 1.86	6.38 +/- 1.61	6.25 – 6.77	0.411
Glucose (mmol/l)	7.19 +/- 3.49	6.75 +/- 3.12	6.61 – 7.41	0.285
Total cholesterol (mmol/l)	4.83 +/- 1.22	5.07 +/- 1.43	4.76 – 5.09	0.147
LDL (mmol/l)	3.03 +/- 1.05	3.10 +/- 1.18	2.92 – 3.19	0.629
HDL (mmol/l)	1.13 +/- 0.72	1.29 +/- 0.46	1.12 – 1.27	0.048
TG (mmol/l)	1.69 +/- 1.06	1.89 +/- 3.16	1.27 – 2.51	0.460
IgA (umol/l)	2.83 +/- 2.14	2.93 +/- 2.46	2.48 – 3.26	0.801

Table 3: Shows the immunological/virology parameters of the 300 chronic kidney disease patients

Parameters	Male (N)	Female (N)	P-value
ANA (Positive)	9	10	0.450
ANCA (Positive)	1	3	0.130
C3 (low)	8	11	0.111
C4 (low)	1	7	0.006
Virology status			
HBV (Positive)	12	5	0.650
HBC (Positive)	5	4	0.809
HIV (Positive)	0	0	

Table 4: Shows the radiological parameters; DEXA Scan and US abdomen of the 300 chronic kidney disease patients

DEXA	Male (N)	Female (N)	Total	Percentage
Normal	56	61	117	39.0 %
Osteopenia	69	57	126	42.0 %
Osteoporosis	31	26	57	19.0 %
Total	156	144	300	100.0
P value			0.863	
Ultrasound				
Normal US	87	88	175	
Abnormal US	35	90	125	
Total	122	178	300	
P value			0.001	

Table 5: Shows the mean (SD) of various biochemical parameters of the 300 chronic kidney disease patients by their thyroid status, normal vs thyroid dysfunction status.

Parameters	Normal thyroid	Thyroid dysfunction	95% CI	P-value
TSH (miu/l))	1.630 +/- 0.863	7.678 +/- 17.069	1.639 – 3.032	0.0000
T4 (pmol/l)	13.05 +/- 3.33	13.41 +/- 4.48	12.01 – 15.26	0.780
Creatinine (umol/l)	311.60 +/- 299.20	322.77 +/- 233.67	279.83 – 345.98	0.831
GFR (ml/min/1.73 m^2)	39.12 +/- 28.19	29.2 +/- 23 77	34.79 – 41.12	0.047
Urea (mmol/l)	13.93 +/- 9.29	17.92 +/- 16.31	13.22 – 15.58	0.032
Urine PCR (mg/mmol)	350.67 +/- 583.26	555.17 +/- 689.48	299.66 – 445.90	0.087
Hematuria (RBC/HPF)	74.70 +/- 35.26	67.03 +/- 89.17	30.96 – 116.70	0.913
Albumin (g/l)	34.61 +/- 6.16	31.91 +/- 7.53	33.57 – 35.02	0.018
ALP (iu/l)	117.87 +/- 145.60	121.08 +/- 90.24	102.32 – 134.17	0.898
Calcium (mmol/l)	2.38 +/- 0.17	2.37 +/- 0.15	2.36 – 2.40	0.773
Phosphate (mmol/l)	1.91 +/- 6.39	1.36 +/- 0.29	1.16 – 2.53	0.615
PTH (pmol/l)	25.24 +/- 31.15	18.12 +/- 21.76	20.60 – 28.12	0.220
HB (g/dl)	11.94 +/- 2.49	10.56 +/- 2.24	11.50 – 12.07	0.004
WCC (x10^9/l)	7.12 +/- 2.68	8.30 +/- 3.53	6.94 – 7.58	0.019
PLT (x10^9/l)	265.27 +/- 92.54	269.14 +/- 93.58	255.21 – 276.23	0.816
HBA1c %	6.45 +/- 1.72	6.94 +/- 1.94	6.25 – 6.77	0.231
Glucose (mmol/l)	6.99 +/- 3.38	7.14 +/- 3.16	6.61 – 7.41	0.811
Total cholesterol (mmol/l)	4.88 +/- 1.27	5.29 +/- 1.58	4.76 – 5.09	0.104
LDL (mmol/l)	3.00 +/- 1.06	3.47 +/- 1.34	2.92 – 3.19	0.031
HDL (mmol/l)	1.19 +/- 0.66	1.21 +/- 0.426	1.12 – 1.27	0.855
TG (mmol/l)	1.79 +/- 2.26	1.64 +/- 1.03	1.51 – 2.03	0.715
IgA (umol/l)	2.86 +/- 2.30	2.98 +/- 2.05	2.48 – 3.26	0.855

Table 6: Shows the mean (SD) of various biochemical and hematological parameters of the 300 chronic kidney disease patients by their thyroid status, normal versus hypothyroidism status.

Parameters	Normal thyroid	Hypothyroid	95% CI	P-value
TSH (miu/l))	1.630 +/- 0.863	12.159 +/- 20.374	1.711 - 3.163	0.0000
T4 (pmol/l)	13.05 +/- 3.33	10.85 +/- 2.22	10.94 – 13.18	0.044
Creatinine (umol/l)	311.60 +/- 299.20	286.22 +/- 210.29	275.60 – 343.72	0.679
GFR (ml/min/1.73 m^2)	39.12 +/- 28.19	34.00 +/- 26.34	35.46 – 41.98	0.411
Urea (mmol/l)	13.93 +/- 9.29	14.55 +/- 10.76	12.89 – 15.07	0.769
Urine PCR (mg/mmol)	350.67 +/- 583.26	570.42 +/- 726.57	203.07 – 441.67	0.122
Hematuria (RBC/HPF)	74.70 +/- 35.26	59.11 +/- 85.33	28.84 – 118.23	0.857
Albumin (g/l)	34.61 +/- 6.16	31.86 +/- 8.24	33.66- 35.14	0.051
ALP (iu/l)	117.87 +/- 145.60	125.81 +/- 109.57	101.86 – 135.09	0.802
Calcium (mmol/l)	2.38 +/- 0.17	2.38 +/- 0.17	2.36 – 2.40	0.946
Phosphate (mmol/l)	1.91 +/- 6.39	1.31 +/- 0.28	1.15 – 2.58	0.664
PTH (pmol/l)	25.24 +/- 31.15	16.00 +/- 12.21	20.63 – 28.31	0.189
HB (g/dl)	11.94 +/- 2.49	11.25 +/- 2.36	11.60 – 12.18	0.215
WCC (x10^9/l)	7.12 +/- 2.68	8.57 +/- 4.10	6.90 -7.56	0.021
PLT (x10^9/l)	265.27 +/- 92.54	271.18 +/- 84.53	255.05 – 276.39	0.772
HBA1c %	6.45 +/- 1.72	7.23 +/- 2.20	6.59 – 7.42	0.855
Glucose (mmol/l)	6.99 +/- 3.38	7.13 +/- 3.72	6.59 – 7.41	0.811
Total cholesterol (mmol/l)	4.88 +/- 1.27	5.52 – 1.64	4.77 – 5.10	0.033
LDL (mmol/l)	3.00 +/- 1.06	3.67 +/- 1.48	2.91 – 3.19	0.011
HDL (mmol/l)	1.19 +/- 0.66	1.31 +/- 0.46	1.12 – 1.28	0.438
TG (mmol/l)	1.79 +/- 2.26	1.70 – 1.20	1.51 – 2.06	0.852
IgA (umol/l)	2.86 +/- 2.30	3.29 +/- 2.48	2.48 – 3.26	0.611

Table 7: Shows the mean (SD) of various biochemical and hematological parameters of 300 chronic kidney disease patients by their thyroid status, normal vs hyperparathyroidism status.

Parameters	Normal thyroid	Hyperthyroid	95% CI	P-value
TSH (miu/l))	1.630 +/- 0.863	0.095 +/- 0.081	1.452 – 1.665	0.0000
T4 (pmol/l)	13.05 +/- 3.33	16.66 +/- 4.58	12.84 – 16.09	0.023
Creatinine (umol/l)	311.60 +/- 299.20	348.61 +/- 240.33	279.98 – 350.05	0.387
GFR (ml/min/1.73 m^2)	39.12 +/- 28.19	21.07 +/- 16.54	34.97 – 41.58	0.023
Urea (mmol/l)	13.93 +/- 9.29	23.64 +/- 22.23	13.16 – 15.61	0.0009
Urine PCR (mg/mmol)	350.67 +/- 583.26	523.00 +/- 644.16	282.73 – 219.51	0.387
Hematuria (RBC/HPF)	74.70 +/- 35.26	80.50 +/- 98.52	28.87 – 121.05	0.959
Albumin (g/l)	34.61 +/- 6.16	32.00 +/- 6.48	33.76 – 35.22	0.136
ALP (iu/l)	117.87 +/- 145.60	113.07 +/- 44.19	100.82 – 134.46	0.905
Calcium (mmol/l)	2.38 +/- 0.17	2.35 +/- 0.14	2.36 – 2.40	0.563
Phosphate (mmol/l)	1.91 +/- 6.39	1.45 +/- 0.30	1.15 – 2.62	0.794
PTH (pmol/l)	25.24 +/- 31.15	21.99 +/- 33.33	21.04 – 29.14	0.736
HB (g/dl)	11.94 +/- 2.49	9.63 +/- 1.63	11.53 – 12.13	0.001
WCC (x10^9/l)	7.12 +/- 2.68	7.86 +/- 2.35	6.84 – 9.28	0.333
PLT (x10^9/l)	265.27 +/- 92.54	265.69 +/- 110.85	254.28 – 276.30	0.987
HBA1c %	6.45 +/- 1.72	6.35 +/- 1.18	6.18 – 6.71	0.884
Glucose (mmol/l)	6.99 +/- 3.38	7.15 +/- 1.95	6.59 – 7.41	0.869
Total cholesterol (mmol/l)	4.88 +/- 1.27	4.8 +/- 1.14	4.71 – 5.04	0.842
LDL (mmol/l)	3.00 +/- 1.06	3.09 +/- 0.89	2.87 – 3.14	0.809
HDL (mmol/l)	1.19 +/- 0.66	1.01 +/- 0.26	1.10 – 1.27	0.400
TG (mmol/l)	1.79 +/- 2.26	1.52 +/- 0.58	1.49 – 2.06	0.704
IgA (umol/l)	2.86 +/- 2.30	2.49 +/- 1.32	2.44 – 3.24	0.720

References

1. Iglesias P, Bajo MA, Selgas R, Diez JJ. Thyroid dysfunction and kidney disease: An update. Rev Endocr Metab Disord. 2017;18(1):131-44.
2. Lim VS. Thyroid function in patients with chronic renal failure. Am J Kidney Dis. 2001;38(4 Suppl 1):S80-4.
3. Lim VS. Renal failure and thyroid function. Int J Artif Organs. 1986;9(6):385-6.
4. Mariani LH, Berns JS. The Renal Manifestations of Thyroid Disease. Journal of the American Society of Nephrology. 2012;23(1):22.
5. Kaptein EM. Thyroid hormone metabolism and thyroid diseases in chronic renal failure. Endocr Rev. 1996;17(1):45-63.
6. Zoccali C, Mallamaci F. Thyroid Function and Clinical Outcomes in Kidney Failure. Clinical Journal of the American Society of Nephrology. 2012;7(1):12.
7. Ramirez G, O'Neill W, Jr., Jubiz W, Bloomer HA. Thyroid dysfunction in uremia: evidence for thyroid and hypophyseal abnormalities. Ann Intern Med. 1976;84(6):672-6.
8. Xu H, Brusselaers N, Lindholm B, Zoccali C, Carrero JJ. Thyroid Function Test Derangements and Mortality in Dialysis Patients: A Systematic Review and Meta-analysis. Am J Kidney Dis. 2016;68(6):923-32.
9. Zoccali C, Mallamaci F. Thyroid function and clinical outcomes in kidney failure. Clin J Am Soc Nephrol. 2012;7(1):12-4.
10. Zoccali C, Tripepi G, Cutrupi S, Pizzini P, Mallamaci F. Low triiodothyronine: a new facet of inflammation in end-stage renal disease. J Am Soc Nephrol. 2005;16(9):2789-95.
11. Sanai T, Nagashima A, Okamura K, Rikitake S, Fukuda M, Onozawa K, et al. Thyroid function in patients on continuous ambulatory peritoneal dialysis in comparison with chronic kidney disease. Clin Nephrol. 2018;89(3):181-6.
12. Sanai T, Okamura K, Rikitake S, Fukuda M, Onozawa K, Sanematsu M, et al. The high prevalence of reversible subclinical hypothyroidism with elevated serum thyroglobulin levels in chronic kidney disease patients. Clin Nephrol. 2017;87 (2017)(5):237-44.
13. de Souza ABC, Arantes MF, Zatz R, Elias RM, Lopes RI, Macedo E. Influence of low free thyroxine on progression of chronic kidney disease. BMC Nephrology. 2020;21(1):36.
14. Al Alawi I, Al Salmi I, Al Mawali A, Al Maimani Y, Sayer JA. End-Stage Kidney Failure in Oman: An Analysis of Registry Data with an Emphasis on Congenital and Inherited Renal Diseases. Int J Nephrol. 2017;2017:6403985.
15. Al Alawi IH, Al Salmi I, Al Mawali A, Sayer JA. Kidney Disease in Oman: a View of the Current and Future Landscapes. Iran J Kidney Dis. 2017;11(4):263-70.
16. Al Ismaili F, Al Salmi I, Al Maimani Y, Metry AM, Al Marhoobi H, Hola A, et al. Epidemiological Transition of End-Stage Kidney Disease in Oman. Kidney Int Rep. 2017;2(1):27-35.
17. Kaptein EM, Quion-Verde H, Chooljian CJ, Tang WW, Friedman PE, Rodriquez HJ, et al. The thyroid in end-stage renal disease. Medicine (Baltimore). 1988;67(3):187-97.
18. Aljabri KS, Bokhari SA, Al MA, Khan PM. An 18-year study of thyroid carcinoma in the western region of Saudi Arabia: a retrospective single-center study in a community hospital. Ann Saudi Med. 2018;38(5):336-43.

19. Chonchol M, Lippi G, Salvagno G, Zoppini G, Muggeo M, Targher G. Prevalence of Subclinical Hypothyroidism in Patients with Chronic Kidney Disease. Clinical Journal of the American Society of Nephrology. 2008;3(5):1296.
20. Naseem F, Mannan A, Dhrolia MF, Imtiaz S, Qureshi R, Ahmed A. Prevalence of subclinical hypothyroidism in patients with chronic kidney disease on maintenance hemodialysis. Saudi J Kidney Dis Transpl. 2018;29(4):846-51.
21. Verhelst J, Berwaerts J, Marescau B, Abs R, Neels H, Mahler C, et al. Serum creatine, creatinine, and other guanidino compounds in patients with thyroid dysfunction. Metabolism. 1997;46(9):1063-7.
22. Kreisman SH, Hennessey JV. Consistent Reversible Elevations of Serum Creatinine Levels in Severe Hypothyroidism. Archives of Internal Medicine. 1999;159(1):79-82.
23. Shirota T, Shinoda T, Yamada T, Aizawa T. Alteration of renal function in hyperthyroidism: Increased tubular secretion of creatinine and decreased distal tubule delivery of chloride. Metabolism. 1992;41(4):402-5.
24. Aizawa T, Hiramatsu K, Ohtsuka H, Kobayashi M, Koizumi Y, Miyamoto T, et al. An elevation of BUN/creatinine ratio in patients with hyperthyroidism. Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et metabolisme. 1986;18(11):771-4.
25. Abdella A, Ekoon B, Modawe G. The impact of thyroid dysfunction on renal function tests. Saudi Journal of Kidney Diseases and Transplantation. 2013;24(1):132-4.
26. Carrero JJ, Qureshi AR, Axelsson J, Yilmaz MI, Rehnmark S, Witt MR, et al. Clinical and biochemical implications of low thyroid hormone levels (total and free forms) in euthyroid patients with chronic kidney disease. J Intern Med. 2007;262(6):690-701.
27. Pan B, Du X, Zhang H, Hua X, Wan X, Cao C. Relationships of Chronic Kidney Disease and Thyroid Dysfunction in Non-Dialysis Patients: A Pilot Study. Kidney and Blood Pressure Research. 2019;44(2):170-8.
28. Sarnak MJ. Cardiovascular complications in chronic kidney disease. Am J Kidney Dis. 2003;41(5 Suppl):11-7.
29. Biondi B, Klein I. Hypothyroidism as a risk factor for cardiovascular disease. Endocrine. 2004;24(1):1-13.
30. Bough EW, Crowley WF, Ridgway C, Walker H, Maloof F, Myers GS, et al. Myocardial function in hypothyroidism. Relation to disease severity and response to treatment. Arch Intern Med. 1978;138(10):1476-80.
31. Liu X-L, He S, Zhang S-F, Wang J, Sun X-F, Gong C-M, et al. Alteration of lipid profile in subclinical hypothyroidism: a meta-analysis. Medical science monitor : international medical journal of experimental and clinical research. 2014;20:1432-41.
32. Sheymaa G. Study of the effect of hypothyroidism on the serum cholesterol and albumin level in women in Najaf. Kufa Journal for Nursing sciences -inhw.
33. Das C, Sahana PK, Sengupta N, Giri D, Roy M, Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Indian journal of endocrinology and metabolism. 2012;16(Suppl 2):S361-S3.
34. Antonijević N, Nesović M, Trbojević B, Milosević R. [Anemia in hypothyroidism]. Med Pregl. 1999;52(3-5):136-40.

35. Kaynar K, Ozkan G, Erem C, Gul S, Yilmaz M, Sonmez B, et al. An Unusual Etiology of Erythropoietin Resistance: Hyperthyroidism. Renal Failure. 2007;29(6):759-61.
36. Iddah MA, Macharia BN, Ng'wena AG, Keter A, Ofulla AVO. Thryroid hormones and hematological indices levels in thyroid disorders patients at moi teaching and referral hospital, Western kenya. ISRN Endocrinol. 2013;2013:385940-.
37. Koga M, Murai J, Saito H, Matsumoto S, Kasayama S. Effects of thyroid hormone on serum glycated albumin levels: study on non-diabetic subjects. Diabetes Res Clin Pract. 2009;84(2):163-7.
38. Kim MK, Kwon HS, Baek K-H, Lee JH, Park WC, Sohn HS, et al. Effects of Thyroid Hormone on A1C and Glycated Albumin Levels in Nondiabetic Subjects With Overt Hypothyroidism. Diabetes Care. 2010;33(12):2546.
39. Gilles R, den Heijer M, Ross AH, Sweep FC, Hermus AR, Wetzels JF. Thyroid function in patients with proteinuria. The Netherlands journal of medicine. 2008;66(11):483-5.
40. Shantha GPS, Kumar AA, Bhise V, Khanna R, Sivagnanam K, Subramanian KK. Prevalence of Subclinical Hypothyroidism in Patients with End-Stage Renal Disease and the Role of Serum Albumin: A Cross-Sectional Study from South India. Cardiorenal Med. 2011;1(4):255-60.