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Evaluation of Thyroid Function Tests in Chronic Kidney Disease Patients in Tertiary Care Centre of Kumaon Region

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Abstract

Background- The physiological association between kidney and thyroid gland functions is well known from many years. Previous studies had reported that chronic kidney disease is associated with different thyroid gland dysfunctions including; low T3 syndrome, low T4 syndrome, Subclinical hypothyroidism. With the inconclusive background the present study was conducted with following objectives.

Objectives- To assess the thyroid function tests of CKD cases and compare them with controls and evaluate the correlation between thyroid profile parameters with kidney function tests in CKD patients.

Methods- This is a cross-sectional study performed on total 254 subjects, out of which 154 were CKD patients and 100 were sex and age matched controls. CKD cases were further divided into 3 sub-groups depending on their GFR values.

Results- Out of 154 CKD cases 58(39%) were euthyroids .47(30%) CKD patients were found to have low T3 syndrome while 37(24%) patients were reported with low T4 syndrome. Subclinical hypothyroidism was observed in 11(7%) CKD cases. The frequency of these dysfunctions was observed to increase with deteriorating Glomerular Filtration Rate. Overt hypothyroidism and hyper thyroidism was not observed in this study. In this study we found a positive, linear and statistically significant correlation with total T3 and T4 level. However the GFR values in CKD showed a negative, linear but in-significant correlation with TSH level.

Conclusions-The data obtained from this study revealed that there is relationship between kidney and thyroid gland function tests. The most common changes in CKD related to the thyroid gland are of low T3, T4 levels followed by subclinical hypothyroidism. Thus early evaluation of CKD patients for thyroid dysfunction followed by replacement therapy will help in improving clinical outcomes in CKD patients.

Keywords: chronic kidney disease (CKD), Thyroid function, thyroid stimulating hormone (TSH), tri-iodothyronine(T3), Thyroxine(T4).

Introduction

Chronic kidney disease (CKD) previously called as chronic renal insufficiency or failure, is characterized by gradual progressive and irreversible loss of excretory, synthetic and regulatory functions of kidney for 3 or more

months and, with or without decreased glomerular filtration rate (GFR) or GFR < 60 ml/min per 1.73 m2 (1,2). It is a silent disease as around 50% CKD patients with severely reduced kidney function but not on dialysis are unaware of harboring the disease and are first seen when the eGFR is <15 ml/min per 1.73 m2 i.e. in End stage renal disease (ESRD), a condition of permanent loss of kidney function requiring dialysis or transplantation(2).The reported prevalence of CKD in different regions in India ranges from <1% to 13% (3) while recently epidemiologic renal data system have demonstrated the kidney disease prevalence of around 17% worldwide (4). The risk factors for development of CKD include hypertension, diabetes mellitus and other endocrine disorders, infections, auto immune diseases, cancer and toxic chemicals (5,6,7). Apart from these, the role of developmental biology, genetics and evolution are also important for development of life time risk of CKD (8). CKD is a chronic condition that leads to high medical costs, increased risks for developing life-altering and life-threatening complications, and contributes to significant morbidity and mortality in patients afflicted with this disease (9).

Thyroid Hormones (TH) plays an important role in growth, development, and physiology of the kidney as these are necessary for the maintenance of electrolyte and water homeostasis, directly by affecting the glomerular /tubular kidney function and the structure of the kidney itself (10,11). Indirectly TH affects the renin–angiotensin system, haemodynamic and cardiovascular alterations that interfere with renal blood flow (12,13).

On the other hand Kidney is involved in the metabolism and regulation of thyroid hormones and is an important target organ for TH actions. Therefore, the impairment of kidney function in CKD patients leads to alterations in regulation of the hypothalamic-pituitary-thyroid axis, changes in the synthesis, secretion, metabolism, and elimination of TH(14,15). The kidney also contributes to the iodine clearance primarily by glomerular filtration. Excess of serum iodine in CKD patients has been correlated with increased prevalence of goiter and hypothyroidism (16). Although several studies have suggested that CKD patients may have various thyroid functional test alterations including low tri-iodo thyronine (T3), normal or reduced thyroxine (T4) levels, and normal or elevated thyroid-stimulating hormone (TSH) yet the results are uncertain(12,17-20).

Material and Methods

This is a cross sectional study performed after permission from institutional ethical committee. Study was conducted on total 254 subjects , of which cases were 154 patients diagnosed to have CKD and on conservative management in the age group 18 -70 years, of both sex, being admitted in Department of Medicine of Susheela Tiwari hospital , a teaching hospital which receives referral from within and outside the state of location, during the period of August 2017 to June 2019. 100 age and sex matched subjects were included as controls for valid comparison.

An informed written consent was taken from the patients and controls before the collection of blood sample. The subjects were selected based on following inclusion and exclusion criteria.

1-Cases

Inclusion criteria - The patients were diagnosed as CKD based on clinical profile and renal function tests as per The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF K/DOQI GUIDELINES)(1). The stages of CKD were defined according to the American National Kidney Foundation(1) Stage 1, eGFR of 90 ml/min/1.73 m^2 or greater;

Stage 2, eGFR 60–89 ml/min/1.73 m^2;

Stage 3, eGFR 30–59 ml/min/1.73 m^2;

Stage 4, 15–29 ml/min/1.73 m^2; and

Stage 5, eGFR less than 15 ml/min/1.73 m^2 or dialysis

CKD patients in stage III, IV and V who were on conservative management were included as cases eGFR was calculated using modified diet and renal disease (MDRD) formula. GFR=186.3× (serum creatinine in mg/dl) -1.154×age in yrs-0.203.Multiply by 0.742 for women. (1)

Exclusion criteria - CKD patients who were on or underwent previous dialysis, subjects younger than 18 years, patients of hyper or hypothyroidism, nephrotic syndrome, taking estrogens, corticosteroids and beta blockers, anti-thyroid drugs, schizophrenia, obesity, cancer, hepatitis, pregnant woman

2- Controls - consisted of 100 non-hospitalized adults matched for age and sex with no history of systemic disease attending medicine OPD for some minor illness.

Laboratory investigations - 5 ml venous blood was withdrawn from each subject after 12-14 hrs fast in EDTA, fluoride and plain vials .On processing the samples, laboratory investigations performed included blood sugar, kidney function tests (urea, creatinine, uric acid), HbA1c,serum proteins (Total protein / albumin / globulin) , Serum electrolytes (sodium, potassium) , Serum calcium, phosphorous and thyroid function tests (T3,T4, TSH). Total T4, T3 level estimations were based on the principle of competitive chemiluminescent immunoassay and that of TSH on ultra sensitive sandwich chemiluminescent immune assay (CLIA). These tests were performed in Roche Cobas E411. Serum Na^+, K^+, Ca^{+2} were analysed in Roche 9180 Electrolyte Analyser and rest of the parameters were estimated in fully auto analyser Roche Cobas - 501.

Statistical Analysis: The results were expressed as Mean ± SD. Data obtained was analyzed using unpaired Student's t-test and Pearsons correlation analysis was performed to elucidate the relationships between eGFR and TSH, T3, T4 levels. A *P* value less than 0.05 was considered statistically significant level and p <0.001 was considered as highly statistically significant.

Results

Table I shows the base line parameters of study subjects; controls (n=100) and CKD subjects (n=154) .121 (78%) of the CKD subjects were males and rest 33 (22%) were females. The mean age of CKD subjects was 54.6 ± 10.66 years and of controls was 59.9 ± 11.72 years. Majority (54%) of the patients were in age group 55-65 years. Body Mass Index in kg/m2 of CKD cases and controls was 26.82 ± 3.35 and 28 .82 ± 5.89 respectively.

Table II shows the mean ± SD values of biochemical tests performed in study subjects. Mean TSH level (µIU/ml) in CKD subjects was not significantly higher than control group 3.12 ± 1.34 vs 2.71 ± 0.79; p =0.142.

A statistical significant decrease in T3 value(ng/ml) in two groups was seen (0.92 ± 0.36 vs 1.37 ± 0.25; p<0.001).

The mean T4 level(µg/dl) was also decreased in CKD cases as compared to controls(6.71 ± 2.54 vs 9.41 ± 1.56; p<0.0001).The mean level of urea (20.31 ± 4.78 vs 104 .41 ± 38.32 mg/dl; p<0.001), creatinine(0.64 ± 0.13 vs 6.51 ± 2.24 mg/dl ; p<0.0001) and GFR (107.8 ± 22.46 vs14.91 ± 6.39 ml/min/1.73 m2 ; p<0.001) level in CKD cases were significantly raised as compared to controls.

Mean ±SD values of total proteins(g/dl), albumin(g/dl) and albumin :globulin ratio were 5.84 ± 0.76 g/dl vs7.12 ± 0.34, 2.81 ± 0.61g/dl vs3.62 ± 0.58 and 0.96 ± 0.34 vs 1.13 ± 0.36 in CKD cases and controls respectively .They were found to be significantly reduced in CKD cases w.r.t controls with p value< 0.001. mean sodium level (meq/l)

was significantly reduced in CKD cases than control group (133.21 ± 7.32 vs142.92 ± 10.89 p<0.05) while potassium level (meq/l) was higher in CKD cases as compared to controls (4.75 ± 1.56 vs 3.68 ± 1.13 ; p<0.05) Statistically significant reduction in mean total calcium (mg/dl)was observed in CKD cases than controls(7.18 ± 0.98 vs 10.72 ± 1.24 ; p< 0.001) while phosphorus level(mg/dl) was raised in CKD cases than control group (7.6 ± 2.34 vs 4.2 ± 1.02; p< 0.001)

In present study 154 chronic kidney disease subjects were divided into following 3 groups based on their CKD grade (GFR in ml/min/1.73m2)

Group I : stage III (GFR ≥ 30)

Group II : stage IV (GFR -15-30)

Group III: stage V (GFR <15)

Table III – shows the comparison of kidney disease thyroid function tests and kidney function tests with each other and with control group . Majority 94 (61%) of CKD subjects were in group III . 22(14 %) and38 (25 %) were in group I and II respectively.

The mean level of TSH in group I was comparable with control group (2.82 ± 0.82 vs 2.71 ± 0.79; p 0.672) and group II(2.82 ± 0.82 vs2.91 ± 0.96; p 0.459)while in group III mean value of TSH (4.01 ± 1.12)was significantly raised in comparison with group II (p<0.05)and III(p<0.05). Total T3 level in group I shows no significant alterations when compared with controls(1.28 ± 0.67 vs 1.37 ± 0.25; p=0.095)and group II (1.28 ± 0.67 vs 1.09 ± 0.34; p=0.084).Statistically low T3 level was also there in group III than group II (1.09 ± 0.34 vs 0.72 ± 0.21;p<0.01). A significant reduction in total T3 level was observed in group III in this study when compared with Group I (0.72 ± 0.21 vs 1.28 ± 0.67; p <0.001) and group II (0.72 ± 0.21 vs 1.09 ± 0.34 p<0.01).

The mean total T4 level in group I was comparable with controls (8.72 ± 3.18 vs 9.41 ± 1.56 p=0.127) as well as with group II (8.72 ± 3.18 vs 7 .94 ± 3.52 ; p=0.178) while statistical significant reduction was seen in total T4 when group III was compared with group I (4.3 ±2.24 vs 8.72 ± 3.18 ;p <0.001) and group II (4.3 ± 2.24 vs 7 .94 ± 3.52 p<0.05).

Mean urea level in controls, group I, II, III was 20.31 ± 4.78, 8.72 ± 3.18, 7.94 ± 3.52 and 4.3 ± 2.24 respectively. Significant elevation levels were seen when compared among each other and controls with p<0.001.

Statistically significant raised creatinine was observed in group I(1.32 ± 0.28), II(2.01±0.91) , III (5.62 ± 2.24) when compared with controls (0.64 ± 0.13) as well with each other (p value < 0.0001).

As shown in table IV, in this study we observed the decrease in GFR with the progression of kidney disease. GFR level showed negative and linear but non-significant correlation with the TSH level in CKD subjects. However with total T3 and total T4 we found a positive linear and significant correlation with the GFR. The urea levels in CKD cases shows a positive but non statistically significant correlation with TSH levels while no correlation was there between urea and total T3 and T4 levels.

As shown in table V- the analysis of thyroid function tests in present study revealed that 61% of CKD cases shows thyroid dysfunctions. Out of which majority (30%) had low T3 levels (low T3 syndrome) followed by 24 % having low T4 levels (low T4 syndrome). Of these 12% of patients had both low T3 and T4 levels with normal TSH values. The remaining 7 % had higher TSH; 4.2-10 µIU/ml with total T3 and total T4 within normal range (subclinical hypothyroidism).

Table-I-Baseline demographic characteristics of study subjects

Parameters	**Controls**		**CKD Cases**	
Age (years)	(n=100)	percentage	(n = 154)	Percentage
25-40	14	14 %	15	10%
41-55	32	32 %	45	30%
56-70	45	45%	83	54%
≥71 (up to 75)	9	9%	11	6%
Mean age	54.6 ± 10.66		59.9±11.72	
No. of males.	72	72%	121	78%
No. of females	28	28%	33	22%
BMI (kg/m2)	26.82 ± 3.35		28 .82 ± 5.89	

Table II: Biochemical parameters analysed in study groups

Biochemical tests	**Normal range**	**Controls**	**CKD Cases**	**p value**
TSH	0.27-4.2 µIU/ml	2.71 ± 0.79	3.12 ± 1.34	0.142
Total T3	0.85-2.02 ng/ml	1.37 ± 0.25	0.92 ± 0.36	<0.001
Total T4	4.8-11.6 µg/dl	9.41 ± 1.56	6.71 ± 2.54	<0.001
Urea	10-45 mg/dl	20.31 ± 4.78	104 .41 ± 38.32	<0.0001
Creatinine	0.8-1.4 mg/dl	0.64 ± 0.13	6.51 ± 2.24	<0.0001
GFR(ml/min/1.73m2)	120-145 ml/min/m^2	107.8 ± 22.46	14.91 ± 6.39	<0.0001
Total proteins	6.0-8.0 g/dl	7.12 ± 0.34	5.84 ± 0.76	<0.001
Albumin	3.5-5.5 g/dl	3.62 ± 0.58	2.81 ± 0.61	<0.001
Albumin: globulin	1.2:1 -1.5:1	1.13 ± 0.36	0.96 ± 0.34	<0.001
Sodium	135-145mEq/l	142.92 ± 10.89	133.21 ± 7.32	<0.05
Potassium	3.5-5.4mEq/l	3.68 ± 1.13	4.75 ± 1.56	<0.05
Total calcium	9-11 mg/dl	10.72 ± 1.24	7.18 ± 0.98	<0.001
Phosphorus	2.5-5.0mg/dl	4.2 ± 1.02	7.6 ± 2.34	<0.001

Table III : Comparison of biochemical parameters among cases of different stages of CKD and with controls

Biochemical parameters	Controls	Group I GFR≥30	Group II GFR=15-30	Group III GFR < 15	P value			
	n=100	n=22(14 %)	n=38 (25%)	n=94(61%)	GI vs Controls	GI vs G II	GI vs G III	GII vs G III
TSH	2.71 ± 0.79	2.82 ± 0.82	2.91 ± 0.96	4.01 ± 1.12	0.672	0.459	<0.05	<0.05
Total T3	1.37 ± 0.25	1.28 ± 0.67	1.09 ± 0.34	0.72 ± 0.21	0.095	0.084	<0.001	<0.01
Total T4	9.41 ± 1.56	8.72 ± 3.18	7 .94 ± 3.52	4.3 ± 2.24	0.127	0.178	<0.001	<0.05
Urea	20.31 ± 4.78	68.82 ± 9.78	81.71 ± 10.76	129.41 ± 24.12	<0.001	<0.001	<0.001	<0.001
Creatinine	0.64 ± 0.13	1.32 ± 0.28	2.01±0.91	5.62 ± 2.24	<0.001	<0.001	<0.001	<0.001

Table IV : Correlation analysis among thyroid function tests, urea and GFR of CKD cases

Thyroid Function	GFR	Urea
TSH	p 0.0065 r - 0.6327	p 0.139 r +0.452
Total T3	p 0.0036 r + 0.721	p 0.265 r - 0.0948
Total T4	p 0.0022 r + 0.086	p 0.382 r - 0.0184

Table V : Interpretation of thyroid function tests and number of CKD patients

Thyroid dysfunction	No. of patients	Percentage of patients
Euthyroids	58	39%
Low T3 syndrome	47	30%
Low T4 syndrome	37	24%
Subclinical hypothyroids	11	7%

Discussion

In the present study when subjects were divided according to age, we found that 54% of CKD cases were in age group of 56-70 years . This finding is in accordance with the study by Zhang and Rothenbacker (21) which reported the prevelance of CKD varying from 23.4% to 35.8% in persons above 60 years in comparison to 7.2% in population less than 30 years. Various epidemiologic studies had revealed that higher prevelance of other non communicable diseases like obesity, hypertension and diabetes in elderly population may contribute to higher morbidity and mortality associated with CKD (5,6,7). In this study majority (78%) of the patients were males .This observation supports study by Kastarinen, Wakaei et al which reported CKD predominance in men than women population(22). Experimental animal studies by Goldberg and Krause had suggested that the gender related contrasts observed in CKD patients may be due to the impact of sex hormones on several mechanisms included in kidney injury (23). Out of 154 CKD patients included in this study 94 (61%) were in stage V according to National Kidney Diseases Foundation guidelines (1). This could be due to the fact that in tertiary care centre most of the patients are referred from remote hilly regions of kumaon . In addition, study conducted by Ene-Lorache et al revealed that due to lack of awareness and low socioeconomic status, patients in developing nations attend hospital when renal disease has already progressed to end stage (24). The serum level of urea and creatinine are routine tests performed to determine the efficiency of kidneys in filtering the blood. The glomerular filteration rate, considered as gold standard to determine CKD and its stage (1,2,25). Beside this calculations of GFR by MDRD equation ,we also used serum creatinine value. In this study ,the serum urea and creatinine values were significantly higher in CKD patients when compared among each other and with controls. These results were in accordance with previous studies which explains that the significant irreversible loss of nephrons leads to decrease in renal clearance of urea, creatinine and other nitrogenous substances and hence their accumulation in the blood (12,14,19,21). In addition hyperuricemia was observed in this study. This is in agreement with observations by Tae Ryom Oh which suggests that reduction in plasma flow and glomerular filteration rate results in decrease uric acid ,renal excretion and its accumulation in plasma with the progression of kidney disease(26).

The serum level of total protein and albumin was significantly lower in CKD patients. Lopez Giacoman et al (27) and other studies explained higher degree of proteinuria, a traditional marker of declining kidney function could be responsible for hypoproteinemia and hypoalbuminemia in CKD patients (28,29). In addition recent studies by Daniela Verzol et al suggested that inflammation in CKD affects cellular signaling and its transcriptional program that promotes protein degradation and decreased synthesis of proteins in CKD (30). According to Chung et al marked alterations of total body water and recurrent changes in plasma volume disturb albumin turn over and subsequently serum albumin values (31). Friedman and Fadem in a study had demonstrated serum albumin serum as a trustworthy and dependable marker of nutritional status as well as response to nutritional medication in patients of kidney diseases (32). In present study derangement of minerals level was observed. Normally calcium and phosphorous are regulated by a complex interaction between kidney, bone and gut in conjunction with a network of endocrine hormones (33). In several studies the balance of these

hormones and minerals were demonstrated to be altered even in early stages of CKD. The serum calcium was reduced while phosphorus level was significantly elevated in this study. This finding further add data to other studies that explained that the declining kidney function leads to reduction of calcitriol production which reduces absorption of dietary calcium that could be responsible for hypocalcemia observed in CKD cases (34,35). The reduction of phosphorous filtration and its excretion with progression of renal failure may explain high phosphate level in this study. In addition, various studies had shown that secondary hyperparathyroidism in response to hypocalcemia or hyperphosphatemia may further disturb mineral metabolism in uremic patients (36). Clinical studies by Hu Mc et al had suggested the derangements of Klotho/fibroblast growth factor-23 axis by various mechanisms affects mineral metabolism in CKD. Such alterations in minerals have been associated with increased risk of cardiovascular diseases in these patients (37).

In present study the principal observation is the alteration in thyroid function tests in chronic kidney disease subjects with the progression of declining renal function tests. We found that 39% of CKD cases were euthyroids. In this study Low total T3 level was the most common thyroid dysfunction observed. This is in consistent with previous authors suggesting low T3 levels as marker of illness in CKD patients (12,14,18,21). Under normal circumstances 80% of T3 is produced by peripheral conversion of T4 hormone produced in thyroid gland by the action of 5'deiodinase, requiring selenium as cofactor (18). In CKD cases Brzezinska-Slebodzinska et al had demonstrated higher free radicals and lower selenium levels which indirectly decreases T3 level (38). In addition certain medications, and in the presence of high serum cortisol and free nonesterified fatty acid levels, it has been suggested that low T3 levels are a marker of illness in CKD patients (39). As investigated in previous studies the deiodinase activity is also affected in chronic metabolic acidosis, fasting, increased level of inflammatory cytokines (20,40,41). Apart from the above mechanisms, protein malnutrition have also been implicated as causative factors for low T3 syndrome in CKD patients (42). Hypoalbuminemia was also observed in this study which further adds data to the earlier studies suggesting impaired protein binding of T3 in CKD cases. In this study the levels of T3 are comparable in controls and CKD patients with GFR >30ml/min/1.73m2. While the T3 level was reduced significantly in group III than group II when compared among each other. This finding supports Song and coworkers showing the decrease in T3 level with advancement of stages in CKD cases (43). In addition, Fan J et al in a study had reported that decreased T3 is associated with inflammation and cardiovascular damage in end stage renal disease patients and so low T3 level can be a marker of disease severity and survival in CKD patients (44).

Low total T4 level was observed in 24% of CKD patients of group III with GFR <30ml/min/m2. No significant reduction was observed in group I and group II patients when compared with controls and with each other. While a statistically significant low level of T4 was seen in group III patients with increased severity of disease when compared with group II and I CKD cases. In study by Allawi et al (45), The reduction in T4 level was explained by the presence of inhibitors of T4 binding to thyroxine binding globulin in these uremic patients. Normal or low levels of T4 may also be due to the monodeiodinase action occurring in the inner benzene ring instead of outer ring of T4, resulting in the formation of reverse T3 (15,18).Since

the vast majority of circulating T4 is bound to proteins, including thyroid-binding globulin, transthyretin, albumin, and lipoproteins, studies suggests that total T4 levels may be false low in low-protein states of CKD patients.(20,29,31,32)

Serum TSH is considered as specific and most sensitive single biochemical measure of thyroid function by the physicians in general population. It is typically used for screening, diagnosis, and treatment monitoring and titration in primary hypothyroidism (25). In present study we had observed that serum TSH was raised in group III patients with GFR < 15ml/min/1.73m2 than in group I and group II. This suggests that TSH remains normal until the onset of end stage renal disease while Total T3 and T4 were decreased in group II patients with moderately reduced GFR. Various studies had demonstrated that certain TSH alterations such as impaired clearance, protracted half-life, blunted pulsatility, altered glycosylation leading to impaired bioactivity, and decreased response to TRH (15,17,46,47).

In present study & 7 % of CKD cases presented with subclinical hypothyroidism. Previous large observational studies had also show that hypothyroidism is highly prevalent in kidney disease patients . In a study of 461,607 US veterans with Stages 3 to 5 CKD who underwent serum TSH testing 23% had hypothyroidism. Across these studies, a large proportion of cases have been due to subclinical hypothyroidism (48). In Third National Health and Nutritional Examination Survey (NHANES III) ,there was an incrementally higher prevalence of hypothyroidism with increasing severity of kidney dysfunction: 5, 11, 20, 23, and 23% with estimated glomerular filtration rates (eGFRs) of ≥90, 60–89, 45–59, 30–44, and <30 ml/ min /1.73m2, respectively. Out of these 56% of hypothyroid cases were due to subclinical disease (49). In another study performed by Chonchol M, demonstrated subclinical primary hypothyroidism as a relatively common condition (~18%) among persons with CKD not requiring chronic dialysis, and it was found to be independently associated with progressively lower estimated GFR(50).

The limitation of this study is that the thyroid function disorders in kidney disease patients were not studied according to the etiology of disease.

To summarize, in this study we observed thyroid dysfunctions with increasing decline of renal function tests in patients with CKD .Low T3 syndrome is the most frequent thyroid function derangement seen, while subclinical hypothyroidism was observed in ESRD subjects. No case of hyper or overt hypothyroidism was observed.

Conclusion

From the data obtained from this study the relationship between kidney and thyroid function tests was observed. It will help to increase clinical knowledge and enable the clinicians to provide better management of their patients who have kidney or thyroid dysfunction. We suggest evaluation of CKD patients for thyroid function tests at all stages, as the appropriate therapeutic intervention for their thyroid disease would decrease chance of developing or exacerbating renal dysfunction.

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