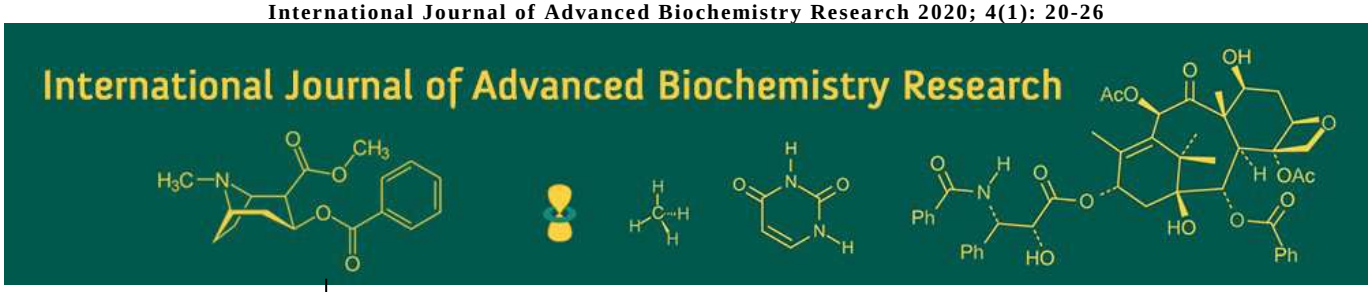

ISSN Print: 2617-4693
ISSN Online: 2617-4707
IJABR 2020; 4(1): 20-26
www.biochemjournal.com
Received: 15-11-2019
Accepted: 17-12-2019

Dr. Aruna Kumari T
Associate Professor,
Department of Biochemistry,
Kakatiya Medical College,
Warangal, Telangana, India

Dr. Anil Kumar G
Assistant Professor,
Department of Biochemistry,
Kakatiya Medical College,
Warangal, Telangana, India

Corresponding Author:
Dr. Anil Kumar G
Assistant Professor,
Department of Biochemistry,
Kakatiya Medical College,
Warangal, Telangana, India

A Study of thyroid dysfunction in chronic kidney disease Patients in a tertiary Care Hospital - A Prospective study

Dr. Aruna Kumari T and Dr. Anil Kumar G

DOI: https://doi.org/10.33545/26174693.2020.v4.i1a.43

Abstract
Background: Abnormal thyroid function tests are frequently observed in patients of chronic kidney disease. Kidneys plays a significant role in thyroid hormone metabolism by conversion of T4 to T3 (the active metabolite). Low plasma free T3 in ESRD is a marker of the inflammation and endothelial activation and is known to predict all cause mortality.
Aim & objective of the study: The present study was done look for the biochemical abnormalities of thyroid function tests in chronic Kidney Disease and to correlate the severity of CKD and alterations of thyroid indices.
Methods: In a cross-sectional study, thyroid function test [TT3, TT4, FT3, FT4, TSH] were estimated by CLIA in 60 patients of chronic Kidney Disease who were in various stages. Symptoms of hypothyroidism, thyroid hormone abnormalities and chronic renal failure patients with different CKD stage were analyzed using Chi square test and ANOVA tests.
Results: Among the mean age was 54.2 ± 12.5 years of which 45 were male and 15 females. The mean value of TT3 in CRF stage 3, 4, 5 were 110.6 ± 17.8; 94.9 ± 29.4; 77.9 ± 29.5 ng/mL respectively (p= 0.02 Significant). The mean value of FT3 in CRF stage 3, 4, 5 were 2.52 ± 0.31; 2.08 ± 0.54; 1.89 ± 0.61 pg/mL respectively (p=0.03 Significant). The mean value of TT4 in CRF stage 3, 4, 5 were 6.47 ± 0.67; 5.12 ± 1.16; 4.41 ± 1.52 µg/dL respectively (p=0.0 significant). The mean value of FT3 in CRF stage 3, 4, 5 were 1.19 ± 0.15; 1.02 ± 0.22; 0.98 ± 0.21 pg/dL respectively (p=0.07 Not significant).
Conclusions: Total T3, total T4 and free T3 were found to be progressively decreased as stage of CKD increased. There was no significant correlation between FT4 and CKD stage. There was a significant correlation between the prevalence of thyroid dysfunction and the stage of chronic kidney disease. Higher the degree of renal insufficiency, the higher was the prevalence of thyroid hormone abnormalities, the levels of thyroid profile i.e T3, T4 decreases and TSH increases as severity of renal failure increases. Thyroid hormone abnormalities could represent a risk factor for cardiovascular disease and might also be implicated in kidney disease progression.

Keywords: Chronic kidney disease, Thyroid Function Test, Hypothyroidism

Introduction
As morbidity and mortality from infectious diseases declined, life expectancy has increased and chronic degenerative diseases have become more prevalent. CKD is unique amongst the chronic non-infectious illnesses [1].
It has been estimated from population survey data that at least 6% of the adult population in the United States has CKD at stages 1 and 2. An unknown subset of this group will progress to more advanced stages of CKD. An additional 4.5% of the U.S. Population is estimated to have stages 3 and 4 CKD. The most frequent cause of CKD is Diabetic Nephropathy, most often secondary to Type 2 DM [2].
India being the diabetic capital of the world, Diabetic Nephropathy is the commonest cause of CKD. There are about 7.85 million CKD patients in India [3].
Patients with End Stage Renal Disease display a variety of endocrine disturbances. However the evidence of endocrine dysfunction commonly consists only of laboratory abnormalities, many of which are not associated with apparent clinical signs and symptoms of the disease [4].
Among which Thyroid function has been extensively evaluated in patients with CRF. CRF is a widely recognized cause of non-thyroidal illness causing thyroid dysfunction, i.e., alteration in thyroid hormones in the absence of underlying intrinsic thyroid disorder [5].

Chronic renal failure affects thyroid function in multiple ways, including low circulating thyroid hormone concentration, altered peripheral hormone metabolism, disturbed binding to carrier protein possible reduction in tissue thyroid content and increased iodine stores in thyroid glands. TT3, TT4, FT3 are decreased more commonly in patients with CRF. But FT4, TSH levels are normal in these patients and indicate thyroid status. We speculate that the low thyroid state in uremia serves to defend against protein wasting and misguided attempts to replete thyroid hormone stores may worsen protein malnutrition [6].

Some studies showed an increased incidence of subclinical hypothyroidism in CKD patients and higher prevalence of hypothyroidism in patients with terminal renal failure. It has been estimated that primary hypothyroidism may occur in up to 9.5% of ESRD patients when compared to 1.1% of general population [7].

When hypothyroidism becomes more severe it can cause reduced cardiac function and lead to progressively worsening kidney function. Thus the prevalence of sub clinical hypothyroidism in patients with CKD might be a risk factor for both cardiovascular disease and progressive kidney disease.

This study is designed to determine the prevalence of thyroid dysfunction in CKD patients in order to intervene at an early stage depending upon the hormone abnormalities and reduce both the cardiovascular risk and progressive worsening of kidney function.

Aims and Objectives of the Study

Study of biochemical abnormalities of thyroid function tests in chronic Kidney disease and also correlate the severity of chronic kidney disease and alterations of thyroid indices.

Materials and Methods

Source of data: 50 patients both male and female patients with CKD over period of 11/2 year admitted in Government General Hospital attached to Kakatiya Medical College, Warangal were included under study.

Study Period: Study was conducted between March 208 and August 2019 for a period of 18 months.

Sample Size: 60 patients both male and female patients with CRF over period of 11/2 year admitted in Government General Hospital attached to Guntur Medical College, Guntur.

Inclusion Criteria

- Symptoms of uremia for 3 months or more.
- Ultrasound evidence of chronic renal failure

1. Bilateral contracted kidneys- size less than 8 cm in male and size less than 7cms in female
2. Poor corticomedullary differentiation.

- Supportive laboratory evidence of CKD like anemia, urine specific gravity, changes in serum electrolytes, etc.,
- Patients with CKD more than 18 years.

Exclusion Criteria

- < 15yrs Patients
- Patients who have been diagnosed to be having thyroid disorder.

Patients on drugs altering thyroid profile like amiodarone, steroids dopamine, phenytoin, oestrogen pills, iodine containing drugs.

- Patients on thyroid hormone replacement or on ant thyroid drugs.

Study Design

Single Centre, cross sectional study. In the study period of 18 months among patients admitted in General Medicine &Nephrology wards after applying inclusion and exclusion criteria 50 patients were included in this study. Patients who fulfilled the criteria for CKD and who are on conservative management and hemodialysis. Informed consent was obtained from all patients.

After selecting the patients, fulfilling the above criteria, about 5ml of blood sample is collected in non heparinised serum bottle and sent for thyroid profile. Components of thyroid profile in this study are serum total triiodothyronine (TT3), serum total thyroxine (TT4), serum thyroid stimulating hormone (TSH), serum free triiodothyronine (FT3), serum free thyroxine (FT4).

Kidney function was assessed by estimated creatinine clearance which was calculated by using the Cockcroft – Gault Equation.

1. Cockcroft – Gault Equation: Estimated creatinine clearance (ml/mt)

$$= \frac{(140\text{-Age}) \text{ X Ideal body weight in K.G.}}{72 \text{ X SCr (mg/dl)}}$$

(Multiply by 0.85 for women)

Thyroid function was assessed by measuring TT3, TT4, FT3, FT4 and TSH level in serum.

Serum TT3, TT4, FT3 and FT4 were estimated by competitive Chemiluminescent immuno assay. TSH estimation was done by ultrasensitive sandwich chemiluminescent immuno assay (CLIA).

Blood urea estimation was done by using diacetyl monoxime (DAM) method. Serum creatinine estimation was done by modified kinetic Jaffe method.

Detailed clinical history and clinical examination was undertaken with preference to thyroid and renal diseases. The following investigations were performed.

1. Urine for specific gravity and broad cast.
2. Peripheral smear for anemia and burr cells.
3. Renal parameters like blood urea, Serum creatinine and Creatinine clearance (using Cockcroft - Gault formula).
4. Serum calcium and phosphorus.
5. Serum cholesterol in hypothyroidism.
6. 24 hours urine protein and serum protein to rule out nephrotic syndrome and Hypoproteinemia respectively.
7. ECG and chest x ray to look for features for hypothyroidism and renal failure, pleural effusion, pericardial effusion.
8. USG abdomen for evidence of chronic renal failure.

Limitations of the study

Small sample size. (Only 60 patients)

Prevalence of hypothyroidism increases as the age advances. So we have to consider the influence of age on hypothyroidism.

Geographical variation of goiter and thyroid problems

Statistical Analysis

The information collected regarding all the selected cases were recorded in the master chart. Data analysis was done with the help of computer using The Statistical software namely SPSS 20.0.

Results

In our study we evaluated 60 patients with various grades of Chronic Renal Failure.

Table 1: Sex distribution

Sex	Cases	
	n =	%
Male	45	75
Female	15	25
Total	60	100

Among 60 patients in the sample 45 patients were males, and 15 patients were females.

Table 2: Age Distribution

Age Group (yrs)	Cases	
	n=	%
21 – 30	6	10
31 – 40	7	11.66
41 – 50	12	20
51 – 60	25	41.66
>60	10	16.66
Total	60	100
Range	21 to 69 yrs	
Mean	52.5 yrs	
S.D	12.5 yrs	

The range was from 21 to 69 years. Most of the patients in the sample were in the age group of 51-60 years. And mean age was 54 years.

Table 3: Prevalence of Diabetes Mellitus and Hypertension

Cases	HTN					
M	YES	%	NO	%	Total	%
YES	15	25%	20	33.33%	35	58.33%
NO	10	16.66%	15	25%	25	41.66%
TOTAL	25	41.66%	35	58.33%	60	100%

Of the 60 patients with CRF, 35 patients (58.33%) were diabetic, and 25 patients (41.66%) were hypertensive. 15 patients (25%) were having both diabetes and hypertension. 10 patients (16.66%) were neither having diabetes nor hypertension.

Table 4: Prevalence of symptoms of hypothyroidism

Symptoms	Cases	
	n=	%
Yes	15	25
No	45	75
Total	50	100

Symptoms of hypothyroidism like tiredness, somnolence, weight gain, cold intolerance, constipation, hoarseness of voice etc., were studied in the study population.

Of the 60 patients with CKD, 15 patients (25%) only were symptomatic and majorities (75%) were asymptomatic. Biochemically 6 patients were hypothyroid and rests 9 were in subclinical hypothyroid range.

Table 5: Prevalence of goitre

Goitre	Cases	
	n=	%
Yes	10	16.66
No	50	83.33
Total	60	100

Of 60 patients with CRF 10 patients (16.66%) had goitre which was present as diffuse thyroid swelling.

Table 6: Prevalence of patients in various CRF stage

CRF Stage	Cases	
	n=	%
3	10	16.66
4	15	25
5	35	58.33
Total	60	100

Of the 60 patients, 10 patients (16.66%) were in stage 3, and 15 patients (25%) in stage 4 and 35 patients (58.33%) in stage 5.

Table 7: Prevalence of thyroid dysfunction based on thyroid function tests

Thyroid status	Cases	
	n=	%
Hypothyroidism	6	10
Subclinical Hypothyroidism	9	15
Some other hormonal abnormalities	20	33.33
Normal	25	41.66
Total	60	100

Of the 60 patients in this sample, 6 patients (10 %) had hypothyroidism 9 patients (15%) had subclinical hypothyroidism 20 patients (33.33%) had some thyroid hormone abnormalities like FT3↓; TT4,TT3↓; TT4,TT3,FT3↓; TT4↓. Totally 35 patients (58.33%) had some thyroid dysfunction.

Out of 60 patients 15 had symptoms suggestive of hypothyroidism, of which 2 patient (13.33%) was in stage 4 CRF and rest 13 patients were in stage 5 CRF. Though symptoms were prominent in advanced renal failure, this correlation was statistically not significant.

Of the 60 patients in this study group, 35 patients had stage 5CKD. The prevalence of goiter was 0% in stage 3 CKD and stage 4 CKD and 18% in stage 5 CKD. The higher the stage of CKD, the higher was the prevalence of goiter, however this relation is statistically not significant of the 60 patients in the study group, 35 patients had stage 5 CKD. 12.1 % of stage 5 CKD pts. had hypothyroidism when compared to stage 3 (0%) and stage 4(0%). A 18% of patients of stage 5 CKD had sub clinical hypothyroidism when compared to stage 3(0%) and stage 4 (10%). Some hormone abnormalities in stage 3 is 0%

and in 4 &5 CKD were 50% and 42.4% respectively. So higher the stage of CKD, higher was the prevalence of thyroid dysfunction. This correlation was found to be statistically significant.

Blood urea and Serum Creatinine in our study

The mean blood urea was 73.7 ± 8.4; 93.2 ± 12.1; 130.2 ± 28.6 mg/dL, and serum creatinine was 2.86 ± 0.49; 3.48 ± 0.37; 7.55 ± 2.09 mg/dL in stages of CRF 3,4,5 respectively. The mean blood urea was 141± 13.5; 121.9 ± 33.8; 94.1 ± 20.8 mg/dL and serum creatinine was 8.73± 2.20; 6.50 ± 2.40; 4.41 ± 1.66 mg/dL in patients with thyroid function tests showing normal, subclinical and overt hypothyroidism respectively. Blood urea and serum creatinine level increased as stage of CKD increases and also in patients with TFT showing hypothyroid compared to normal patients. This correlation was statistically significant.

T3 in our study

The average Total T3 (TT3) value was 85.66 ng/mL. The mean value of TT3 in CRF stage 3, 4, 5 were 110.6 ± 17.8; 94.9 ± 29.4; 77.9 ± 29.5 ng/Ml respectively.

TT3 was decreased in 14 patients of whom 4 were hypothyroid. 10 patients who were in CRF stage 5 without symptoms of hypothyroidism had decreased TT3 of which 6 patients had associated decreased TT4 and 4 patients had decreased TT4 and FT3 (graph15). According to our study as CKD stage increases there was progressive decrease in TT3 levels and is statistically significant.

The average Free T3 (FT3) value was 2.02 pg /mL. The mean value of FT3 in CRF stage 3, 4, 5 were 2.52± 0.31; 2.08 ± 0.54; 1.89 ± 0.61 pg/mL respectively.

FT3 was decreased in 14 patients of which 4 were hypothyroid and rest 10 had decreased FT3 without any symptoms of hypothyroidism. 2 patients had isolated decrease in FT3 who were in stage 4, 4 patients had associated decrease in TT4 and 4 patients had decreased TT4 and TT3 (graph15). There was progressive decrease in FT3 as renal dysfunction increases and was statistically significant.

T4 in our study

The average Total T4 (TT4) value was 4.84 µg/dL. The mean value of TT4 in CRF stage 3, 4, 5 were 6.47 ± 0.67; 5.12 ± 1.16; 4.41 ± 1.52 µg/dL respectively. TT4 was decreased in 21 patients of which 4 were hypothyroid and rest 17 had decreased TT4 without any symptoms of hypothyroidism. 3 patients had isolated decrease in TT4 who were in stage 4, and 6 patients had associated decrease in TT3 and 4 patients had associated decreased FT3 and 4 patients had decreased TT3 and FT3. There was progressive decrease in TT4 as renal dysfunction increases and was statistically significant.

The average Free T4 (FT4) value was 1.02 pg/dL. The mean value of FT3 in CRF stage 3, 4, 5 were 1.19± 0.15; 1.02 ± 0.22; 0.98 ± 0.21 pg/dL respectively. Only 4 patients had decreased FT4 levels and all were hypothyroid. There was decrease in FT4 as CKD stage increases but this was statistically not significant.

TSH in our study

Values of TSH vary from 0.77-22.4 µIU/m L with mean value in 5.43 µIU/mL. Among the 50 patients, TSH was normal in 39 patients (78%) and In 7 patients (14%) with subclinical hypothyroidism TSH values were between 9.62 and 12.34 µIU/ml and 4 patients with hypothyroidism TSH values varied between 12.1 to 22.4 µIU/ml.

TSH level increased as stage of CKD increased and this correlation was statistically significant. Ultra sound abdomen showed evidence of CRF in all patients. Bilateral contracted kidney was present in 86% of the patients and remaining 14% patients had poor corticomedullary differentiation.

This study was designed to determine the prevalence of thyroid dysfunction in CKD patients in order to intervene at an early stage depending upon the hormone abnormalities and reduce both the risk of cardiovascular disease and progression of kidney dysfunction.

Discussion

The kidney normally plays an important role in the metabolism, degradation, and excretion of several thyroid hormones. It is not surprising therefore that impairment in kidney function leads to disturbed thyroid physiology. All levels of the hypothalamic-pituitary-thyroid axis may be involved, including alterations in hormone production, distribution, and excretion [8].

A large number of hormonal systems are affected by CKD, yet it remains unclear to what extent these changes are responsible for manifestations of uremic syndrome.

Patients with CKD often have signs & symptoms suggestive of thyroid dysfunction & hence the diagnosis of thyroid disease in these patients has obvious prognostic implications.

Several investigators have studied thyroid hormone levels in CKD and obtained variable results. Overall 15% of patients with CKD had subclinical hypothyroidism. 10% of patients with mild CKD had low thyroid function, compared to 18% of those with moderate CKD.

Sinha *et al.* [9] studied 90 patients with CKD and found thyroid dysfunction in 38.6% patients with CKD. The most common thyroid dysfunction being subclinical hypothyroidism 27.2%. Prevalence of subclinical hypothyroidism in stage 3, stage 4 & stage 5 was 15.2%, 32% and 43.3% respectively.

Higher prevalence of thyroid dysfunction was observed in patients with CKD. Increasing trend for TSH level across CKD stage 3-5 which suggest that TSH level increases with progression of renal impairment.

In our study 58.33% of the patients with CKD had thyroid dysfunction and the most common being the subclinical hypothyroidism. 15% were subclinical hypothyroid and the prevalence of subclinical hypothyroidism in stage 4& stage 5 was 10.1% and 18% respectively differed from sinha *et al.* due to small number of patients in the study. Our study correlated with Sinha *et al.* [10] in TSH level which has increasing trend across CKD stage 3-5 that suggest TSH level increases with progression of renal impairment.

In our study, 25% of subjects with stage 4 are subclinical, 12.1% with stage 5 are hypothyroid, 18.2% with stage 5 were subclinical.

Ng *et al.* [11] reported that 98(80.3%) were having euthyroidism, 19 (15.6%) were subclinical hypothyroidism, 5 (4.1%) were subclinical hyperthyroidism, in peritoneal dialysis patients of Taiwan.

In Our study 9 (15%) were subclinical hypothyroidism which correlated with Ng *et al*. Differed from that study in

view of subclinical hyperthyroidism which was not seen in our study [11].

Balaji R *et al.* [12] reported that there was significant decrease in levels of T3, T4 in CKD patients when compared to controls. Reduction in T3 concentrations has linked to a decrease in the peripheral synthesis of T3 from T4.

In Our study also there is significant decrease in levels of TT3, TT4 in CKD patients which correlated with Balaji R *et al.* Mean values of TT3 were 110.6,94.9,77.9 in CKD patients with stage 3,stage 4,stage 5 respectively. Mean values of TT4 were 6.47,5.12,4.41 in CKD patients with stage 3, stage 4, stage 5 respectively.

Singh P A *et al.* [13] reported that 75% of undialysed CRF patients presented with diminished T4 levels. Low levels of both T3 and T4 could also be due to defective release in response to TSH.

Our study reported significant decrease in levels of TT3, TT4, FT3 and no significant variation in FT4 levels in CKD patients with stage 3 to stage 5.

In our study prevalence of subclinical hypothyroidsm (14%) and overt hypothyroid (8%).There is increased prevalence of subclinical 10% in stage 4, 18.2% in stage 5 CKD patients and overt hypothyroidism in 12.1% in stage 5 CKD patients.

In a study by Ramesh C [14] the prevalence of subclinical hypothyroidism in patients with GFR >90ml/min/1.73m^2 is 7% where as in patients with an eGFR <60ml/min/1.73m^2 the prevalence of hypothyroidism is 17.9%.There was significant inverse association between estimated GFR and TSH levels throughout the normal and high ranges.

In Our study the prevalence of subclinical hypothyroidism 14% and hypothyriodism 8%.The mean TSH levels increased with severity of renal failure i.e 2.07, 3.68,6.29 in CKD stage 3,stage 4 and stage 5 respectively but in normal and high ranges.

Jingxian Fan *et al.* [15] studied 279 CKD patients 149 males, 130 females with mean age 67.8.Among all patients 4.7% (n=13) had subclinical hypothyroidism, 5.4% (n=15) had low T4 syndrome and 47% had low T3 syndrome. The prevalence of low T3 syndrome increased as kidney function decreased ranging from 22.2% for persons with CKD 1 to 76% in persons with ESRD. By contrast there was no significant change in TSH, TT4 & FT4 across the estimated GFR

Our study conducted in 50 CKD patients with 37 males, 13 females with mean age 51.2 years. Among all patients 14% (n=7) had subclinical hypothyroidism, 8% (n=4) had hypothyroidism. There is significant change in TT4 and TSH but no significant change in FT4.

In Chonchol *et al.* [16] study the prevalence of subclinical hypothyroidism is 18%. It has been estimated the prevalence of subclinical hypothyroidism ranges from 4 & 10 % in general population &between 7 and 26% in elderly.

In Our study the prevalence of subclinical hypothyroidism is 14% somewhat correlated with chonchol *et al*. study.

In Singh S *et al.* [17] study serum TSH concentration was within normal range in 36(94.73%).Study also found low FT3 in 44.73% as well as low FT4 in 28.94% with TSH normal in 94.73%.5.26% stage 5 CKD patients had TSH level increased above normal range with FT3 & FT4 within the normal limit.

In our study 12.1% stage 5 CKD patients had increased TSH and were hypothyroid and 18.2% stage 5 CKD patients had slight increase in TSH values and were considered as subclinical hypothyroid.

Lim V S *et al.* [18] demonstrated that marked reduction in serum TT3 concentration are common in CKD. Decreased TT3 result from

1. Decreased T3 binding capacity.
2. Increased hormone catabolism.
3. Reduced T3 secretion.
4. Decreased peripheral T4 to T3 conversion.

Our study also showed significant decrease in TT3 in CKD patients and is correlated with Lim *et al*. study. The mean values of TT3 were 110.6, 94.9,77.9 in stage 3, stage4, stage5 CKD patients respectively.

In Rajeev *et al.* [19] study serum TT3 concentration was significantly lower than normal range in majority of CKD patients. One third of CKD patients had significantly lower TT4 concentration. Serum TSH concentration was significantly increased in 60% of CKD patients.

Our study correlated with Rajeev *et al.* study in that there is significant reduction in serum TT4 concentration in majority of CKD patients.

Quion-verde *et al*. have also reported higher prevalence of up to 5% of frank hypothyroidism in patients with chronic Kidney disease, in comparison with hospitalized patients with normal renal function (0.6%) [20].

In the majority of studies, TT4 concentrations were found to be low or low normal. However, FT4 levels were within normal limits. This is attributed to lowering of thyroxine binding globulin concentration as well as presence of inhibitors of thyroid hormone bindings to the thyroid binding proteins.

Avasthi *et al.* [21] showed that mean T3 level was reduced below normal in GFR less than 10 ml/min. In higher GFR, it was present in low normal and there was no linear correlation between T3 level and GFR.

In our study, study of thyroid dysfunctions in chronic renal failure is done with 50 cases. Cases were selected according to inclusion and exclusion criteria which are mentioned earlier. The cases and controls included different age groups. The range was from 21 to 69 years. Most of the patients in the sample were in the age group of 51-60 years.

Of the 50 patients studied, 4 patients (8%) had hypothyroidism, 7 patients (14%) had subclinical hypothyroidism and 19 patients (38%) had some thyroid hormone abnormalities in the form of reduction in TT3, TT4 and FT3 levels. So totally 60% of patients with CKD had some thyroid hormone abnormalities.

Among 19 patients with some thyroid hormone abnormalities 2 patients (4%) had only decreased FT3, 3 patients (6%) had only decreased TT4, 6 patients(12%) had decreased TT3 and TT4, 4 patients(8%) had decreased TT4 and FT3, 4 patients (8%) had decreased TT3,TT4 and FT3.All these patients were thyroid and TSH levels were within normal limits.

Excluding hypothyroidism and subclinical hypothyroidism, the mean TSH level in our study is within normal limits. The mean TSH levels are also within normal limits for the various ranges of GFR. But TSH level does show any linear correlation with the severity of

renal failure. This is consistent with the study conducted by Joseph *et al.* and Hardy *et al.* [22].

These studies demonstrated abnormality in hypophyseal mechanism of TSH release in uremic patients as the TSH response to the TRH was blunted.

Other studies conducted by Ramirez *et al.* [23] revealed low T3 T4 level with high TSH level suggesting maintenance of pituitary thyroid axis.

In our study total 10 patients were having symptoms suggestive of hypothyroidism of which 4 were hypothyroid biochemically and rest 6 patients had TFT was in subclinical range. Thus some of the symptoms of CKD tend to be overlap with hypothyroidism and may pose difficulty in diagnosis.

Out study is consistent with the results Ramirez *et al.* [23] study showing low T3, low T4 and normal or mild elevation of TSH.

Ramirez *et al.* [23] and associates, reported high prevalence up to 58% of goitre in patients with CKD as compared to 8% in control are as from the same geographic area especially those on chronic dialysis. The possible explanation is due to accumulation of iodides in Thyroid gland due to decreased renal clearance in CRF patients.

In our study, out of the 60 patients studied, 5 patients (10%) had goitre all were in stage 5 CRF. Out of 5 patients with goiter 4 were hypothyroid and one was sub clinically hypothyroid.

Relationship between CRF stage and thyroid dysfunction

Higher the stage of CKD, there is an increased prevalence of thyroid dysfunction in CRF patients [24].

In our study, 12.1% of stage 5 CKD patients had hypothyroidism when compared to stage 3 (0%) and stage 4 (0%). 6 patients of stage 5 patients had subclinical hypothyroidism when compared to no patients in stage 3 and 1 patient in stage 4. Some hormone abnormalities according to stage 4 found in 5 and 14 patients respectively.

TT3, TT4, FT4 levels progressively decreased as the CRF stage increased but FT4, TSH levels were normal except in patients with overt hypothyroidism. Even though symptoms of hypothyroidism were prominent in advanced stage of renal disease, statistical analysis did not show significant correlation.

So many traditional and nontraditional risk factors are therefore cardiovascular disease and its related morbidity and mortality.

A part from them hypothyroidism and subclinical hypothyroidism are linked to an increased risk of cardiovascular disease and reduced cardiac function.

Patients with CKD are at greatly increased risk of thyroid dysfunction. ― Thyroid hormone abnormalities could represent a risk factor for cardiovascular disease and might also be implicated in kidney disease progression‖. [16]

Conclusions

In our study, the overall prevalence of thyroid dysfunction is 60% in patients with chronic kidney disease. 8% of CKD patients had hypothyroidism. There is no hyperthyroidism in our study. 14% had subclinical hypothyrodism. 38% had some thyroid hormone abnormalities. 10% of CKD patients had goiter. There was a significant correlation between the prevalence of thyroid dysfunction and the stage of chronic kidney disease. Higher the degree of renal insufficiency, the higher was the prevalence of thyroid hormone abnormalities, the levels of thyroid profile i.e. T3, T4 decreases TSH increases as severity of renal failure increases (i.e., as serum creatinine increases). Excluding hypothyroidism and subclinical hypothyroidism, the mean TSH level in our study is within normal limits which indicate abnormality in hypophyseal mechanism of TSH release in uremic patients as the as the TSH response to the TRH was blunted.

Acknowledgement

The author is thankful to Department of Biochemistry for providing all the facilities to carry out this work.

Conflict of interest: None

References

1. Ashok L.K, Hardik S. Chronic kidney disease, API text book of medicine, 9th edition, 2 page, 2012; 19(4) 1295-1301.
2. Joanne M.B, Karl S, Chronic kidney disease, Harrison‘s principles of internal medicine, 19th edition, part 13, chapter 335; 1811 to 1821.
3. Suresh C and Sanjay K.A, Incidence of chronic kidney disease in India, Nephrol Dial Transplant. 2006; 21(1):232-233.
4. Knochell JP. Endocronic changes in patients on chronic dialysis, In: replacement of function by dialysis‖, W. Drukker, FM Parsons, JF Maher, editors, 2nd edition, Boston: Martinus Nijhoff Publishers. 1983; 712- 723.
5. De Groot LJ: Dangerous Dogmas in Medicine: The non-thyroidal illness syndrome, J.Chin endocrine metabol. 1999; 84: 151-164.
6. Lim VS: Thyroid function in patients in CRF; Am J Kidney disease. 2001; 38(Supplement 1):880-884.
7. Lo JC, Cherton GM, Go AS, HSU CY: Increased prevalence of subclinical and clinical hypothyroidism in persons with chronic kidney disease, Kidney Int 2005; 67(3):1047-1052.
8. J Larry Jameson, Anthony P, Weetman. Disorders of the thyroid gland, Harisson‘s Endocrinology. 2nd Edn; chapter 4; 2010, 62-98.
9. Sinha V, Kumar A, Kachhawa P, Agrawal S. Thyroid dysfunction and dyslipidemia in patients with chronic kidney diseases. International Journal of Medical Science and Public Health. 2016; 5(12).
10. Sinha V, Kumar A, Kachhawa P, Agrawal S. Thyroid dysfunction and dyslipidemia in patients with chronic kidney diseases. International Journal of Medical Science and Public Health. 2016; 5(12).
11. Ng YY, Wu SC, Lin HD, Hu FH, Hou CC, Chou YY *et al.* Prev-alence of clinical and subclinical thyroid disease in a peritoneal dialysis population. Perit Dial Int 2012; 32(1):86-93.
12. Rajagopalan B, Dolia PB, Arumalla VK, Seshadri Reddy V. Renal function markers and thyroid hormone status in undialyzed chronic kidney disease, Al Ameen J Med Sci. 2013; 6(1):70-4.
13. Singh PA, Bobby Z, Selvaraj N, Vinayagamoorthi R.An evaluation of thyroid hormone status and oxidative stress in undialyzed chronic renal failure

patients, *Indian Journal of Physiology and Pharmacology*. 2006; 50:279–284.
14. Ramesh C, Kumar MP, Batthini G. Study of Hypothyroidism in Chronic Kidney Disease Patients, Indian Journal of Applied Research. 2016; 13:6(6).
15. Fan J, Yan P, Wang Y, Shen B, Ding F, Liu Y. Prevalence and Clinical Significance of Low T3 Syndrome in Non-Dialysis Patients with Chronic Kidney Disease, Medical science monitor: International Medical Journal of experimental and Clinical Research. 2016; 22:1171.
16. Chonchol M, Lippi G, Salvagno G, Zoppini G, Muggeo M, Targher G. Prevalence of subclinical hypothyroidism in patients with chronic Kidney disease. Clin J Am Soc Nephrol. 2008; 3:1296-300.
17. Singh S, Verma A, Aryal G, Thapa S. Prevalence of thyroid hormone abnormalities in stage 5 chronic kidney disease: a tertiary care center study of Nepal, International Journal of Research in Medical Sciences. 2016; 4(9):3929-33.
18. Lim VS, Fang VS, Katz AI, Refetoff SA. Thyroid dysfunction in chronic renal failure, J Clin Invest. 1977; 60:522-34.
19. Rajeev G, Rayappa WD, Vijayalakshmi R, Swathi M, Kumar S. Evaluation of thyroid hormone levels in chronic kidney disease patients. Saudi Journal of Kidney Diseases and Transplantation. 2015; 1;26(1):90.
20. Kaptein EM, Quion-verde H, Chooljian CJ: The thyroid in end-stage renal disease. Medicine (Baltimore). 1988; 67:187–197,
21. G Avasthi, S Malhotra, APS Narang, S Sengupta. Study of thyroid function in Patients of chronic renal failure; Indian J Nephrol. 2001;11: 165-169
22. Hardy MJ. Pituitary – Thyroid function in chronic renal failure assessed by a highly sensitive thyrotropin assay; J clin Endocrinol metab. 1988; 66:233-6.
23. Ramirez G. Thyroid dysfunction in uraemia. Evidence for thyroid and hypophyseal abnormalities. Ann Inter med. 1976; 84:672-6.
24. Hollander JG, Wulkan RW, Mantel MJ, Berghout A. Correlation between severity of thyroid dysfunction and renal function Clin Endocrinol. 2005; 62(4):423-7.