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Correlation of Serum T3, T4, TSH with Chronic Kidney Disease

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Abstract
Aims and Objectives: *Correlation of serum T3, T4, TSH with Chronic kidney disease patients.*
Material and Methods: *The present study was undertaken at Maharana Bhupal Govt. Hospital, attached to R.N.T. Medical College Udaipur (Raj.).*

- *Patients admitted with sign and symptoms due to deranged renal functions were stratified into stages of CKD according to guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)]*
- *Methods of measurement of GFR: Cockroft-Gault formula was used.*
- *Clinical history was recorded including age, sex, weight, height, primary renal diagnosis, and Blood pressure, history of diabetes and smoking.*
- *Blood samples were collected in the non-fasting state.*
- *Descriptive statistical analysis was carried out in this study.*

Observation and Conclusion: *In this study population, 100 patients of various stages of CKD (II to V) were included. They were non-diabetic, and were not on dialysis.*
Serum T3 differed between chronic kidney disease stages, being more commonly decreased in more advanced chronic kidney disease. Serum T4 differed between chronic kidney disease stages, being more commonly decreased in more advanced chronic kidney disease. Serum TSH differed between chronic kidney disease stages, being more commonly increased in more advanced chronic kidney disease. Prevalence of hypothyroidism with chronic kidney disease was 31% .31 out of 100 patients had hypothyroidism. Out of which 29 had subclinical hypothyroidism (0% in stage II, 16% in stage III, 40% in stage IV, and 60% in stage V) and 2 had overt hypothyroidism (8% in stage V).
According to this study all CKD patients should undergo for thyroid function evaluation as these patients are definitely associated with development of hypothyroidism.

Introduction

Chronic renal failure (CRF) refers to an irreversible deterioration in renal function which classically develops over a period of years. Initially it manifests only as a biochemical abnormality eventually loss of excretory, metabolic & endocrine functions of the kidney. This leads to the development of the clinical symptoms &signs, which are referred to as uremia. Death is likely to occur without renal replacement.

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a

progressive decline in Glomerular Filtration Rate (G.F.R).

In 2002, the NKF (National Kidney Foundation) defined CKD: (1) Kidney damage for ≥ 3 months, as confirmed by kidney biopsy or markers of kidney damage with/without a decrease in G.F.R.

And/or

(2) G.F.R < 60 ml/min/1.73m^2 for ≥ 3 months with/without kidney damage. (Kidney damage is ascertained by either kidney biopsy or markers of kidney damage such as proteinuria, abnormal urinary sediments or abnormalities on imaging studies).

There is a widely accepted classification, based on guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)], in which stages of CKD are defined according to the estimated G.F.R.

Classification of Chronic Kidney Disease (CKD)

STAGE	0	I	II	III	IV	V
GFR(ml/min/1.73m^2)	>90	≥90	60-89	30-59	15-29	<15 ESRD

Thyroid Function in Chronic Kidney Disease

Patients with CRF often have signs and symptoms of thyroid dysfunctions. Various studies of thyroid functions in uremic patients have been carried out which have shown conflicting results. Hypothyroidism, hyperthyroidism & euthyroid state have all been reported by various workers.

Serum Tri-iodothyronine (T3) level were consistently found to be low, serum total &free thyroxine (T4) concentration have been reported as low, normal or high. Serum thyroid stimulating hormone (TSH) levels were found to be normal in most of the patients of CRF even in those whose CRF is complicated by low T3 concentration.

Serum hormonal concentration may be altered by changes in the binding capacity of serum proteins. In CRF there is massive proteinuria mainly albuminuria. Globulin levels are not much altered. Hypothyroidism in CRF is mainly due to decreased level of albumin & thyroid binding pre-albumin.

In CKD Circulating thyroid binding inhibitors are increased, which inhibits the binding of thyroid hormones to carrier proteins; it may be an additional cause for hypothyroidism.

Plasma TSH levels are not increased in spite of low T3 & T4 levels. It is notdue to dysfunction in hypothalamo-pitutary axis but because truly hypothyroid renal failure patients can mount a high TSH response. But some studies show that normal TSH response is due to blunted TSH response to TRH. Suggesting probability of pituitary dysfunction as well. Duration & Severity of renal failure affects the Serum thyroid hormone levels. Restoration of normal functions with renal transplant resulted in normalisation of all parameters of thyroid function with exception of blunted or absent TSH response to TRH. The latter may be a direct consequence of glucocorticoid administration.

Because of these variabilities in previous studies a definite change in thyroid hormone levels in CRF is yet to be determined. So study of thyroid hormone levels in CKD taken in various 2nd, 3rd, 4th and 5th stages.

Aims and Objectives

This study was conducted at Maharana Bhupal Govt. Hospital attached to R.N.T Medical College, Udaipur (Raj.) to know "Correlation of serum T3 , T4 , TSH in Chronic kidney disease patients.''

1. To estimate thyroid hormone levels i.e. T3, T4 and TSH in patients of chronic renal failure.
2. Estimation of blood urea and serum creatinine for selection of patients.

Material and Methods

The present study entitled "correlation of serum T3, T4, TSH with chronic kidney disease" was undertaken at Maharana Bhupal Govt. Hospital, attached to R.N.T. Medical College Udaipur (Raj.).

(1) Patients

1. Patients admitted with signs and symptoms due to deranged renal functions were stratified into stage IICKD (GFR =60-89 mL/min/1.73m^2), stage III CKD (GFR = 30-59 mL/min/1.73 m^2), stage IV CKD (GFR = 15-29 mL/min/1.73 m^2) and end stage, V (GFR =<15 mL/min/1.73m^2) according to guidelines of the National Kidney Foundation [Kidney Dialysis Outcomes Quality Initiative (KDOQI)]

2. Methods of measurement of GFR:

Cockroft-Gault formula as follows:

Males: (140 - age) x weight (kg)/ 72 x serum creatinine (mg/100 mL)

Females: 0.85 (140 - age) x weight (kg)/ 72 x serum creatinine (mg/100 mL)

3. Clinical history was recorded including age, sex, weight, height, primary renal diagnosis, and Blood pressure, history of diabetes and smoking.

(2) Sample Analysis

1. Blood samples were collected in the non-fasting state.

2. Serum creatinine was measured by buffered kinetic Jaffe's reaction method on SIEMENS AUTOANALYSER.

3. Blood urea estimation- Urea nitrogen method employs a urease/glutamate dehydrogenase coupled enzymatic activity done on SIEMENS AUTOANALYSER.

4.Thyroid function test was measured with the COBAS e 411 ANALYSER, which is an automated random-access; multi-channel analyzer for immunological assay (Roche Diagnostic Ltd).It is designed for both qualitative and quantitative in vitro determination of a wide range of analytes by use of electro-chemiluminescence technology.

Statistical Methods

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Inclusion Criteria

1. Patients with chronic kidney disease stage II to stage V who were non-diabetic, non – pregnant and not on dialysis.
2. Patients who himself or his relatives given consent.

Exclusion Criteria

1. Patients having acute renal failure.
2. Patients on dialysis.
3. Patients having GFR >90 ml/min. per 1.73 m^2.
4. Patients with diabetic nephropathy, patients on treatment with estrogen, corticosteroids, sulphonylurea, phenol barbitones & beta-blocker.
5. Patients with chronic liver diseases.
6. Patients having high bilirubin level.

Observations

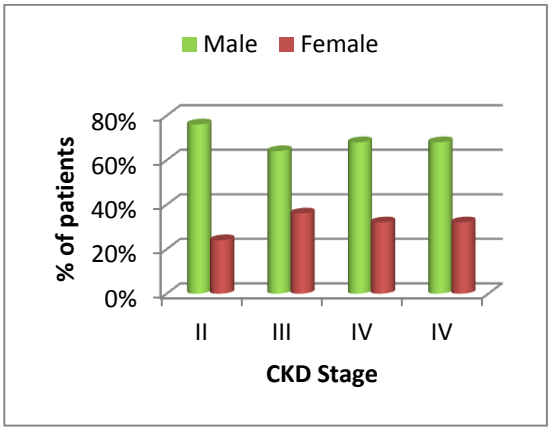
The present study constitutes 100 patients with chronic kidney failure who met inclusion criteria and exclusion criteria. They were selected from the patients admitted in medical wards, nephrology ward and OPD of M.B.G. Hospital, attached to R.N.T. Medical College, Udaipur (Rajasthan). The following tables highlight the most pertinent observations:-

Table 1. Distribution of patients in study

CKD stage	GFR(mL/min/1.73 m^2)	No. of patients	%
II	80-89	25	25.0
III	30-59	25	25.0
IV	15-29	25	25.0
V	<15	25	25.0
Total		100	100.0

100 patients were divided into various CKD stages (stage II –V).Each stage contains 25 patients. Out of 100 patients 69 (69%) were male. Out of these 69(69%) male patients 19 belong to

CKD stage II, 16 patients belong to stage III,17 patients were in stage IV and 17 patients were in stage V. Out of 100 patients 31(31%) were female patients and in this group 6 females were in stage II,9 were in stage III,8 females were in stage IV,and another 8 females were in stage V.



Patient's age ranged from 18-85 yrs. 16 (16%) patients were in age group18-29 yrs. 54 (54%) patients were in age group 30-49yrs. 30(30%) patients were in age group 50 yrs. and above.

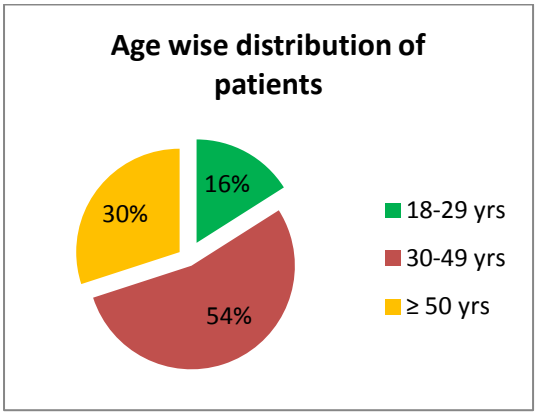


Table 2. Distribution of patients according to blood urea level

Blood Urea level (mg/dl)	No. of patients	%
<100	26	26.0
100-200	48	48.0
>200	26	26.0
Total	100	100

Blood urea ranged between 65 to 377 mg/dl. 26 (26%) patient's blood urea level was <100mg/dl, 48(48%) patient's blood urea level was in 100-200 mg/dl range,26 (26%) patient's urea level was >200 mg/dl. The mean of urea was 163.49±85.54 mg/dl. Mean of blood urea level increases as the stage of CKD increases. (p-0.001).

Table-3.Distribution of patients according to S. creatinine level

S. creatinine level (mg/dl)	No. of patients	%
<3.0	51	51.0
3.1-5.0	19	19.0
>5.0	30	30.0
Total	100	100

Serum creatinine ranged from 1.42-12.7 mg/dl. 30(30%) patient's s.creatinine was >5mg/dl, 19(19%) patient's s.creatinine level was 3.1-5.0 mg/dl range, 51(51%) patient's s.creatinine was <3.0 mg/dl range. Mean s.creatinine was 3.99±2.64mg/dl. Mean of serum creatinine increases as the stage of CKD increases. (p-0.002).

Table-4. Distribution of patients according to S.T3 levels

S.T3 levels(nmol/L)	Stage				Total
	II	III	IV	V	
1.30-3.10	24 96.0%	20 80.0%	15 60.0%	9 36.0%	68 68.0%
<1.30	1 4.0%	5 20.0%	10 40.0%	16 64.0%	32 32.0%
Total	25 100.0%	25 100.0%	25 100.0%	25 100.0%	100 100.0%

P value = 0.0009

24 patients of stage II,20 patients of stage III,15 patients of stage IV,9 patients of stage V had serum T3 level within normal range(1.30-3.10nmol/L).1 patient of stage II,5 patients of stage III,10 patients of stage IV, and 16 patients of stage V had serum T3 level below 1.30nmol/L. Mean T3 was 1.62±0.74nmol/l. Mean of serum T3 level decreases as the stage of CKD increases.

Table 5 Distribution of patients according to S.T4 levels

S.T4 levels(nmol/l)	Stage				Total
	II	III	IV	V	
66.0-180.0	24	23	19	14	80
	96.0%	92.0%	76.0%	56.0%	80.0%
< 66.0	1	2	6	11	20
	4.0%	8.0%	24.0%	44.0%	20.0%
Total	25	25	25	25	100
	100.0%	100.0%	100.0%	100.0%	100.0%

P value = 0.001

24 patients of stage II,23 patients of stage III,19 patients of stage IV,14 patients of stage V had serum T4 level within normal range (66.0-180 nmol/L). One patient of stage II,2 patients of stage III,6 patients of stage IV, and 11 patients of stage V had serum T4 level below 66.0nmol/L. Mean T4 was 1.0001 ± 26.26nmol/l. Mean of serum T4 decreases as the stage of CKD increases.

Table-6. Distribution of patients according to serum TSH level

Serum TSH levels(µIU/ml)	Stage				Total
	II	III	IV	V	
0.270-4.20	25	21	15	8	69
	100.0%	84.0%	60.0%	32.0%	69.0%
4.21-10.0	0	4	10	15	29
	.0%	16.0%	40.0%	60.0%	29.0%
> 10.0	0	0	0	2	2
	0.0%	0.0%	0.0%	8.0%	2.0%
Total	25	25	25	25	100
	100.0%	100.0%	100.0%	100.0%	100.0%

P value = 0.000

25 patients of stage II,21 patients of stage III,15 patients of stage IV,8 patients of stage V had serum TSH level within normal range (0.27-4.20µIU/ml) 4 patients of stage III,10 patients of stage IV,15 patients of stage V had serum TSH level between 4.21-10.0µIU/ml. Only 2 patients of CKD stage V had serum TSH level >10.0 µIU/ml. Mean TSH was 4.69 ± 6.61 µIU/ml. Mean of serum TSH increases as the stage of CKD increases.

Table 7. Comparison of study variables according to the stage of chronic kidney disease

Variables	CKD stages				P value
	II	III	IV	V	
Age (years)	34.84±8.68	44.92±14.18	45.08±15.38	46.88±11.75	0.007
Male	19 (76%)	16 (64%)	17 (68%)	17 (68%)	0.828
Female	6 (24%)	9 (36%)	8 (32%)	8 (32%)	
Weight (kg)	65.00±4.78	66.04±7.97	63.40±9.58	65.84±6.88	0.591
Blood urea (mg/dl)	89.68±16.55	125.68±41.24	188.56±76.01	250.05±82.51	0.001
S. creatinine (mg/dl)	1.51±0.12	2.26±0.47	4.55±0.99	7.64±1.98	0.002
S.T3 (nmol/L)	2.34±0.54	1.91±0.71	1.29±0.33	0.94±0.40	0.002
S.T4 (nmol/L)	1.41E2±26.26	1.11E2±29.96	79.41±18.88	67.88±21.87	0.004
S.TSH (µIU/ml)	2.90±0.84	3.01±1.19	4.37±0.67	8.48±12.52	0.007

As above data showed, among different study variables of CKD stage II,III,IV and V patients, significant P value (< 0.05) seen in of Blood urea, serum creatinine, serum T3,serum T4 and serum TSH level measurements.

Discussion

In our study prevalence of hypothyroidism with chronic kidney disease was 31%.31 out of 100 patients had hypothyroidism. Out of which 29 had subclinical hypothyroidism and 2 had overt hypothyroidism. It shows that prevalence of hypothyroidism increases with decrease in GFR which is comparable to the study done by Lo JC, Chertow GM, Go AS, Hsu CY.

32 patients were having low T3 syndrome which signifies that T3 is the first parameter to get deranged in CKD which is comparable to previous studies by G Avasthi, S Malhotra, APS Narang, S Sengupta.2001.k

Out of 100 patients 32 patients had thyroid dysfunction in which 32 patients had low T3, 20 patients had low T4 and 10 patients had normal T4. This finding is comparable with previous study showing that hypothyroid patient can have low or normal T4.Thus is comparable to the study of Neuhaus et al.

The serum T4 level can be normal or low in non-dialysis patients which is comparable to the previous study by German Ramirez, William O Neill, William Jubiz, Ramirez etal, Alvarez-udeetal, Czernichow etal and Lim VS et al.Studies conducted by G. Avasthietalin CKD patients have low T3 and normal or reduced T4 levels, and consequently elevated TSH to maintain the pituitary thyroid axis. Sakurai S et al (1988) reported decreased serum values of Total T3, Total T4, Free T3 and Free T4 in their study however TSH was increased.

The mean of T3 level was 1.62±0.74 nmol/l. The mean of T3 in this study decreases as the GFR decreases or B.urea, s.creatinine increases. Findings were comparable with the previous study (Lim VS, Fang VS, Katz AL, Brenner and Rector, Kohli HJ, Mehta HJ et al.

Conclusion

According to our study all CKD patients should undergo for thyroid function evaluation as these patients are definitely associated with development of hypothyroidism.

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