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ORIGINAL RESEARCH

A HOSPITAL BASED PROSPECTIVE STUDY TO CORRELATE THE SEVERITY OF CHRONIC RENAL FAILURE AND ALTERATIONS OF THYROID INDICES AT TERTIARY CARE CENTRE

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ABSTRACT

Background: The evaluation of thyroid function in systemic illness remains complex because the changes occur at all levels of the hypothalamic-pituitary-thyroid axis. So, it is prudent for the internist and treating physician to be aware of thyroid dysfunction so that early intervention can be instituted to improve the outcome. The aim of this study to correlate the severity of chronic renal failure and alteration of thyroid indices at tertiary care centre.

Materials& Methods: A hospital based prospective study done on 40 chronic renal failure patients admitted in medical ward at KPC Medical College, Jadavpur, Kolkata, West Bangal, India during one year period. Patients who fulfill the criteria for CRF and who are on conservative management were taken for the study. The correlation between the thyroid indices were analyzed and interpreted by the Karl Pearson's coefficient(r). The interpretation of statistical procedures was performed by the statistical package SPSS (22.0 V). The value of P<0.05 was considered as significant.

Results: Among 40 patients, 10 patients were female, and 30patients were male. The mean age of the male and female patients was 52.76±11.65 and 50.45±7.32 years respectively. The prevalence of low T3 syndrome was 52.5% (21 cases) and the low T4 syndrome was 22.5 % (9 cases). The prevalence of TSH in hypothyroidism range was 5% (2cases). Among the males 46.66% of patients had low T3 syndrome. And among the females was 70%. The difference was not statistically significant P>0.05. The prevalence of low T4 among the males was 20% and among the females was 30%. The difference among the sexes was not statistically significant i.e. P>0.05. Theprevalence of

TSH in clinical hypothyroidism range among males was 3.33% and among the females was 10%. The prevalence between the sexes was not statistically significant(P>0.05).
Conclusion: We concluded that serum level of total T3 and free T4 is directly proportional to creatinine clearance level. Alteration in the values of T3 and T4 occurs as a part of body adaptation mechanism to conserve energy.
Keywords: Total T3, Free T4, TSH, Creatinine clearance.

INTRODUCTION

Chronic kidney disease (CKD)[1] encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function, and a progressive decline in glomerular filtration rate (GFR). Patients with chronic renal failure often have signs & symptoms suggestive of thyroid dysfunction. These findings include dry skin, sallow complexion, low temperature, cold intolerance, decreased basal metabolic rate, lethargy, fatigue, edema & hyporeflexia.

Serum triiodothyronine (T3) levels were consistently found to be low without any regard to treatment of CRF. Serum total & free thyroxine (T4) concentrations have been reported as low, normal or high. Serum thyroid stimulating hormone (TSH) levels were found to be normal in most patients of CRF even in those whose CRF is complicated by low T3 concentration.[2] A reduction in total T3, but not in free T3 concentrations was associated with an increased all-cause and cardiovascular mortality in euthyroid CKD patients.[3] Total and free T3 behave assurvival markers in patients with CKD both in HD and in PD.

Prevalence of hypothyroidism in end stage renal disease (ESRD) have been estimated between 0 and 9%. There is also increased prevalence of goiter in patients with ESRD. Though there are multiple factors which predicts the overall mortality and severity of renal disease, one among the important factor is thyroid dysfunction.[4] So it is prudent for the internist and treating physician to be aware of thyroid dysfunction so that early intervention can be instituted to improve the outcome. The aim of this study to correlate the severity of chronic renal failure and alteration of thyroid indices at tertiary care centre.

MATERIALS & METHODS

A hospital based prospective study done on 40 chronic renal failure patients admitted in medical ward at KPC Medical College, Jadavpur, Kolkata, West Bangal, India during one year period. Patients who fulfill the criteria for CRF and who are on conservative management were taken for the study. Thyroid profile is done in all patients who fulfill the criteria.

INCLUSION CRITERIA FOR CHRONIC RENAL FAILURE

1. Symptoms of uremia for 3 months or more.
2. Elevated blood urea, serum creatinine and decreased creatinine clearance.
3. Ultrasound evidence of chronic renal failure:

a) Bilateral contracted kidneys – size less than 8 cm in male and female.
b) Poor corticomedullary differentiation.

4. Supportive laboratory evidence of CRF like anemia, low specific gravity, changes in serum electrolytes, etc.,

5. Radiological evidence of renal osteodystrophy.

EXCLUSION CRITERIA

1. Patients underwent peritoneal dialysis or hemodialysis.
2. Nephrotic range of proteinuria.
3. Low serum protein especially albumin.
4. Other conditions like: Recent surgical trauma/burns, acute illness, Diabetes mellitus, Liver disease, drugs altering thyroid profile.

METHODS

Detailed clinical history and examination is undertaken with preference to thyroid and renal diseases. The following investigations are performed:

- Urine for specific gravity and broad cast
- Renal parameters like blood urea, serum Creatinine and creatinine clearance (using Modified diet and renal disease)
- Serum calcium
- Serum cholesterol for hypothyroidism
- 24 hours urine protein and serum protein to rule out nephrotic syndrome and hypoproteinemia respectively
- ECG and chest X ray to look for features for hypothyroidism and renal failure like pleural effusion, pericardial effusion.
- X ray wrist, forearm and spine for evidence of renal osteodystrophy
- USG abdomen for evidence of chronic renal failure.

After selecting the patients, fulfilling the above criteria, about 5 ml of blood sample is collected in non-heparinised serum bottle and sent for thyroid profile.

STATISTICAL ANALYSIS

The analytical data was interpreted by students unpaired and students proportion‘t’ test. The relations between the related biochemical variable in CKD were analyzed and interpreted by the point biserial correlation coefficient (rp1bis). The correlation between the thyroid indices were analyzed and interpreted by the Karl Pearson’s coefficient(r). The interpretation of statistical procedures was performed by the statistical package SPSS (22.0 V). The value of $P<0.05$ was considered as significant.

RESULTS

40 patients with chronic kidney disease who were on conservativemanagement were studied. Among 40 patients, 10 patients were female, and30patients were male. The mean age of the male and female patients was 52.76±11.65 and 50.45±7.32 years respectively. The difference between the mean age of the male and female was statistically not significant $P>0.05$. The male participation was 75% and the female participation was 25% (table 1).

Table 1: Sex wise age distribution of patients taken for study

Age group in years	Male		Female		Total	
	frequency	%	frequency	%	frequency	%
30-39	6	20%	0	Nil	6	15%
40-49	3	10%	4	40%	7	17.5%
50-59	8	26.66%	5	50%	13	32.5%
60-69	13	43.33%	1	10%	14	35%
total	30	100%	10	100%	40	100%
mean±S.D.	52.76±11.65		50.45±7.32		52.23±10.58	
Significance	P>0.05					

The prevalence of low T3 syndrome was 52.5% (21 cases)and the low T4 syndrome was 22.5 % (9 cases). The prevalence of TSH in hypothyroidism range was 5% (2cases). Among the males 46.66% of patients had low T3 syndrome. And among the females was 70%. The difference was not statistically significant P>0.05. The prevalence of low T4 among the males was 20% and among the females was 30%. The difference among the sexes was not statistically significant i.e. P>0.05. Theprevalence of TSH in clinical hypothyroidism range among males was 3.33% and among the females was 10%. The prevalence between the sexes was not statistically significant(P>0.05) (table 2).

Table 2: Sex wise prevalence of thyroid dysfunctionin CKD patients

Thyroid hormones	Level of hormone	No	Males, n=30		Females=10		Significance
			frequency	%	frequency	%	
T3	low	21	14	46.66%	7	70%	P>0.05
	normal	19	16	53.33%	3	30%	
T4	low	9	6	20%	3	30%	P>0.05
	normal	31	24	80%	7	70%	
TSH	high	2	1	3.33%	1	10%	P>0.05
	normal	38	29	96.66%	9	90%	

Table 3: Distribution of total T3 free T4 and TSH in various stages of CKD

Stages of CKD	Frequency	Mean Total T3	Mean free T4	Mean TSH
1-3	4	102.8±29.74	1.22±0.13	1.65±1.78
4	13	90.45±35.6	1.09±0.18	1.14±0.56
5	23	68.56±23.87	0.93±0.26	4.46±13.34

The mean T3 is decreased significantly with reducedcreatinine clearance. The free T4 is also significantly decreased in stage 5CKD (table 3). A positive correlation between total T3 and Creatinine clearance and it is statistically significant. The free T4 and creatinine clearance shows positive correlation, and it is statistically significant. A negative correlation of TSH with creatinine clearance and it is not statistically significant (figure 1 & 2).

Figure 1: Correlation of Total T3 With Creatinine Clearance

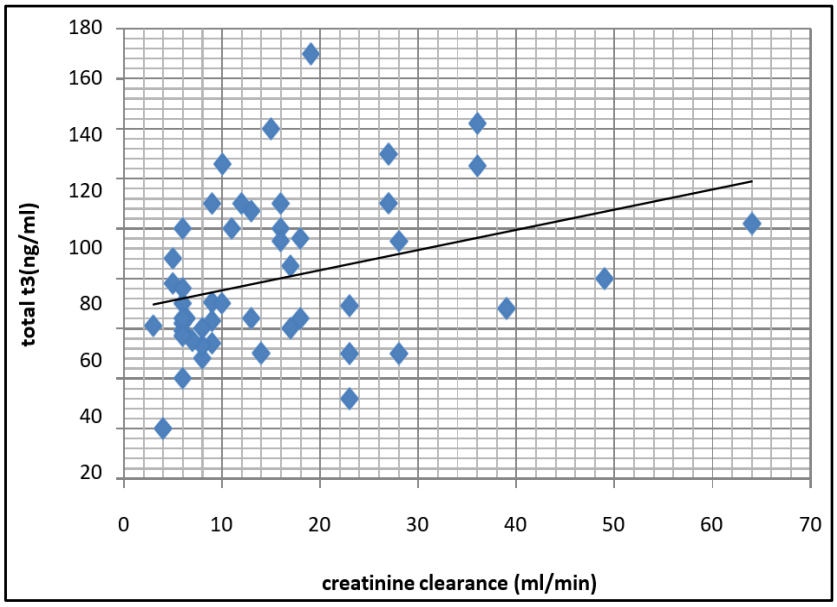
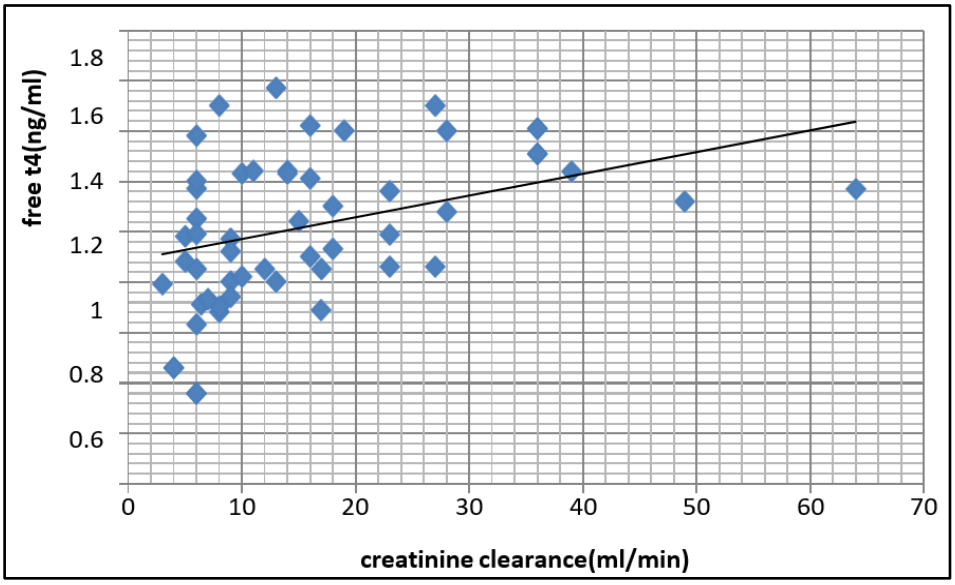


Figure 2: Correlation of Free T4 With Creatinine Clearance



DISCUSSION

Patients with CRF often have signs & symptoms suggestive of thyroid dysfunction & hence the diagnosis of thyroid disease in these patients has obvious prognostic implications. A large number of hormonal systems are affected by CRF, yet it remains unclear to what extent these changes are responsible for manifestations of uremic syndrome.

In uremia the mean values of both serum T3&T4 were significantly low. This is comparable to Ramiraz etal[5] and Lim VS et al[6]study. In our study, outof 40 patients 21 patients (52.5%) had low T3 syndrome.The prevalence oflow T3 in stage 1- 3 is 10 %, for stage 4 is 32.5%, and stage 5 is 57.5%. This observation is consistent with Sang Heon Songetal.[7] in which the prevalence of low T3 will be increased according to the increase in stage of CKD. In our study there is a positive correlation between Total T3 and creatinine clearance and it is

statistically significant P<0.05. This shows serum T3 levels were associated with severity of CKD even in the normalTSHlevel.

In our study there is a positive correlation between Free T4 and creatinine clearance and it is statistically significant P<0.05. Out of the 40uremic patients 2 patients showTSH>10µIU/ml. The high serum TSH level is > 75 µIU/ml. Both these patients had very lowserum T3 concentration which can be explained by the normal feed back regulation of the pituitary thyroid axis. This observation is consistent with Joseph et al.[8] who studied 175 patients of CRF who had low T3, T4, fT4 but had high TSH levels suggested maintenance of pituitary thyroid axis. These results areconsistent with study of Spector et al.[9] and Ramirez et al.[5] reported normal level of serum TSH in patients of CRF inspite of lowserumT3levels.

In Mehta H.J. Joseph et al.[10] study low TT3, FT3 and TT4 values isseen in clinically euthyroid CKD patients. However, finding of normal T4 values and TSH would indicate function al euthyroid status. It can be presumed that free T4values would fall if these patients'developed hypothyroidism and TSH values would rise simultaneously. Thus, Free T4and TSH levels combined can be used for the diagnosis of hypothyroidism inpresenceof CKD.

Ramirez et al.[5] reported high prevalence of goiter in CRF patientsespecially those on chronic dialysis. Incidences were increased in end stagerenal disease. The possible explanation is due to accumulation of iodides in thyroid gland due to decreased renal clearance in CRF patients. Study conducted by Hegedusetal.[11] showed thyroid gland volume was significantly increased in patients with CRF.

As stated previously, He modialysis and continuous ambulatory peritoneal dialysis have shown to affect the thyroid profile independently of CRF. Also, drugs like heparin, furosemide used during dialysis will affect thethyroid profile. Kayimaetal.[12] and Giordanoetal.[13] have conducted studies regarding effect of dialysis on CRF patients with thyroid dysfunction.

This study showed no significant improvement in thyroid profile after repeated hemodialysis. But in the patients who have undergone renal transplant surgery, most of the thyroid function parameters returned to normal with TSH below normal.

CONCLUSION

We concluded that serum level of total T3 and free T4 is directly proportional to creatinine clearance level. Alteration in the values of T3 and T4 occurs as apart of body adaptation mechanism to conserve energy.

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