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STUDY OF THYROID FUNCTION IN PATIENTS OF CHRONIC RENAL FAILURE AT DMCH, LAHERIASARAI, BIHAR

Biochemistry

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ABSTRACT

Thirty patients with chronic renal insufficiency underwent clinical evaluation & studies of thyroid function The results were compared with age & sex-matched controls. Two patients had clinical hypothyroidism with low serum T3, T4, FT4 & high serum TSH. Four patients had clinical goitre but were euthyroid. The remaining 24 patients did not have goitre & they were clinically euthyroid. All the members of the control group were clinically euthyroid. The mean values of serum T3, T4 & FT4 were significantly lower & mean serum TSH was significantly higher as compared to controls. There was no correlation of thyroid functions with decrease in renal function. To conclude thyroid dysfunction occurs both clinically & biochemically in patients with chronic renal insufficiency.

KEYWORDS

INTRODUCTION

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. Various studies of thyroid functions in uremic patients have been carried out which have shown conflicting results.

Hyperthyroidism, hypothyroidism & euthyroid state have all been reported by various workers [1-5].

Serum triiodothyronine (T3) levels were consistently found to be low without any regard to treatment of CRF[5].

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. The incidence of goitre has also been variably reported in literature[4-8]. A

study had reported reversion of thyroid function to normal after successful renal transplantation[4].

In view of the variability of thyroid function tests in patients with CRF in previous studies, it was decided to undertake a prospective clinical & biochemical study of various thyroid functions & to establish a correlation, if any between thyroid dysfunction & severity of renal disease. Serum organic iodine & urinary iodine levels were studied in all patients of CRF & detailed dietary content of iodine (including salt & water) were studied in patients with manifestations of goitre to evaluate the aetiological relationship of iodine metabolism in uremia.

Material And Methods

Present study was conducted at Department of Biochemistry, Associated with Department of Medicine, Darbhanga Medical College, Laheriasarai, Bihar from October 2020 to September 2021. Thirty patients of chronic renal failure (CRF) admitted in the department of Medicine, DMC&H, Laheriasarai, Bihar were studied after taking informed consent. The diagnosis of CRF was established on the basis of clinical profile, biochemical tests (serum creatinine, blood urea, creatinine clearance) and radiological investigations (plain Xray abdomen, USG abdomen, infusion pyelogram). The severity of the chronic renal failure was based on creatinine clearance values of >13ml/min, 5-13ml/min, & <5ml/min. Patients with diabetes mellitus, nephrotic syndrome & those known for the consumption of estrogens, corticosteroids & β blockers were excluded from the study. None of the patients had history of using iodine containing drugs, contrast or nuclear studies containing iodine. An equal number of age & sex matched subjects from the same geographical area without renal disease were taken as controls.

Evaluation Of Thyroid Status

Clinical profile

Sign and symptoms of thyroid dysfunction were evaluated by previously established clinical indices[9-11]. Each patients was evaluated for hypothyroid and hyperthyroid scores by separate questionnaires. The presence of weighted symptoms and signs were recorded. Summed scores of plus 20 or above either the hyperthyroid or hypothyroid questionnaires indicated a high likelihood of thyroid dysfunction.

Laboratory Parameters

The following investigations were carried out on serum for each patient & controls:

(1) Serum triiodo thyronine T3
(2) Serum thyroxine T4
(3) Serum TSH; all by Boehringer Mannhein immunodiagnostic method
(4) Serum free thyroxine (FT4) as calculated according to the method elucidated by Kaplan et al[9].

Iodine studies included measurements of serum organic iodide (PBI) & urinary iodine by zinc hydroxide precipitation for both cases & controls. All cases with goitre were studied for iodine contents in their salt, diet, water & urine & compared with age and sex matched controls from the same geographical areas. Samples of all foods, water & salt consumed by these cases were collected by duplication sampling technique in labeled polythene bags for analysis.

Statistical analysis was done by using student's 't' test.

RESULTS

Thirty patients of chronic renal failure of varying etiologies were studied. (Table 1). Twenty two patients were men & 8 were women. They ranged in age from 22-70 years (mean 51.17 ± 13.53 years). The control group was matched for age, sex and physical characteristic of weight & height (Table 2).

Table 1 : Spectrum Of Chronic Renal Failure In 30 Patients

Primary Disease (Likely diagnosis)	Patients	
	Number	Percentage
Benign nephrosclerosis	14	46.67
Chronic glamerulonephritis	9	30.00
Chronic pyelonephritis	4	13.33
Obstructive uropathy	2	6.67
Polycystic kidney disease	1	3.33

Table 2 : Physical Characteristics Of Chronic Renal Failure Patients And Control Subjects

Parameters	Male		Female		Total	
	Controls	Patients	Controls	Patients	Controls	Patients
Number	22	22	8	8	30	30
Age range (yrs.)	21-75	22-70	31-70	35-70	21-75	22-70
Age (yrs) (Mean±SD)	49.38±15.32	51.55±14.09	50.78±14.24	50.13±11.79	49.80±15.20	51.17±13.53
Weight (kg) Range	52-80	54-80	48-60	52-62	48-80	52-80
Weight (kg) (Mean±SD)	66.14±7.46	65.23±8.84	51.00±5.14	56.63*±2.87	61.60±9.75	62.93±8.60
Height (cm) Range	155-196	155-179	150-160	150-158	150-196	150-179
Height (cm) (Mean±SD)	169.10±9.61	167.05±6.55	155.44±3.79	152.63±2.55	165.00±10.39	163.20±8.59

* p<0.05

Two patients of chronic renal failure had clinical sign symptom index scores suggestive of hypothyroidism. One patient had hypothyroidism index score of +44 and another patient had +32. Both these patients with clinical hypothyroidism had low serum T3, T4,fT4 and high serum TSH. Four patients of CRF had clinical goitre (13.34%).

Thyroid was diffusely enlarged and smooth in all with no bruit. All these were clinically found to be euthyroid. The remaining 24 patients did not have goitre and they were clinically euthyroid. All the members of the control group were clinically euthyroid.

The mean value of serum T3 level was significantly less in patients of CRF as compared to controls (patients of CRF 0.80±.25ng/ml, controls 1.12±.17ng/ml; p<0 05).

Fourteen patients (46.67%) of CRF had serum T3<0.8ng/ml, whereas none of the control group had serum T3, concentration below the normal range. Similarly mean serum T4 value & serum free T4 was significantly less in patients of CRF as compared to controls (serum T4 in CRF 5.99±.92,µg/dl, controls 8.55±0.97µg/dl, p<0.05;) free T4 in CRF 0.83+.32ng/dl controls1.55 ±.34 p<.05.

Twelve (40%) of the CRF patients as compared to none in the control group had serum T4 concentration below the normal range.

Serum mean TSH level and free T4 was significantly increased in patients of CRF as compare to controls (4.73±2.60ug/ml, vs 2.69±.34ug/ml p<0.05). Thirteen patients (43 33%) of CRF group had high TSH levels of >5ug/ml as compared to two controls (6.67%) Table 3.

Table 3 : Thyroid Function Tests In Chronic Renal Failure Patients And Control Subjects (mean±sd)

		Serum concentrations			
Group	No. (n)	T_3(ng/ml)	T_4(mg/ml)	FT_4(ng/ml)	TSH(mU/ml)
Control	30	1.12±0.17	8.55±0.97	1.15±0.34	2.69±1.34
Patients	30	0.80±8.25*	5.99±1.92*	0.83±0.32*	4.73±2.60*

* p<0.05

Table 4 : Thyroid Function Tests And Severity Of Chronic Renal Failure

	Control	5ml/min (ESRD) n=12	5-13ml/min n=4	>13ml/min n=14
T_3 ng/ml	1.12±0.17	081±0.27**	0.79±0.10***	0.83±0.30**
T_4 mg/ml	8.55±0.97	5.88±1.71***	6.53±1.92**	5.77±1.76***
FT_4 ng/dl	1.51±0.34	0.90±0.34**	0.91±0.23*	0.89±0.36**
TSH mU/ml	2.69±1.34	5.06±3.00***	5.65±2.20***	4.82±3.20

* All values are mean ±SD
*All values are in relation to control group
*<0.05 **<0.005 ***<0.0005

The relation of mean serum T3, T4, fT4 and TSH with varying severity of renal failure are shown in Table 4. A significant difference was seen with the varying severity

of renal failure and controls but no statistically significant difference in between the groups with varying renal failure (creatinine clearance).

There was no significant difference between the mean values of serum organic iodine levels of patients (0.87±0.32µg/dl) as compared to controls (0.88±0.23µg/dl). The mean value of urinary iodine in CRF patients (16.33±13.54µg/dl urine) (Table 5). On comparing the iodine content in the food stuffs in the four uraemic goitre patients as compare to age and sex matched controls, it was seen that iodine intake in the diet of four uraemic patients was significantly less as compared to controls (Table 6).

Table 5 : Iodine Levels (mg/dl; Mean±sd) In Chronic Renal Failure Patients And Control Subjects

	Control	5ml/min (ESRD) n=12	5-13ml/min n=4	>13ml/min n=14
T_3 ng/ml	1.12±0.17	081±0.27**	0.79±0.10***	0.83±0.30**
T_4 mg/ml	8.55±0.97	5.88±1.71***	6.53±1.92**	5.77±1.76***
FT_4 ng/dl	1.51±0.34	0.90±0.34**	0.91±0.23*	0.89±0.36**
TSH mU/ml	2.69±1.34	5.06±3.00***	5.65±2.20***	4.82±3.20

* p<0.05 as compared to control group.

Table 6 : Daily Iodine Intake And Urinary Excretion Inuraemic Goiter Patients And Control Subjects

Subjects	Salt iodine (ppm)	Dietary iodine (mg/day)	Water iodine (mg/day	Total iodine (Diet±water) (mg/day	Urinary Iodine (mg/day
Control	0.94±0.74	130.96±45.13	7.30±2.54	138.26±45.38	34.74±13.30
Uraemic goiter patients	0.78±0.36	63.39±36.88	7.05±3.15	70.45±39.34	11.87±4.55

There was no significant difference in the mean values of serum organic iodine levels in both the groups (CRF patients 0.87±0.32ug/dl, controls 0.88±0.23ug/dl;p>0.05). The urinary excretion of iodine was significantly decreased in patients of CRF as compared to normal controls (CRF 1 6.33±3.54ug/100ml; controls 33.10±21.90ug/100ml p<0.05).

Discussion

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

Patients with CRF often have signs & symptoms suggestive of thyroid dysfuction & hence the diagnosis of thyroid disease in these patients have obvious prognostic implications. The data reported deals primarily with the clinical symptoms sign index & biochemical parameters. Two patients were clinically & biochemically confirmed to be hypothyroid.

In uremia the mean values of both serum T3 & T4 were significantly low. This is comparable to various studies done earlier[6,8,12,13]. There was no significant variation with worsening of renal disease in our study. The likely explanations for low levels of both T3 & T4 could be defective release in response to TSH. FT4 is the most active biological fraction, constituting 0.03% of T4 and its levels are unaffected by variations of concentration of carrier proteins and hence, reflects thyroid status accurately. On studying FT4 concentration in patients of CRF, ten patients (33%) had low FT4 concentrations (<0.6ng/ml) compared to none of the controls and was comparable to studies done by various authors[13,14] whereas Schmidt et al2 have reported normal levels of FT4.

Out of the thirty uraemic patients, thirteen patients (43.33%) had high serum TSH levels (> 5 uu/ml). The highest serum TSH was 11.55 uu/ml. Seven of these thirteen patients had very low serum T3 concentrations which can be explained by the normal negative feedback regulation of the pituitary thyroid axis. In addition, four of these thirteen patients had diffuse goitre but their serum T3 and T4 concentrations were within the normal range and this number is too small to draw any definite conclusion.

In contrast to our study, Spector et al5 and Tamirez et al[6] reported normal levels of serum TSH in patients of CRF inspite of low serum T3 levels. They demonstrated abnormality in the hypophyseal mechanism of TSH release in uraemic patients as the TSH response to the administration of thyotropin releasing hormone (TRH) was blunted. Our results are comparable with Joseph et al[16]., who studied 127 patients of CRF, who had low T3,T4,fT4 but had high TSH levels

suggesting maintenance of pituitary-thyroid axis.

Earlier studies done in animal models of uraemia[17] and in human subjects 6 had proposed that presence of goiter could be related to accumulation of inorganic iodine caused by impaired renal excretion but our study has shown normal serum organic iodine levels in both the patients and the controls Urinary iodine excretion was

lower in patients of CRF as in previous studies15 probably due to decreased GFR. Goitre in 4 patients out of 30 reflects high incidence of goitre in our area, but the inherent bias of hospital based study remains in the present report also.

Moreover, our hospital drains patients from nearby cities of North Bihar like Madhubani, Sitamarhi & Samastipur which have high incidence of goitre[18]. On studying the dietary contents of iodine in the four patients of CRF having goitre, it was seen that two of them had low intake of iodine in their diet. Therefore, the likely explanations for goitre in patients of CRF are deficient iodine intake in the diet[15], high serum inorganic iodine levels[6] and presence of unknown goitrogenic substances in the blood[6].

CONCLUSION

To conclude thyroid dysfunction occurs both clinically and biochemically in patients with chronic renal insufficiency.

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