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A Study of Evaluation of Thyroid Function Status In Patients With Chronic Kidney Disease

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Abstract: *A Cross sectional observational study was done to analyze the prevalence of thyroid dysfunction in patients with chronic kidney disease. In our study consisting of 100 patients with CKD, Thyroid dysfunction occurs in 35% of the patients. The alteration in the values of T3 and T4 in CKD can be viewed as a protective mechanism, promoting conservation of protein.Incidence of hypothyroidism is increased in patients with chronic kidney disease.Low T3 syndrome is seen in 15% of the patients, Low T4 syndrome is seen in 3% of the patients, combined low T3 and T4 is seen in 4% of the patients in our study group. Sub clinical hypothyroidism is seen in 6% and overt hypothyroidism is seen in 7% of patients in the study group. Serum level of T3 has correlation with the severity of chronic kidney disease which was statistically significant.*

Keywords: *Thyroid function, chronic kidney disease, cross sectional study, protective mechanism*

I. Introduction

Thyroid dysfunction affects renal physiology and development, whereas kidney disease could result in thyroid dysfunction. Kidney and thyroid function and dysfunction are interrelated through several mechanisms[1]. It is not difficult for physicians to diagnose and treat patients with overt hypothyroidism or hyperthyroidism presenting significant biochemical derangements and clinical symptoms. In the spectrum of subclinical thyroid dysfunction and nonthyrodial illness syndrome (i.e. alterations in thyroid hormones without any underlying intrinsic thyroid disorder), however it is not always an easy task. The interpretation of thyroid functions in patients with CKD or ESRD is even more complicated by the declination in GFR, the difference in dialysis modalities, and co morbid associations[2]. The present study was taken to assess the clinical and biochemical profile of thyroid abnormalities in patients with chronic kidney disease.

II. Materials And Methods

The study is conducted on 100 patients of, who are diagnosed to have chronic kidney disease (In Stages 3-5 with or without dialysis) and being admitted in Government Rajaji Hospital attached to Madurai Medical College, Madurai.Patients with chronic kidney disease and patients who fulfill the criteria for CKD and who are on conservative management are included in the study.Criteria for CKDare symptoms of uremia for 3 months or more or elevated blood urea, serum creatinine and decreased creatinine clearance with Ultra sound evidence of chronic renal failure like bilateral contracted kidneys – size less than 8 cm in male and size less than 7 cm in female, Poor corticomedullary differentiation, type 2 or 3 renal parenchymal changes.Patients with nephrogenic range of proteinuria, low serum protein especially albumin, conditions like acute illness, recent surgery, trauma or burns, diabetes mellitus, liver diseases which affect thyroid function test and on drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, beta blocker, estrogen pills, iodine-containing drugs and Patients with known thyroid disease on treatment are excluded from the study. Details of clinical history and clinical examination are undertaken with preference to thyroid and renal diseases. Venous blood sample was collected and sample was sent for analysis for T3, T4, TSH using Chemiluminescence immunoassay. Data analysis was done with the help of computer using Epidemiological Information Package EPI 2012.Using this software, frequencies, percentage, mean, standard deviation, chi square and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

III. Results And Interpretation

Table 1:Distribution Of T3

T3	No. of cases
>0.6	23
0.6 - 2.0	77
> 2.0	0

Table 2: Distribution Of T4

T4	No. of cases
> 4.5	14
4.5 - 12.5	86
> 12.5	0

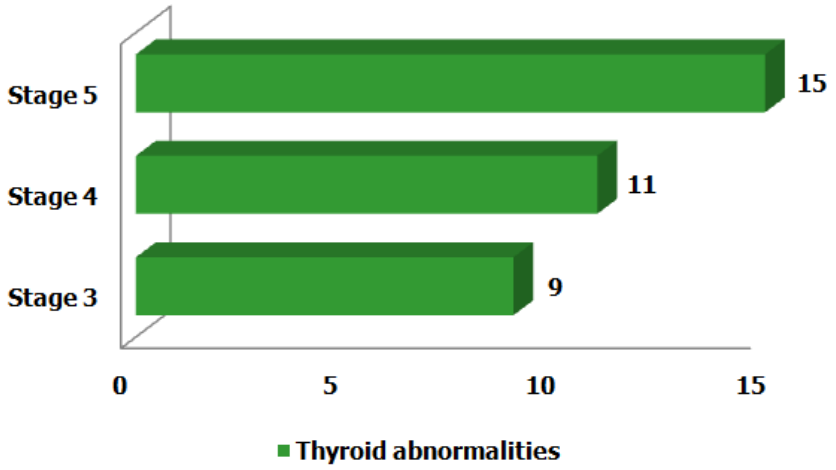
Table 3: Distribution Of Tsh

TSH	No. of cases
> 0.5	0
0.5 - 5.5	87
> 5.5	13

Table 4: Distribution Of Various Thyroid Abnormalities In Various Stages On Ckd

Stage	T3		T4		TSH	
	Mean	SD	Mean	SD	Mean	SD
3	0.973	0.314	6.32	2.09	3.67	3.678
4	0.923	0.35	6.67	2.17	3.957	2.789
5	0.828	0.37	6.298	1.87	4.96	4.32

Figure 1: stage vs thyroid abnormalities



The mean age of males in our study group was 48.24±9.18 years. The mean age of females in our study group 47.8±9.13 years. Mean T3 level in our study is within normal limits in all stages of CKD, but significantly decreases as the stage of CKD advances and was statistically significant hence exhibiting a linear correlation with the severity of renal failure. Mean T4 level in our study is within normal limits in all stages of CKD, and it does not correlate with the severity of renal failure. In our study, not all the patients with CKD have low T3 and T4. Only 35% (35 patients) of patients had altered Thyroid Profile. Remaining 65% of patients had normal thyroid profile. Among 35% of these patients, 15% have only low T3 level with normal T4 level. Remaining 4% have both low T3 and T4 level. The percentage of patients having low T3 and T4 gradually increase with increase in stage. The patients who will develop such changes in thyroid profile is not known. 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 mean TSH levels were not statistically significant and hence don't show any linear correlation with the severity of renal failure. This is consistent with the study conducted by "Spector DA et al" and "Ramirez et al"[45], "Dudani et al"[19], "Karunanidhi et al"[34]. These studies demonstrated abnormalty in hypophyseal mechanism of TSH release in uremic patients as the TSH response to the TRH was blunted. Our study is consistent with the results of "Ramirez et al"[45] study showing low T3, low T4 and normal or mild elevation of TSH. Various studies had shown that this thyroid profile derangements is a part of our body adaptation mechanism. In our study 5% of patients had symptoms of hypothyroidism and 2% of patients had goiter. Previous studies by "Quionverde et al"[43] reported high prevalence of hypothyroidism in CKD. It was

estimated to be about 5% in patients with terminal renal failure. In our study 7% had hypothyroidism. Detailed study by "Kaptein et al"[32,33] estimated the prevalence of primary hypothyroidism was about 2.5 times much frequent in chronic kidney disease. The hypothyroidism in CKD was estimated to range between 0 and 9.5%.

IV. Discussion

CKD is associated with a higher prevalence of primary hypothyroidism both overt and sub clinical, but not with hyperthyroidism. In fact the prevalence of primary hypothyroidism, mainly in the sub clinical form, increases as GFR decreases[3]. Chronic renal failure is one among the condition causing low T3 syndrome. As with other low T3 syndromes, CRF produces decrease in T3 when GFR falls below 50%. There is marked decrease of T3 than T4 as the GFR deceases. Despite decreased circulating T4 and T3, thyroid stimulating hormone (TSH) level in serum is not elevated[5]

CRF as low T3 syndrome differs from other conditions causing similar illness, by two unique features[4].

1. rT3 is usually low or normal in CRF due to redistribution into the extravascular compartment.
2. Increased incidence of goiter is present in CRF, probably due to decreased clearance of iodine by the kidney[5,6].

Thyroid hormone metabolism normality's with renal transplantation. Goiter and hypothyroidism may be induced by iodide excess due to reduced iodide excretion by the kidneys.

According to the postulates, CRF affect thyroid at all levels.

A. Change in Hypothalamic – pituitary – thyroid axis

1. Sensitivity of TSH secretion to low thyroid hormone is decreased.
2. Limited TSH reserve[7,8,9].
3. Due to changes in thyrotrophs or to decreased TRH secretion, as manifested by decrease in nocturnal pulses of TSH secretion[10].
4. Tissue concentration of the hormone may be appropriate for the patient, so the patient is in euthyroid state.
5. Serum FT3 and FT4 appears normal by sensitive methods[10,12].

B. Changes in hormone Transport

1. Presence of protein and non-protein inhibitors preventing the binding of thyroxin with thyroxin binding protein. Non-protein inhibitor is non-esterified unsaturated fatty acid.
2. Acquired intrinsic structural alternation in the T4 binding site.
3. Decrease in concentration of thyroxin binding globulin[11,13].

C. Changes in metabolism

1. Decrease in the activity of lodothyronine 5 – Deiodinase leading to low T3
2. Increase in Non-deiodinative pathways of iodothyronine degradation leading to increased serum T3 sulphate, diiodotyrosine, triiodothyroacetic acid and tetraiodothyroacetic acid[15,16].

Complications of CKD worsened by coexisting hypothyroidism are,

I. Cardiovascular complications like secondary hypertension, LV failure and pulmonary edema, accelerated atherosclerosis, myocardial infarction, pericarditis, uremic cardiomyopathy.
II. CNS and neuromuscular complications like Dementia, uremic encephalopathy, peripheral neuropathy, proximal muscle weakness.
III. Hematological complications like anemia
IV. Electrolyte imbalance like hyponatremia
V. Fluid overload – edema
VI. Effects on Vascular System include increased Systematic Vascular Resistance (SVR), increased arterial stiffness, endothelial, all these factors predispose to diastolic HTN.

High serum T4 with low T3 in the presence of CRF should make the possibility of T4 thyrotoxicosis.This is because serum T3 level will be suppressed in low T3 syndrome with serum T4 unaffected.Low serum T3 level in patients with severe renal failure is metabolically protective and it is interpreted as physiological adaptation to reduce basal metabolic rate (BMR) and to conserve energy in an adverse environment.Experiments performed to correct the low serum T3 level by administration of small doses of LT3 resulted in lesser nitrogen balance and protein degradation. So we speculate that low thyroid state in uremia serves to defend against protein wasting and that misguided attempts to replete thyroid hormone stores may worsen protein malnutrition[17,18].

Although no recommendations are available regarding the treatment of mild abnormalities of thyroid hormone levels in patients with CKD, these abnormalities could represent a significant risk factor for cardiovascular disease and might also be implicated in kidney disease progression[18]

In CKD patients,Hypothyroidism should be diagnosed only if the following prevails,

1) Basal TSH level should be more than 20 ml U/ml.
2) Both total and free T4 are distinctly low in the presence of normal TBG[18].
3) Presence of anti-thyroid antibodies can provide clue for hypothyroidism[18].

V. Conclusion

Incidence of hypothyroidism is increased in patients with chronic kidney disease. Number of patients with low T3 syndrome progressively increases with the severity of chronic kidney disease

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