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Clinical Evaluation Of Thyroid Function Tests In Patients With Chronic Kidney Disease

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Abstract

Introduction: People with Chronic Kidney Disease (CKD) are hypothyroid, according to estimates. Patients with CKD also have a higher prevalence of goitre. The current study examined thyroid function tests in patients with chronic renal failure in light of the variability of thyroid function tests in patients with CKD in other investigations.

Material and Methods: This study was an observational, prospective, hospital-based study that included patients on conservative therapy and who met the criteria for CKD. T3, T4, and TSH were all quantified using an enzyme-linked immunosorbent assay.

Results: 28 patients (56%) of the 50 patients had low serum T3 levels, and 5 of those patients also had high TSH values > 20 U/ml with low T levels and symptoms indicative of hypothyroidism. The range of the creatinine clearance was 6 to 34 ml/min. Twenty patients (40%) had GFRs of 10 ml/min or less, twenty patients (40%) had GFRs of 10–20 ml/min, and ten patients (20%) had GFRs of more than 20 ml/min. It was shown that patients with GFR less than 10 ml/min are the only ones with a low mean value of blood T3 (0.538 ng/ml). Despite low T3 levels, the number of patients with low T3 rises as the degree of renal failure increases.

Conclusion: The number of patients with low T3 and T4 syndrome increased over time as renal failure became more severe. However, there was no relationship between serum levels of T3 and T4 and the degree of renal failure.

Keywords: Low T3, hypothyroidism, chronic kidney disease

Introduction

A Chronic Kidney Disease (CKD) is manifested by irreversible renal impairment that culminates in metabolic and excretory failure and manifests clinically as a build-up of non-protein nitrogenous chemicals (1). Despite having several causes, CKD is the one common pathway that leads to the irreversible death of nephrons and, ultimately, the modification of all bodily systems. In that the kidney is the only other organ that competes with the thyroid for iodide elimination, it is intimately related to the thyroid (2).Numerous symptoms and indicators of thyroid dysfunction are present in CKD patients, including edema, dry skin, cold sensitivity, reduced BMI, asthenia, and hyporeflexia. It is therefore challenging to rule out thyroid dysfunction in CKD cases based solely on clinical history. Between 0% and 9% of people with end-stage renal disease are hypothyroid, according to estimates. Patients with CKD also have a higher prevalence of goitre (3).The goal of the current study was to examine thyroid function tests in people with chronic renal failure in light of the diversity of thyroid function tests in individuals with CKD in prior studies.

Materials And Methods:

The present study was an observational, prospective, hospital-based study carried out in the Department of General Medicine at Assam Medical College and Hospital, Assam, India. The study lasted for 12 months (July **2021-June 2022).**

Inclusion criteria:

1. All adult patients who fulfil the criteria for CRF and on conservative management

Exclusion Criteria:

1. Patients with nephrotic range of proteinuria.

2. Patient with any acute illness, Recent surgery, trauma or burns, Chronic Liver disease

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

Patients were briefed about the study, and their written consent was obtained. The focus of the thorough clinical history and examination was on thyroid and renal disorders. The subsequent investigations were carried out. Peripheral smear for anaemia and burr cells, urine (specific gravity and broad cast), Renal indicators such as serum calcium and phosphorus, blood urea, serum creatinine and creatinine clearance, ECG, chest X-ray, 24-hour urine protein and serum protein, USG abdomen, serum cholesterol for hypothyroidism. In a non-heparinized serum vial, 5 cc of blood are drawn and sent for a thyroid profile. Triiodothyronine, thyroxine, and thyroid-stimulating hormone levels in the blood. T3, T4, and TSH were quantified using an enzyme-linked immunosorbent assay. The thyroid function tests were checked 2 monthly for the patients.

Microsoft Excel was used to collect and compile the data, and SPSS 23.0 was used to analyse it. The continuous variables were analysed using frequency, percentage, means, and standard deviations (SD), while the categorical variables were computed using ratios and proportions. Descriptive statistics were used in the statistical analysis.

Results:

A study was conducted on 50 CKD patients receiving conservative treatment. There were 50 patients, of which 10 were female and 40 were male. The range of ages was 12 to 70. 50 patients were treated; 10 had ages below 30, 33 had ages between 30 and 60, and 7 had ages over 60.

In this study, T3 levels ranged from 0.2 to 2 ng/ml. T3 has a mean concentration of 0.67 ng/ml. The mean value is 0.71 ng/ml when patients with primary hypothyroidism are excluded. This value was within the low normal range. In this investigation, serum T4 levels ranged from 0.5 to 9.5 g/dl. 50 patients' serum T4 levels averaged 5.62 g/dl. The mean value is 5.99 g/dl when hypothyroid patients are excluded. This number falls within the T4 low normal range. TSH levels range from 0.6 to 27 IU/ml, with a mean of 6.53 IU/ml. The typical value, when hypothyroidism is excluded, is 4.75 IU/ml.

28 patients (56%) of the 50 patients had low serum T3 levels, and 5 of those patients also had high TSH values > 20 U/ml, low serum T3 levels, and symptoms indicative of hypothyroidism. According to the criteria, these people were classified as having "primary hypothyroidism." The remaining 6 individuals had TSH levels that were slightly high, ranging from 9 to 14 IU/ml. Only 3 of these 6 patients had low T3 levels, and only one of them showed a few clinical signs of hypothyroidism. Therefore, these 6 patients didn't entirely meet the hypothyroidism requirements. Hence, all 23 individuals were categorised as "Low T3 syndrome" or "sick Euthyroid syndrome".

The time span of CKD in this study ranged from 3 months to 5 years. The range of the creatinine clearance was 6 to 34 ml/min. Twenty patients (40%) had GFRs of 10 ml/min or less, twenty patients (40%) had GFRs of 10–20 ml/min, and ten patients (20%) had GFRs of more than 20 ml/min. Creatinine levels ranged from 3 mg to 17.2 mg/d1, and blood urea ranged from 64 to 170 mg/dL. All patients had a 24-hour urine protein excretion of less than 1 g/day.

It was shown that patients with GFR less than 10 ml/min are the only ones with a low mean value of blood T3 (0.538 ng/ml). The mean is low normal in patients with GFR >10 ml/min. The study found that despite low T3 levels, the number of patients with low T3 rises as the degree of renal failure increases.

The number of low T4 patients is not related to the severity of renal illness. At all phases of renal failure, the mean T4 level, excluding patients with hypothyroidism, was normal. The mean TSH values

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in various stages of renal failure are within the normal range in patients with low Ts syndrome. TSH values, however, did not exhibit a linear relationship with GFR. GFR and hypothyroidism did not correlate linearly. Only two individuals had hypothyroidism with a GFR of less than 10 ml/min, compared to an increased number of 4 hypothyroid patients with a GFR of 11 to 20 ml/min. Nine (21.33%) other patients had T4 levels below normal and low T3 syndrome after excluding the five hypothyroidism patients with low T4 values.

Tables:

Table 1: Age of the study population

Age (years)	Number of patients	Percentage
<=30	10	20 %
31-60	33	66%
>60	7	14%

Table 2: Gender of the study population

Sex	Number of patients	Percentage
Male	40	80
Female	10	20

Table 3: Serum Thyroid levels

Thyroid levels	Range	Mean ± SD	Mean ± SD (excluding hypothyroidism)
Serum T3 (ng/ml)	0.2 - 2	0.673 ± 0.414	0.7122 ± 0.4368
Serum T4 (µg/ml)	0.5 – 9.5	5.622 ± 2.27	5.99 ± 2
Serum TSH (µIU/ml)	6 -27	6.53 ± 6.96	4.75 ± 4.15

Table 4: Serum T3, T4 and TSH excluding hypothyroidism in the study

Thyroid dysfunction	No. of Patients with Normal values (%)	No. of Patients with low values	No. of Patients with high values
Serum T3 (ng/ml)	22 (44 %)	23 (46 %)	0
Serum T4 (µg/ml)	35 (70 %)	10 (20 %)	0
Serum TSH (µIU/ml)	38 (76 %)	0	7 (14 %)

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Table 5: TFTs with creatinine clearance

Creatinine Clearance ml/min	Mean Serum T3 (ng/ml)	Mean Serum T4 (µg/ml)	Mean TSH µIU/ml
<10 (n=20)	0.538 ± 0.40	5.02 ± 2.10	5.22 ± 4.25
11-20 (n=20)	0.82 ± 0.43	6.69 ± 2.17	3.77 ± 3.78
> 20 (n=10)	0.8 ± 0.31	6.32 ± 2.04	5.72 ± 5.00

Discussion:

Iodide removal is typically aided by the kidney, especially through glomerular filtration. Iodide absorption by the thyroid gland is enhanced in renal failure patients due to decreased iodide excretion and an increase in plasma inorganic iodide. Increases in the body's overall amount of inorganic iodide may prevent the generation of thyroid hormone (the Wolff-Chaikoff effect). A shift like this could explain why people with chronic renal illness have a slightly increased incidence of goitre and hypothyroidism (4). Ramirez G et al undertook considerable research on thyroid dysfunction in CKD, and in addition to their findings, other studies in this field have produced conflicting findings. Only patients receiving conservative treatment were examined in this study. This is owing to the fact that changes to the thyroid profile brought on by dialysis are distinct from those brought on by chronic renal failure (5). In individuals with renal failure, dialysis also alters the thyroid hormone levels that were previously present in the serum. Several studies have compared conservative management and hemodialysis for CKD patients. Low T3 readings were found in numerous research done on CKD patients. Low T3 had been linked to severe renal failure as observed in those studies. The degree of renal failure linearly correlated with the mean blood T3 and T4 levels, according to studies by Ramirez G et al. and Spector DA et al (5,6). The mean T level in our study was dropped below normal with GFR less than 10 ml/min, similar to other studies. It was present in low normal in cases of greater GFR, and there was no linear relationship between T3 level and GFR, which is similar with the findings of other studies (7). The mean T level in this study is within normal ranges for all GFR levels, however it is at a low normal level, and it also has no relationship to how severe renal failure is. Not all of the CRF patients in this study had low T3 and T4, although 58% of them had abnormal thyroid scans. After eliminating patients with primary hypothyroidism from the sample of 58% of these patients, 28% have only low T3 levels with normal T4 levels. The remaining 20% have low levels of both T3 and T4. As GFR declines, the proportion of patients with low T3 and T4 steadily rises. The mean TSH level in our study is within normal ranges, with the exception of hypothyroidism (8).

For the various GFR ranges, the mean TSH levels are also within normal ranges. Yet, there is no linear relationship between the TSH level and the degree of renal failure. This is in line with other studies. As the TSH response to the TRH was attenuated, these findings showed abnormalities in the hypophyseal mechanism of TSH release in uremic patients (9). Low T3 and T4 levels were seen in other investigations, however high TSH levels indicated that the pituitary thyroid axis was still functioning. Seven patients in this study, excluding those with hypothyroidism, had a modest TSH rise and low T3 level. Four of these individuals had normal T4 levels, while three of them had T4 levels below normal. These patients lacked any clinical indicators of hypothyroidism. These patients can have tests like FT4, FT3, TH response, and antithyroid auto-antibodies performed to diagnose hypothyroidism. Our findings are in line with other major studies, which also showed low T3 and low T4 levels as well as normal or mild TSH increase. However, it is not apparent to what extent these alterations are to blame for the Uremic syndrome symptoms. It has been hypothesised from a number of studies that the abnormal thyroid profile is a result of a body adaptive mechanism (10,11).

As previously mentioned, continuous ambulatory peritoneal dialysis and hemodialysis have both been found to have an impact on the thyroid profile separately from CKD. The thyroid profile will also be

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impacted by medications used during dialysis, such as heparin and furosemide. Studies on the impact of dialysis on CKD patients with thyroid dysfunction have been done in the above studies. These studies revealed that after repeated hemodialysis, the thyroid profile did not significantly improve. Nonetheless, most thyroid function measures reverted to normal in individuals who underwent kidney transplant surgery, whereas TSH was below normal. High frequency of hypothyroidism in CKD was observed in them. In individuals with end-stage renal failure, it was estimated to be around 5% (12).

According to a detailed study by Kaptein et al, chronic renal failure and dialysis patients are around 2.5 times more likely to have primary hypothyroidism. Estimates of the hypothyroidism in CKD ranged from 0 to 9.5%. Anti-thyroid antibody titre was also determined to be present in 6.7% of CKD. In our study, 10% of the patients had hypothyroidism, but it had no relation to how severe their renal failure was (13). In our study, patients with hypothyroidism and CKD both experienced a similar distribution of hypothyroid symptoms. In CKD without hypothyroidism, signs of hypothyroidism were more prevalent than in CKD with hypothyroidism. Hence, the TSH level, which should be very high (>20 MIU/dl) with low blood T4, is the key factor in the diagnosis of hypothyroidism in CKD. No patient in this research demonstrated biochemical or clinical signs of hyperthyroidism (9,14).

Conclusion:

CKD patients have a higher incidence of hypothyroidism. For individuals with CKD, it is critical to detect hypothyroidism using both clinical and biochemical markers. The prevalence of low T3 and T4 syndrome patients increases over time as renal failure becomes more severe. There is no relationship between serum levels of T3 and T4 and the degree of renal failure (15).

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