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CORRELATION OF THYROID FUNCTION TEST WITH BIOCHEMICAL MARKERS OF RENAL FUNCTION IN CKD PATIENTS ON HEMODIALYSIS

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Abstract

Introduction: Thyroid replacement therapy when it comes to chronic kidney disease (CKD) patients has the potential to save renal function. It is therefore of utmost importance to identify such cases and recognize when to initiate thyroid replacement therapy. **Methods:** This observational study was conducted on a cohort of 70 CKD patients from June 2020 to July 2020. All clinically stable patients for the last six months and on hemodialysis were included. **Results**: Around 30 (42.9%) cases belonged to stage 5, 37 (52.9%) belonged to stage 4, and 3 (4.3%) belonged to stage 3 of CKD. Hypothyroidism was seen in 17 (24.3%) cases. **Conclusion**: We found that the T3 hormone is inversely correlated with blood urea, creatinine levels, and positively correlated with hemoglobin levels.

Keywords: Thyroid Function test, biochemical markers, renal function, chronic kidney disease, hemodialysis

INTRODUCTION:

Thyroid disorders in CKD patients are of multifactorial origin.[1] As compared to the general population, hypothyroidism is prevalent among CKD patients.[2,3] Kidney is involved in the production of T_3 hormone by deiodination of T4 by the isoform D1 of the enzyme T4-5′ -deiodinase.[4] Previous researches have assumed that Thyroid disorders like clinical and subclinical hypothyroidism and low T3 syndrome in patients suffering from CKD has been happening because there has been lesser activity on the part of enzyme T4-5′ -deiodinase.[2,3,5] It has been noted earlier too that patients suffering from CKD show any variation in case of Hyperthyroidism as compared to general population.[6] The prevalence of subclinical and clinical hypothyroidism is reported from 5% up to 25%.[2] Other causes implicated in thyroid dysfunction in CKD are- abnormal TSH response to TRH, uremic toxins[7], metabolic acidosis[8], malnutrition[8], heparin (used in hemodialysis)[7], advanced age[7], HCV infection[1], chronic inflammation[1], and certain drugs[7] like amiodarone, steroids, beta-blockers. Hypothyroidism or hyperthyroidism may affect renal tubular function, glomerular filtration rate (GFR), and cause proteinuria.[9]

There is a significant alteration in thyroid hormone function tests in CKD patients especially if they are on dialysis. Thyroid replacement therapy when it comes to Chronic kidney disease patients has the potential to save renal function.[10–12] It is therefore of utmost importance to identify such cases and recognize when to initiate thyroid replacement therapy. Also, the correlation with other biochemical markers like urea and electrolytes does not show consistent results across the literature. Indian studies are also less in number. By this study, we aim to estimate the prevalence of abnormalities in thyroid hormone in CKD patients and evaluate the correlation of thyroid hormone profile with other biochemical markers of renal function like urea, creatinine, electrolytes, albumin, and globulin levels in CKD patients on hemodialysis at our institute which is a tertiary care center in the southern part of Maharashtra state.

METHODS:

This observational study was conducted on a cohort of 70 CKD patients from June 2020 to July 2020. All clinically stable patients for the last six months and on hemodialysis were included. Thyroid function test (T3, T4, and TSH), hemoglobin, urea, creatinine, electrolytes (sodium and potassium), total proteins, albumin, and globulin levels were measured. Written informed consent was taken from all patients. Data entry and analysis was done in SPSS version 22.0 (IBM). Statistical significance was considered with a $p < 0.05$. Pearson's correlation coefficient and scatter plots were used to determine the relationship between thyroid hormone levels and other clinical parameters as well as the duration of dialysis.

RESULTS:

This observational study consisting of 70 CKD patients with 43 (61.4%) males and 27 (38.6%) females yielded the following results. Around 30 (42.9%) cases belonged to stage 5, 37 (52.9%) belonged to stage 4, and 3

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(4.3%) belonged to stage 3 of CKD. The description of the study participants is given in **Table 1**. The mean age of participants in our study was 46.87 ± 14.99 years (range 20-84).

Table 1: Characteristics of the study participants (N=70)

Variables	Male (43)	Female (27)	Total		p-value independent t -test
	Mean ± S.D	Mean ± S.D	Mean ± S.D	Range	
Age (years)	46.53 ± 14.77	47.41 ± 15.619	46.87 ± 14.99	20 - 84	0.815
Hemoglobin (g/dl)	8.19 ± 2.05	8.12 ± 1.99	8.17 ± 2.01	4.30 – 15.50	0.886
Blood urea (mg/dl)	123.81 ± 41.34	103.33 ± 43.54	115.91 ± 43.07	23 - 229	**0.052**
Creatinine (mg/dl)	9.94 ± 3.69	7.40 ± 2.99	8.96 ± 3.64	1.90 – 18.20	**0.004**
Sodium(mEq/L)	133.47 ± 5.19	135.93 ± 4.49	134.41 ± 5.05	122 - 145	**0.046**
Potassium (mmol/L)	4.72 ± 0.94	4.62 ± 1.34	4.68 ± 1.10	2.40 – 7.00	0.722
Total Proteins (g/dl)	6.14 ± 0.67	6.22 ± 0.87	6.17 ± 0.76	4.20 – 8.30	0.683
Albumin (g/dl)	3.25 ± 0.51	3.29 ± 0.61	3.27 ± 0.54	2.00 – 4.30	0.752
Globulin (g/dl)	2.89 ± 0.62	2.92 ± 0.59	2.90 ± 0.61	1.50 – 4.50	0.823
T3 (ng/dl)	90.76 ± 52.04	95.74 ± 61.89	92.68 ± 55.66	28.00 – 383.00	0.719
T4 (µ/dl)	5.01 ± 1.79	5.0437 ± 1.63	5.02 ± 1.72	1.20 – 10.70	0.941
TSH (µIU/ml)	4.23 ± 2.89	6.60 ± 5.19	5.15 ± 4.07	0.24 -23.00	**0.017**
Duration of dialysis (months)	29.35 ± 27.28	36.30 ± 24.25	32.03 ± 26.20	4 - 120	0.283

Hypothyroidism was seen in 17 (24.3%) cases. Hyperthyroidism was seen in one (1.4%) case. T3 was normal in 32 cases (45.7%). The prevalence of low T3 was 48.6 % (34 cases). Hypothyroidism was more prevalent among female patients (40.74%) of CKD than male (13.95%) patients. (p=0.03) Mean TSH levels in the study group was 0.24 -23.00 µIU/ml. On applying independent sample t-test, there was a significant difference in TSH levels among males and females (p=0.017). Mean T3 and T4 levels in the study group were 92.68 ± 55.66 ng/dl and 5.02 ± 1.72 µ/dl respectively. T3 and T4 levels were comparable among males and females. There was a significant difference in levels of blood urea and creatinine too among males and females (p=0.052 and p=0.004 respectively).

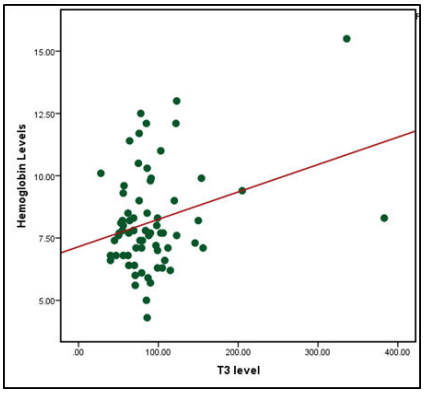

Figure 1: Scatter plot showing a positive correlation between hemoglobin and T3 levels in study participants.

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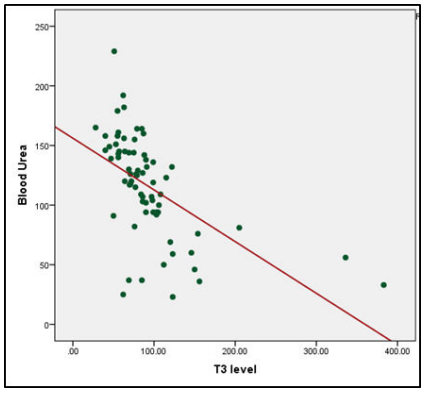

Figure 2: Scatter plot showing the inverse correlation between blood urea and T3 levels in study participants.

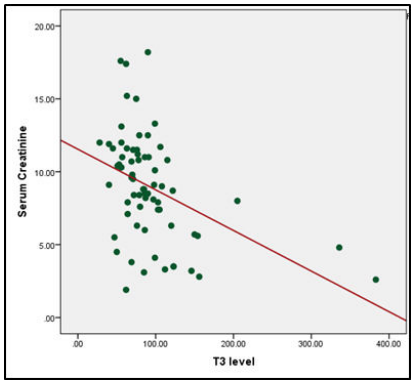

Figure 3: Scatter plot showing the inverse correlation between serum creatinine and T3 levels in study participants.

We found no significant correlation between levels of thyroid hormone and stage of CKD. Correlation was also used to study the relationship between thyroid hormone levels and other biochemical parameters. A positive correlation was found between hemoglobin levels and T3 levels (Pearson's correlation coefficient, r=0.304, p=0.011). Urea and creatinine levels were found to be inversely correlated with T3 levels (r=-0.56 and -0.43 respectively, both p<0.001). This has been represented in scatter plots. (Figure 1-3) There is no correlation between thyroid hormone levels and other parameters.

DISCUSSION:

This observational study consists of 70 CKD patients with 61.4% males and 38.6% females. Around 42.9% were in stage 5, followed by 52.9% in stage 4, and 4.3% in stage 3 of CKD. Previous studies have shown that hypothyroidism is prevalent among CKD patients.[2,3] The prevalence of hypothyroidism in the general population is 4-10%,[13] with a 3% prevalence in men, and 8% in women.[14] There is a significant alteration in thyroid hormone function in CKD patients. In our study, the prevalence of hypothyroidism was 24.3%, hyperthyroidism was 1.4%, and T3 hormone deficiency was 48.6 %. Hyperthyroidism in CKD patients does not vary from the general population.[6] **Lim et al** reported the prevalence of goiter in end-stage renal disease (ESRD) as 0%–58%, and that of sub-clinical hypothyroidism as 0%–9.5%. [15] **Lao et al** reported the prevalence of subclinical and clinical hypothyroidism is reported from 5% up to 25% in CKD patients.[2] In another study, **Chonchol et al** reported that 18% of the patients with CKD not requiring dialysis had subclinical primary hypothyroidism.[3] In India, **Gupta et al**, conducted a study on 100 pre-dialysis CKD patients and reported a prevalence of 53% for thyroid dysfunction, 33% subclinical hypothyroidism, and 20% for clinical hypothyroidism. Even the CKD patients on dialysis, have significant alterations in the thyroid function test. **Kang et al,** in their study on ESRD patients receiving continuous ambulatory peritoneal dialysis, reported a prevalence of 27.5% of subclinical primary hypothyroidism. In a study by **Naseem et al** in Karachi, the prevalence of subclinical hypothyroidism in patients on maintenance hemodialysis was found to be 30.6%.[16] Even in India, **Shantha et al**, reported the prevalence to be 24.8% in patients on maintenance hemodialysis.[17] In our study we found that hypothyroidism was more prevalent among female (40.74%) patients of CKD than male (13.95%) patients. Similar findings were reported by **Naseem et al**, where they reported the prevalence of

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hypothyroidism as 21.6% in males, and 46.2% in females (P=0.03). Low T3 levels have been reported in CKD patients with or without alteration in other thyroid hormones like T4 and TSH.[7,18,19] In our study the prevalence of low T3 was 48.6 %. **Manohari et al** reported an overall incidence of hypothyroidism as 16.2 % in CKD patients. They also proved the association of lower T3 syndrome with CKD.[18] **Fan et al** also reported a high prevalence of serum T3 (47%) in CKD patients.[19]

Some studies have reported that the prevalence of hypothyroidism increases with the duration of dialysis.[16] It is reported that 3-5% of patients of CKD who have subclinical hypothyroidism progress to overt hypothyroidism every year. [20] We found no association with the duration of dialysis with the thyroid hormone levels in our study.

The incidence of anemia in hypothyroidism is reported as 23%-60%. The etiology is multifactorial. [21] Our study has shown a positive correlation (r=0.304) between hemoglobin levels and T3 levels. A study by **Chandra A** also reported lower hemoglobin levels in the hypothyroid group of CKD patients, the results however were not significant (p=0.06). [22] **Fan et al** also reported a positive correlation between T3 levels and anemia (r^2=0.15).[19] We also found that blood urea and creatinine levels were inversely correlated with T3 levels (r=-0.56 and -0.43 respectively, both p<0.001). These results are consistent with previous studies. **Srivastava et al** reported a significant inverse correlation between the blood urea and free T3 (r = −0.749) and creatinine and free T3 (r = −0.692) in CKD patients but, they were not on dialysis. **Mehta et al**, however, observed no linear relationship between these variables. [23] Proteinuria and hypoalbuminemia have been associated with hypothyroidism. Previous studies show a positive correlation between albumin levels and TSH levels[17], however, no such correlation was found in our study.

CONCLUSION:

Our study contributes to previous evidence of thyroid dysfunction in CKD patients on hemodialysis and its relationship with other biochemical parameters. We found that the T3 hormone is inversely correlated with blood urea, creatinine levels, and positively correlated with hemoglobin levels. However, our study has certain limitations like small sample size and non-availability of a control group. The thyroid profile also changes with the dialysis technique and this could not be assessed as all patients were on hemodialysis only. Larger studies that can be extrapolated on the patients of CKD on hemodialysis are needed. Thyroid replacement therapy in these patients can lead to significant improvement of renal function and thus it is important to identify such cases and initiate thyroid replacement therapy where indicated.

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