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CROSS SECTIONAL STUDY OF ALTERATION OF T3 LEVEL IN PATIENTS WITH UNDERLYING CHRONIC KIDNEY DISEASE.

General Medicine

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ABSTRACT

Background: Chronic kidney disease (CKD) is associated with multiple systemic complications, including thyroid dysfunction, which can further impact metabolism and disease progression. The interplay between CKD and thyroid abnormalities is complex, with significant alterations in thyroid hormone metabolism observed as renal impairment advances. **Aim:** To assess T3 abnormalities in patients with chronic kidney disease. **Methodology:** This cross-sectional study was conducted in the Department at a tertiary care hospital. Forty CKD patients on conservative management were enrolled based on predefined inclusion and exclusion criteria. Clinical history, physical examination, and laboratory investigations, including renal function tests and thyroid hormone levels (TSH, T3, T4), were conducted. CKD severity was classified based on the estimated glomerular filtration rate (eGFR). **Results:** This study examined T3 abnormalities in CKD patients, revealing that 65% had low T3 levels. Serum T3 correlated inversely with blood urea ($r = -0.42$) and creatinine ($r = -0.47$) but drop in eGFR ($r = 0.53$) coincided with fall in T3. These correlations were statistically significant ($p < 0.05$), indicating T3 abnormality worsens with declining renal function. **Conclusion:** Thyroid dysfunction is prevalent in CKD patients and low T3 syndrome strongly correlates with declining renal function. These findings emphasize the need for routine assessment of T3 in CKD management. Further research is required to explore the clinical significance of T3 in CKD and its impact on disease progression and patient outcomes.

KEYWORDS

Chronic kidney disease, Thyroid dysfunction, Hypothyroidism, Renal impairment.

INTRODUCTION

Chronic kidney disease (CKD) is a major global health issue, with an estimated prevalence of 9.1%. It is defined by persistent structural or functional kidney abnormalities lasting over three months, leading to significant health implications. CKD is strongly linked to increased mortality, cardiovascular diseases, and progression to end-stage renal disease (ESRD).[1] Understanding the factors influencing CKD development and the decline in estimated glomerular filtration rate (eGFR) is essential for developing preventive and therapeutic strategies.[1,2]

Thyroid hormones play a crucial role in kidney growth, regulation of renal blood flow, and overall maintenance of kidney function. Several epidemiological studies and clinical trials have examined their influence on renal function decline.[3] Thyroid dysfunctions can significantly impact both kidney and cardiovascular health. Conversely, CKD can alter thyroid function through various mechanisms, including non-thyroidal illness, metabolic disturbances, impaired hormone metabolism, decreased peripheral conversion of thyroid hormones, hormone loss during dialysis, and increased iodine accumulation in the thyroid gland.[4,5] The study of T3 will enable us to focus on the role of this active hormone in various pathophysiological mechanisms in CKD.

Thyroid hormones play a crucial role in renal development and function by modulating various physiological processes. They contribute to the regulation and activity of multiple co-transport systems within the renal tubules, including the sodium-phosphate (Na-P) co-transporter, sodium-hydrogen (Na-H) exchanger, and sodium-potassium ATPase (Na/K ATPase) in the proximal convoluted tubule.[6] T3 being an active hormone plays the major role in these processes. So estimating the value of T3 will help us in understanding its role in patients suffering from CKD.

The systemic effects of thyroid hormones particularly T3 on renal function are largely mediated through their influence on the cardiovascular system, the renin-angiotensin system, and renal hemodynamics.[6,7] Experimental studies have demonstrated that T3 may enhance beta-adrenergic receptor expression and its coupling with adenylate cyclase, thereby modulating the renin-angiotensin system and influencing renal blood flow.[8]

Research, predominantly cross-sectional, has highlighted a link between both overt and subclinical hypothyroidism with decreased estimated glomerular filtration rate (eGFR) and subsequently higher occurrence of CKD .[9] T3 with conversion to T4 which ultimately impacts TSH may play a significant role in decline of eGFR. However, longitudinal studies have yielded mixed results, with some indicating that both reduced and elevated thyroid function may contribute to renal dysfunction. The concurrent presence of CKD and abnormalities of T3 has prompted the potential benefits of thyroid hormone replacement therapy in improving renal function.[10,11]

Given the considerable impact of CKD and the possible influence of thyroid dysfunction on renal health, evaluating the prevalence and patterns of T3 abnormality in CKD patients is crucial. This study seeks to analyze T3 levels in individuals with CKD and determine its relationship with the degree of renal impairment. Recognizing low T3 values could contribute to more effective therapeutic strategies by replacement of T3 hormone for managing CKD patients.

AIM:

To assess T3 abnormalities in patients with chronic kidney disease.

OBJECTIVES:

1. To determine the prevalence of T3 disturbances in CKD patients.
2. To study the relationship between T3 level and stage of CKD.

METHODOLOGY

This cross-sectional study was conducted in the Department at a tertiary care hospital. The study included both male and female patients admitted with chronic kidney disease (CKD) who were on conservative management. A total of 40 patients were enrolled based on predefined inclusion and exclusion criteria.

The inclusion criteria comprised patients presenting with symptoms of uremia for at least three months, elevated blood urea and serum creatinine levels with decreased creatinine clearance, and ultrasound evidence of chronic renal failure, including bilaterally contracted kidneys (size <8 cm in males and <7 cm in females) and poor corticomedullary differentiation. Supportive laboratory findings such as anemia, altered urine specific gravity, and electrolyte disturbances were also considered. Additionally, participants were required to provide informed consent and be between 18 and 80 years of age.

Patients were excluded if they had undergone peritoneal dialysis or hemodialysis, were on medications affecting thyroid function (such as amiodarone, steroids, dopamine, phenytoin, beta-blockers, estrogen pills, or iodine-containing drugs), were pregnant, or had conditions like acute illness, recent surgery or trauma, diabetes mellitus, or liver diseases.

Following informed consent, detailed clinical history and examination was conducted, focusing on thyroid and renal diseases. The history assessment included symptoms of uremia , disease duration, comorbidities, lifestyle factors (smoking, alcoholism), drug intake, and prior treatment taken. Physical examinations included height, weight, and blood pressure measurements, along with renal function tests and an electrocardiogram (ECG).

Blood samples (5 mL) were collected from the antecubital vein using plain vacutainers under strict aseptic precautions. The samples were transported to the laboratory, centrifuged to separate serum, and stored at 4°C for further analysis. Serum urea and creatinine levels were measured using enzymatic methods, and thyroid profiles particularly T3 were assessed using a fully automated analyzer. Renal function was evaluated based on blood urea, serum creatinine, creatinine clearance, and estimated glomerular filtration rate (eGFR), which was calculated using the CKD-EPI creatinine equation, known for its accuracy, particularly in patients with higher GFR levels.

Thyroid function was assessed by measuring Triiodothyronine (T3) levels using chemiluminescence immunoassays. The reference range used was T3 (0.40–2.04 ng/mL). Additional investigations such as ECGs and chest X-ray was done to detect features of renal failure, such as pleural or pericardial effusion. X-rays of the wrist, forearm, and spine were examined for renal osteodystrophy, and abdominal ultrasound imaging was performed to assess structural abnormalities in the kidney associated with chronic renal failure.

All the data was systematically collected and analysed.

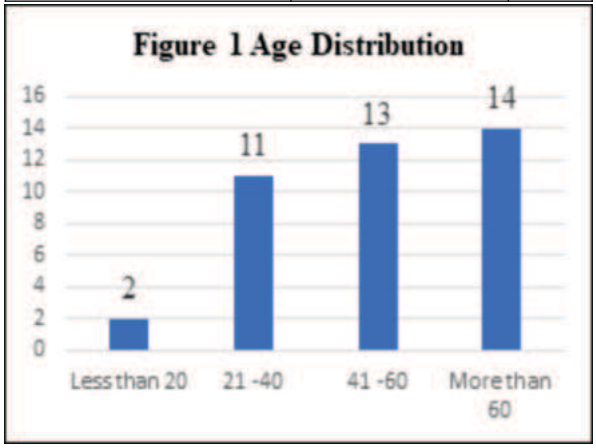
RESULTS

This cross-sectional study explores changes in T3 hormone in patients with chronic kidney disease (CKD) by analyzing T3 hormone levels and their correlation with renal parameters. Understanding T3 abnormalities in CKD patients is crucial, as they can impact metabolic balance and disease progression.

The present study analyzed the demographic characteristics of participants, focusing on age, gender distribution, and symptom duration. The mean age of participants was 46.10 ± 14.84 years, ranging from 18 to 74 years. **(Ref Table 1)** The majority (35%) were aged over 60 years, while 27.5% were between 21 and 40 years. Males constituted 65% of the study population, while females made up 35%. **(Ref Fig 1).** The average symptom duration was 5.7 ± 1.45 months, with a range of 4 to 8 months.

Table 1 Demographic Data

Variable	Mean ± SD	Range
Age (Years)	46.10 ± 14.84	18 – 74
Gender Distribution	Male: 26 (65%) Female: 14 (35%)	-
Symptoms Duration (Months)	5.7±1.45.7	4 – 8



The present study analyzed renal function parameters in patients with chronic kidney disease (CKD). The mean blood urea level was 65.82 ± 13.92 mg/dL, with values ranging from 43 to 89 mg/dL. Serum creatinine levels averaged 2.99 ± 0.87 mg/dL, with a range of 1.6 to 5.76 mg/dL. The estimated glomerular filtration rate (eGFR), a key indicator of kidney function, had a mean value of 25.18 ± 7.67 mL/min/1.73m², ranging from 10 to 41 mL/min/1.73m².

Based on eGFR classification, moderate impairment (eGFR 30-44 mL/min/1.73m²) was observed in 12 (30%) patients, while severe impairment (eGFR 15-29 mL/min/1.73m²) was the most common category, affecting 24 (60%) patients. Additionally, 4 (10%) patients had kidney failure (eGFR <15 mL/min/1.73m²), highlighting the high disease burden in the study population.

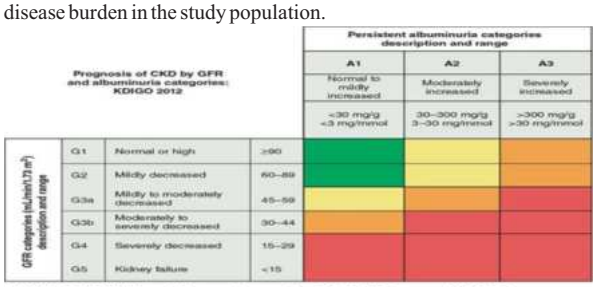


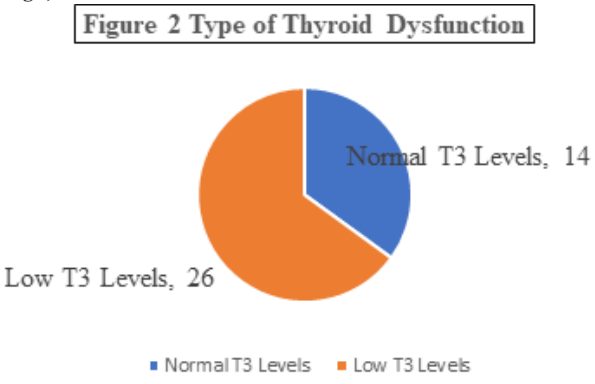
FIGURE 311-1 Kidney Disease Improving Global Outcome (KDIGO) classification of chronic kidney disease (CKD). Gradation of color from green to red corresponds to increasing risk and progression of CKD. GFR, glomerular filtration rate. *(Reproduced with permission from KDIGO 2012 Clinical Practice*

The study categorized chronic kidney disease (CKD) patients into different stages based on disease severity. Among the 40 participants, 12 (30%) were in CKD Stage 3b, 24 (60%) were in Stage 4, and 4 (10%) had reached Stage 5, indicating end-stage renal disease. The majority of patients (70%) had advanced CKD, highlighting the progression of renal dysfunction in the study population. **(Refer Table 2)**

Table 2 – Stages Of CKD

CKD Stage	Frequency (n = 40)	Percentage (%)
Stage 3b	12	30.00
Stage 4	24	60.00
Stage 5	4	10.00

Out of the total cases, 14 individuals (35%) had normal T3 levels, while a majority, 26 individuals (65%), exhibited low T3 levels. **(Ref Fig 2)**



Serum T3 levels have a mean of 0.66 ± 0.56 ng/mL, with values ranging from 0.06 to 4.54 ng/mL. Serum T4 levels show a mean of 5.81 ± 2.24 mcg/dL, with a minimum of 1.35 mcg/dL and a maximum of 13.68 mcg/dL. Serum TSH levels have a mean of 4.54 ± 2.92 mcIU/mL, ranging from 0.21 to 13.68 mc IU/mL.

Table 4 Correlation Between low T3 Levels and Renal Parameters

Renal Parameter	Correlation Coefficient (r)	Significance (p-value)
Blood Urea (mg/dL)	-0.42	$p < 0.05$
Serum Creatinine (mg/dL)	-0.47	$p < 0.05$
eGFR (mL/min/1.73m²)	0.53	$p < 0.05$

As blood urea and serum creatinine levels increase, the T3 hormone level decreases. The statistically significant p-value ($p < 0.05$) confirms that these correlations are meaningful.

The eGFR (estimated glomerular filtration rate) has a positive correlation (+0.53), indicating that lower eGFR values correspond to fall in T3 levels.

All correlations are statistically significant ($p < 0.05$), which indicates a meaningful relationship between renal function and the variable being analyzed.

DISCUSSION

Patients with chronic kidney disease (CKD) are at an increased risk of developing thyroid dysfunction due to multiple interrelated mechanisms. One major factor is iodine retention, which occurs due to impaired renal clearance, leading to disruptions in thyroid hormone synthesis. Additionally, metabolic acidosis, a common complication of CKD, can negatively impact thyroid function by altering hormone production and peripheral conversion.

The dysregulation of the hypothalamic-pituitary-thyroid (HPT) axis is observed in CKD patients, leading to alterations in T3 hormone secretion and metabolism. Lastly, changes in thyroid hormone degradation and excretion due to impaired renal function can result in abnormal circulating T3 hormone levels. These complex interactions underscore the importance of routine T3 level assessment in CKD patients to ensure timely diagnosis and management of thyroid-related complications.

The present study aimed to assess T3 abnormalities in patients with chronic kidney disease Since T3 dysfunction often remains undiagnosed in CKD due to symptom overlap with uremia—such as fatigue, cold intolerance, and cognitive decline . Assessment and treatment with T3 will help us in preventing this decline.

In the present study, the mean age of participants was 46.10 ± 14.84 years (range: 18 to 74 years), with a higher proportion of males (65%) compared to females (35%). The average duration of symptoms was 5.7 ± 1.45 months, ranging from 4 to 8 months. Age distribution analysis revealed that 5% of patients were below 20 years, 27.5% were between 21-40 years, 32.5% were in the 41-60 years group, and 35% were above 60 years, indicating a predominance of middle-aged and elderly individuals.

A comparison with previous studies revealed similarities and differences. **Sinjari et al.** reported a higher mean age (53.99 ± 14.59 years) than our study, suggesting an older CKD population in their cohort.[13] Their gender distribution (Male/Female = 54/50) was also more balanced compared to the male predominance observed in our study. Another study by **Mohamedali M et al.** also reported comparable findings, supporting the idea that T3 dysfunction in CKD patients is common and often remains undiagnosed due to overlapping clinical presentations.[14]

The present study analyzed renal function parameters and T3 dysfunction in chronic kidney disease (CKD) patients, revealing significant findings in both aspects. The mean blood urea level was 65.82 ± 13.92 mg/dL (range: 43–89 mg/dL), while the mean serum creatinine was 2.99 ± 0.87 mg/dL (range: 1.6–5.76 mg/dL). The estimated glomerular filtration rate (eGFR) averaged 25.18 ± 7.67 mL/min/1.73m², with most patients having severe impairment (60%) or kidney failure (10%), indicating a high disease burden.

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Regarding CKD stages, T3 dysfunction was most common in Stage 4, with a statistically significant association (p=0.012). Prior studies also reported a strong correlation between worsening CKD and T3 dysfunction, particularly hypothyroidism. The present study supports findings from **Cotoi L et al.** and other epidemiological studies, reinforcing that T3 abnormalities increase with CKD severity.[16]

In this study, a significant proportion of CKD patients (65%) exhibited low T3 levels, while only 35% had normal T3 levels. This finding aligns with the concept of low T3 syndrome or non-thyroidal illness syndrome (NTIS), which is frequently observed in patients with chronic illnesses, including CKD.[16] The mean serum T3 level was 0.66 ± 0.56 ng/mL, with a wide range from 0.06 to 4.54 ng/mL, indicating variability in T3 level among the study population. The reduction in T3 levels in CKD patients may be attributed to impaired peripheral conversion of T4 to T3 due to systemic inflammation, uremic toxins, and alterations in protein metabolism.

T3 level was analyzed in correlation with renal parameters. A negative correlation was observed between T3 levels and blood urea ($r = -0.42$, $p < 0.05$) as well as serum creatinine ($r = -0.47$, $p < 0.05$), suggesting that worsening renal function is associated with lower T3 levels. This could be due to metabolic disturbances, reduced deiodinase activity, and increased cytokine production, all of which contribute to T3 abnormalities in CKD. A positive correlation was found between T3 levels and estimated glomerular filtration rate (eGFR) ($r = 0.53$, $p < 0.05$), indicating that better kidney function is associated with relatively preserved T3 levels.

These findings highlight the interplay between thyroid and kidney function, reinforcing the need for T3 level assessment in CKD patients. The decline in T3 levels may serve as a potential marker for disease severity and progression in CKD. Recognizing low T3 syndrome in CKD patients is crucial, as it may have prognostic implications, including increased cardiovascular risk and mortality. Further studies are needed to determine whether T3 hormone supplementation could improve outcomes in these patients.

CONCLUSION

The present study highlights a significant prevalence of T3 disturbances , particularly low T3 syndrome, in patients with chronic kidney disease (CKD). The findings suggest a strong association between declining renal function and alterations in T3 levels, with worsening kidney function correlating with lower T3 levels. This relationship underscores the impact of CKD on overall metabolic regulation and thyroid function. The routine assessment of T3 level in these patients may be beneficial for early detection and management. Recognizing and addressing T3 abnormalities in CKD could potentially improve clinical outcomes and overall metabolic stability. Future research is needed to explore the therapeutic implications of T3 hormone alterations in CKD and its role in disease progression.

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