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Effect of Thyroid Hormone Replacement Therapy on Glomerular Filtration Rate in Patients with Hypothyroidism

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ABSTRACT

Introduction: Thyroid hormones exert widespread effects on almost all organ systems of the body and are essential for normal growth, development, and metabolic regulation. Among these systems, the kidneys are particularly influenced by thyroid hormone activity. **Aim**: The aim of the study is to evaluate the effect of thyroid hormone replacement therapy on glomerular filtration rate in patients with hypothyroidism Methodology: This study was designed as a prospective cohort study conducted in the Department of General Medicine, Government Medical College, Palakkad. The study population comprised patients attending the outpatient department as well as those admitted as inpatients during the study period. **Result**: At baseline, most patients had elevated TSH levels with increased serum creatinine and reduced eGFR. Following thyroid hormone replacement therapy, there was a progressive normalization of TSH accompanied by a decrease in serum creatinine and improvement in eGFR. **Conclusion**: Hypothyroidism was associated with elevated serum creatinine and reduced eGFR at baseline, indicating impaired renal function. Thyroid hormone replacement therapy led to progressive normalization of TSH levels with a parallel improvement in serum creatinine and eGFR, suggesting that renal dysfunction in hypothyroidism is largely reversible.

Keywords: hypothyroidism, renal, eGFR.

INTRODUCTION

Thyroid hormones exert widespread effects on almost all organ systems of the body and are essential for normal growth, development, and metabolic regulation. Among these systems, the kidneys are particularly influenced by thyroid hormone activity. Thyroid hormones play an important role in renal growth and maturation and are involved in the regulation of water and electrolyte balance, particularly sodium handling.[1] Through these mechanisms, thyroid hormones significantly affect renal plasma flow (RPF) and glomerular filtration rate (eGFR), which are key indicators of kidney function.In patients with hypothyroidism, several functional and hemodynamic changes occur in the kidneys. Reduced cardiac output, increased systemic vascular resistance, and impaired renal perfusion lead to a decrease in RPF and eGFR. Hyponatremia is also commonly observed in hypothyroid patients due to impaired free water excretion. These renal abnormalities are largely functional in nature and have been shown to improve following thyroid hormone replacement therapy.[2] Several studies have demonstrated that restoration of euthyroidism with L-thyroxine results in normalization of renal hemodynamics, improvement in serum creatinine levels, and an increase in eGFR.Previous literature has highlighted the close relationship between thyroid dysfunction and renal disease. L-thyroxine therapy has been shown to correct cases of acute renal failure associated with severe hypothyroidism[3]. Additionally, it has been observed that underlying chronic kidney disease may worsen rapidly in the presence of untreated hypothyroidism, emphasizing the importance of early diagnosis and management of thyroid dysfunction in patients with impaired renal function. These observations suggest that hypothyroidism may act as a reversible cause of renal dysfunction and may mask true renal status if left untreated.Thyroid disorders primarily affect the cardiovascular and renal systems, both of which are closely linked through hemodynamic regulation.[4] The renin–angiotensin system (RAS) plays a central role in maintaining cardiovascular stability and renal function[5]. Thyroid hormones influence the activity of the RAS by regulating the synthesis of renin and angiotensin-converting enzyme (ACE), particularly in the kidney and lung, which are the principal sites of their production.[6] Alterations in thyroid hormone levels may therefore lead to significant changes in renal blood flow and glomerular

filtration.Hypothyroidism is more prevalent in the elderly population and shows a clear female predominance[7]. The incidence of elevated thyroid-stimulating hormone (TSH) levels increases with advancing age. Large population-based studies have reported a higher prevalence of hypothyroidism in older adults, with a significant proportion of elderly men and women exhibiting TSH levels above the normal reference range.[8,9] Data from the National Health and Nutrition Examination Survey (NHANES) further support these findings, demonstrating that a substantial percentage of individuals aged 80 years and above have elevated TSH levels even in the absence of autoimmune thyroid disease.[10]Although advancing age is considered a risk factor for chronic kidney disease, the decline in eGFR observed in elderly individuals may represent a physiological aging process rather than true pathological renal disease[11]. While correction of hypothyroidism has been shown to improve eGFR in several studies, data specifically evaluating renal function changes following thyroid hormone replacement in older patients remain limited. Therefore, the present study aims to evaluate the effect of achieving euthyroid status on renal function parameters in elderly patients with hypothyroidism[12].

AIM

The aim of the study is to evaluate the effect of thyroid hormone replacement therapy on glomerular filtration rate in patients with hypothyroidism.

METHODOLOGY

This study was designed as a prospective cohort study conducted in the Department of General Medicine, Government Medical College, Palakkad. The study population comprised patients attending the outpatient department as well as those admitted as inpatients during the study period. All participants were screened and selected based on predefined inclusion and exclusion criteria.

Patients aged more than 18 years who were diagnosed with primary hypothyroidism were included in the study. Primary hypothyroidism was defined by elevated thyroid-stimulating hormone (TSH) levels along with a decrease in any one of the four thyroid hormone levels. Only those patients with normal serum creatinine levels and an estimated glomerular filtration rate (GFR) of less than 90 ml/min/1.73 m² were enrolled. Patients were excluded if they had any known kidney disease or conditions directly affecting renal function, such as diabetes mellitus, systemic hypertension, heart failure, or chronic liver disease. Pregnant women were also excluded from the study.

The duration of the study was six months, commencing after obtaining approval from the institutional ethical committee. Sampling was done by enrolling all eligible patients who attended the Department of General Medicine and fulfilled the inclusion criteria during the study period. An approximate sample size of 100 patients was planned for this study.

RESULT

Table 1: Demographic distribution of participants

Age	Number	Percentage
≤30	15	15%
31-40	29	29%
41-50	23	23%
51-60	17	17%
61-70	12	12%
>70	4	4%

The majority of patients belonged to the 31–40 year age group (29%), followed by those aged 41–50 years (23%). Smaller proportions were observed in the younger (≤30 years, 15%) and older age groups, with only 4% of patients aged above 70 years.

Table 2:Sex distribution of participants

Sex	Number	Percentage
Male	39	39%
Female	61	61%

Females constituted the majority of the study population, accounting for 61% of the patients, while males comprised 39%. This demonstrates a clear female predominance in the study group.

Table 3: Duration of disease

Duration	Number	Percentage
<1 year	24	24%
1-10 year	56	56%
11-20 year	17	17%
>20 year	3	3%

The majority of patients had a disease duration of 1–10 years, accounting for 56% of the study population. Shorter disease duration of less than one year was seen in 24% of patients, while long-standing disease of more than 20 years was observed in only 3%.

Table 4: Serial Distribution of Patients According to TSH Levels Before and After Thyroid Hormone Replacement Therapy

TSH	TSH 1	TSH 2	TSH 3
0.5-4.5	00	12	59
4.6-10	37	57	27
<10	63	31	14

At baseline (TSH1), the majority of patients had TSH levels >10 mIU/L, indicating overt hypothyroidism. Following thyroid hormone replacement therapy, there was a progressive shift toward lower TSH ranges, with most patients achieving euthyroid levels (0.5–4.5 mIU/L) by the third follow-up.

Table 5:Distribution of Patients According to serum creatinine Levels Before and After Thyroid Hormone Replacement Therapy

Cr	Cr 1	Cr 2	Cr 3
≤0.9	00	19	52
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]

At baseline (Cr1), most patients had serum creatinine levels in the 1–1.2 mg/dL range, with a notable proportion showing values ≥1.3 mg/dL. Following therapy, there was a progressive shift toward lower creatinine levels, with an increasing number of **patients** achieving values ≤0.9 mg/dL by the third follow-up.

Table 6:Distribution of Patients According to GFR Levels Before and After Thyroid Hormone Replacement Therapy

GFR	GFR 1	GFR 2	GFR 3
<60	39	16	6
60-89	54	71	59
≥90	7	13	35

At baseline (GFR1), a large proportion of patients had reduced or mildly reduced eGFR values, with only a small number showing normal eGFR. Following therapy, there was a progressive improvement in renal function, with an increasing number of patients achieving eGFR values ≥90 mL/min/1.73 m² by the third follow-up.

DISCUSSION

The age of the patients ranged from 19 to above 70 years. The largest proportion of patients belonged to the 31–40 year age group, accounting for 29% of the study population. This was followed by patients aged 41–50 years, who constituted 23%. Patients in the 51–60 year age group formed 17% of the total. Younger patients aged 30 years or less comprised 15% of cases. Only a small proportion of patients (4%) were above 70 years of age.

The study population showed a clear female predominance. Females constituted 61% of the total patients included in the study. Males accounted for the remaining 39% of the study population. This distribution indicates that hypothyroidism was more commonly observed among females than males. The findings are consistent with the known higher prevalence of thyroid disorders in women. The sex distribution of the patients was representative of the typical epidemiological pattern of hypothyroidism.Eşme M et al[13] 285 patients were included in the study, the median age was 73(65–84), and 234 patients were female.

The duration of disease among the study population varied widely. Most patients had a disease duration of 1–10 years, constituting 56% of the total cases. A shorter duration of less than one year was observed in 24% of patients. Seventeen percent of patients had a disease duration ranging from 11–20 years. Only a small proportion of patients (3%) had a disease duration of more than 20 years. This distribution indicates that the majority of patients were diagnosed and treated within the first decade of the disease.

At baseline (TSH1), most patients had TSH levels greater than 10 mIU/L, indicating uncontrolled hypothyroidism. After initiation of thyroid hormone replacement therapy, a clear improvement in TSH levels was observed at the second assessment (TSH2). There was a reduction in the number of patients with TSH levels above 10 mIU/L and a corresponding increase in patients in the 4.6–10 mIU/L range. By the third follow-up (TSH3), the majority of patients achieved TSH levels within the euthyroid range of 0.5–4.5 mIU/L. Only a small proportion of patients continued to have elevated TSH levels at this stage. These findings demonstrate a progressive normalization of TSH levels with ongoing hypothyroid therapy.

At baseline (Cr1), the majority of patients had serum creatinine levels in the range of 1–1.2 mg/dL, and a considerable proportion showed elevated values of ≥1.3 mg/dL. After initiation of therapy, improvement in serum creatinine levels was observed at the second assessment (Cr2). The number of patients with creatinine levels ≥1.3 mg/dL reduced markedly by the second follow-up. By the third assessment (Cr3), no patients had creatinine values in the ≥1.3 mg/dL range. There was a progressive increase in the number of patients with creatinine levels ≤0.9 mg/dL over time. These findings indicate a clear improvement in renal biochemical parameters following therapy.Naguib R, et al [14]demonstrated a statistically significant reduction in the average serum creatinine level in the hypothyroid patients after treatment compared to before treatment .

At baseline (GFR1), a substantial number of patients had reduced renal function, with 39 patients showing eGFR values below 60 mL/min/1.73 m². The majority of the remaining patients had mildly reduced eGFR values between 60 and 89 mL/min/1.73 m², while only a few had normal eGFR levels. Following therapy, improvement in eGFR was observed at the second assessment (GFR2), with a marked reduction in patients with eGFR below 60 mL/min/1.73 m². There was a corresponding increase in patients with eGFR in the 60–89 mL/min/1.73 m² range. By the third follow-up (GFR3), a significant number of patients achieved normal eGFR values of ≥90 mL/min/1.73 m². Overall, these findings demonstrate progressive improvement in renal function following therapy.Eşme M et al [13]The median eGFR of the patients in hypothyroid cases was 66.59 (14.62–116.07), while the median eGFR value of patients was 69.6 (12.91–109.31) in the euthyroid state. This value obtained after thyroid replacement was significantly improved when compared to the first eGFR (p: 0.001). Charak, R., et al[15] the hypothyroid group showed a significant increase in creatinine levels (1.04 ±0.05) (p value < 0.001), leading to a decrease in eGFR (102.05 ±5.38) compared to the control group.

Bulur O, et al[16] The correlation analyses revealed that creatinine and ΔTSH levels were significantly correlated before and after levothyroxine treatment (r: 0.288, $p < 0.0001$). ΔeGFR and ΔTSH levels were significantly correlated before and after LT4 treatment (r: -0.272, $p < 0.0001$).

CONCLUSION

The present study demonstrates that hypothyroidism is associated with significant alterations in renal function. At baseline, most patients showed elevated TSH levels along with increased serum creatinine and reduced eGFR, indicating impaired renal function. Following initiation of thyroid hormone replacement therapy, there was a progressive normalization of TSH levels at subsequent follow-up assessments. This improvement in thyroid status was accompanied by a consistent reduction in serum creatinine levels and a corresponding increase in eGFR values.These findings suggest that the renal dysfunction observed in patients with hypothyroidism is largely functional and reversible with appropriate treatment. The parallel improvement in thyroid and renal parameters highlights the close physiological relationship between thyroid hormones and

renal hemodynamics. Early diagnosis and timely initiation of thyroid hormone replacement therapy may therefore play a crucial role in improving renal function and preventing unnecessary labeling of patients as having chronic kidney disease.

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