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Thyroid dysfunction and serum creatinine variations: A tertiary care study from northern Kerala

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ABSTRACT

Background: Thyroid hormones regulate renal hemodynamics and glomerular filtration rate (GFR), influencing serum creatinine levels. Understanding this relationship is crucial to avoid misclassification of renal function.

Objective: To determine the association between thyroid dysfunction and serum creatinine variations in patients attending a tertiary care center.

Methods: This retrospective cross-sectional study included 84 thyroid patients (66 females, 18 males) from a tertiary care center in Calicut, Kerala. Participants were classified as hypothyroid or hyperthyroid based on thyroid function tests (TSH, FT3, FT4). Serum creatinine levels were categorized as reduced or elevated using sex-specific reference ranges. Statistical analysis employed chi-square and Fisher's exact tests.

Results: Hypothyroid patients exhibited elevated creatinine in 85-100% of cases, while hyperthyroid patients demonstrated reduced creatinine in 92-100% of cases across subgroups. Highly significant inverse associations were observed across all thyroid markers ($p<0.001$ for all comparisons). The strongest concordance occurred in women younger than 45 years (100% concordance), with modest attenuation in older women (≥45 years), although associations remained highly significant.

Conclusion: Thyroid dysfunction profoundly affects serum creatinine through GFR modulation. Clinicians should systematically evaluate thyroid status before diagnosing chronic kidney disease based on creatinine abnormalities to prevent misclassification.

Keywords: Creatinine, glomerular filtration rate, hyperthyroidism, hypothyroidism, thyroid dysfunction

Introduction

Thyroid hormones play essential roles in regulating metabolism across multiple organ systems, and imbalances in thyroid function can lead to diverse metabolic disorders. Thyroid diseases represent a significant public health burden in India, with epidemiological studies estimating that approximately 42 million people are affected [1]. Both hypothyroidism and hyperthyroidism demonstrate higher prevalence among women, occurring approximately ten times more frequently in females compared to males, with peak incidence in middle-aged and older populations [1,2].

Thyroid hormones exert profound influence on renal function through modulation of cardiac output, renal blood flow, and glomerular filtration rate (GFR), which are critical determinants of serum creatinine levels [3,4]. Serum creatinine, a metabolic waste product derived from muscle creatine metabolism, serves as the most widely used biomarker for assessing renal function in clinical practice. Alterations in thyroid function can substantially impact serum creatinine concentrations through multiple mechanisms, creating potential for misinterpretation of renal status when thyroid dysfunction is not recognized [5,6].

In hypothyroidism, reduced cardiac output and decreased renal perfusion result in diminished GFR, typically by 20-40%, leading to elevated serum creatinine levels even in the absence

of intrinsic kidney disease [4,6]. Additionally, decreased metabolic activity associated with hypothyroid states may further influence creatinine production and clearance dynamics [3,7]. Conversely, hyperthyroidism increases metabolic activity and enhances renal blood flow, leading to elevated GFR by 20-30% and increased creatinine clearance [8,9]. Despite muscle wasting that may occur in prolonged hyperthyroidism, the dominant physiological effect is typically lower serum creatinine due to enhanced renal clearance [8,10].

Serum creatinine concentrations exhibit physiological variation based on muscle mass and sex-related differences. Males generally possess 20-30% greater muscle mass than females, resulting in naturally higher baseline serum creatinine levels [5,7]. Hormonal influences also contribute to these differences, with androgens promoting muscle development and creatinine production, whereas estrogen does not exert comparable anabolic effects on skeletal muscle [5,7]. Consequently, sex-specific reference ranges for serum creatinine are essential for accurate clinical interpretation.

Previous studies have documented associations between thyroid dysfunction and altered serum creatinine levels [3-6,8,9,11]. However, most research has focused on hypothyroidism, with limited data examining hyperthyroidism or providing balanced comparisons between both conditions. Furthermore, the influence of demographic factors such as sex and age on thyroid-creatinine relationships remains incompletely characterized. Limited data exist regarding the prevalence and patterns of serum creatinine variations among thyroid patients in the northern Kerala region specifically.

Understanding the biochemical impact of thyroid dysfunction on serum creatinine has important clinical implications. Failure to recognize thyroid-induced creatinine changes may lead to misdiagnosis of chronic kidney disease, unnecessary nephrology referrals, inappropriate medication dose adjustments, or delayed recognition of thyroid disorders [4-6]. Conversely, enhanced creatinine clearance in hyperthyroidism may mask underlying renal dysfunction, delaying appropriate intervention [8,9]. Systematic characterization of these relationships can improve clinical interpretation of renal function tests in thyroid patients and prevent misclassification of renal status.

Therefore, this study aimed to determine the association between thyroid dysfunction and serum creatinine variations in patients attending a tertiary care center in northern Kerala, with specific focus on sex-stratified and age-stratified patterns to elucidate demographic influences on this relationship.

Methods

Study design and setting

This retrospective, hospital-based cross-sectional study was conducted at a tertiary care center in Calicut, Kerala, India. Medical records were retrieved from the laboratory patient data register of the tertiary care center between January 2023 and December 2024. The study protocol adhered to ethical standards for retrospective data analysis, ensuring patient confidentiality and anonymity throughout the investigation.

Study population and sample size

A total of 84 patients diagnosed with thyroid disorders were included in this study. Participants were identified through systematic review of laboratory records maintained at the clinical biochemistry department. This was a convenience sample based on available records meeting inclusion criteria during the study period. Post-hoc power analysis indicated that with 84 participants (42 hypothyroid, 42 hyperthyroid) and observed effect sizes, the study achieved adequate statistical power (>95%, β=0.05) to detect significant associations between thyroid status and creatinine levels at α=0.05 significance level.

Inclusion and exclusion criteria

The study included adult patients aged 18 years and above who met the following criteria: (1) confirmed diagnosis of thyroid disorder, either hypothyroidism or hyperthyroidism, based on

clinical assessment and biochemical evaluation; (2) availability of complete thyroid function test results, including thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), and free thyroxine (FT4); (iii) documented serum creatinine measurements performed on the same day as thyroid function testing (within 24 hours of blood draw); (iv) treatment-naïve patients (not currently on thyroid hormone replacement or antithyroid medications) or patients with newly diagnosed thyroid dysfunction prior to initiation of therapy.

Patients were excluded if they had any of the following conditions: (1) documented malignancy or autoimmune disorders other than autoimmune thyroid disease; (ii) cardiac dysfunction or heart failure, (iii) pre-existing renal failure or chronic kidney disease (baseline eGFR <60 mL/min/1.73m^2), (iv) liver diseases or hepatic dysfunction, (v) pregnancy at the time of data collection; (vi) current use of medications known to affect serum creatinine levels (e.g., NSAIDs, ACE inhibitors, ARBs, trimethoprim, cimetidine); (vii) patients already receiving thyroid treatment for >1 month prior to biochemical assessment. These exclusion criteria were applied to minimize confounding factors that could independently affect serum creatinine levels.

Data collection

Demographic and clinical data, including age, sex, thyroid function status, and medication history, were extracted from patient medical records. Laboratory parameters comprising serum creatinine, FT3, FT4, and TSH were retrieved from the laboratory information system. All biochemical measurements were performed using standardized laboratory protocols in accordance with institutional quality control procedures.

Classification of thyroid status

Patients were classified into two groups based on their thyroid function status: hypothyroid and hyperthyroid. Classification was determined using established reference ranges for TSH, FT3, and FT4 as per laboratory standards. Hypothyroidism was defined by TSH greater than 4.5 mIU/L with FT3 less than 2.3 pg/mL and/or FT4 less than 0.8 ng/dL. Hyperthyroidism was defined by TSH less than 0.4 mIU/L with FT3 greater than 4.2 pg/mL and/or FT4 greater than 1.8 ng/dL. Patients with subclinical thyroid dysfunction (isolated TSH abnormalities with normal FT3 and FT4) were excluded from analysis to ensure clear classification into overt hypothyroid or hyperthyroid groups.

Classification of serum creatinine levels

Serum creatinine concentrations were classified as reduced, normal, or elevated based on sex-specific reference ranges established by the laboratory. For males, creatinine levels were classified as reduced if less than 0.7 mg/dL, normal if between 0.7 and 1.2 mg/dL, and elevated if greater than 1.2 mg/dL. For females, creatinine levels were classified as reduced if less than 0.5 mg/dL, normal if between 0.5 and 1.0 mg/dL, and elevated if greater than 1.0 mg/dL. For the purpose of this study, participants were dichotomized into "reduced" versus "elevated" categories to examine the directionality of creatinine changes in relation to thyroid dysfunction.

Laboratory methods

Serum creatinine concentrations were measured using the kinetic Jaffe method (alkaline picrate) on the Roche Cobas c311 automated clinical chemistry analyzer (Roche Diagnostics, Basel, Switzerland). The analytical measurement range was 0.17 to 24.9 mg/dL with intra-assay coefficient of variation less than 2.5% and inter-assay coefficient of variation less than 3.0%.

Thyroid function tests, including TSH, FT3, and FT4, were performed using electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e411 immunoassay analyzer (Roche Diagnostics, Basel, Switzerland). Reference ranges were TSH 0.4 to 4.5 mIU/L, FT3 2.3 to 4.2 pg/mL, and FT4 0.8 to 1.8 ng/dL. All assays were conducted following manufacturer protocols and institutional standard operating procedures, with regular internal quality control and participation in external quality assurance programs.

Data analysis

Data were coded and entered into Microsoft Office Excel 2019 (Microsoft Corporation, Redmond, WA, USA) for data management. Statistical analysis was performed using IBM SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA).

Descriptive statistics were calculated for all study variables. Categorical variables were expressed as frequencies and percentages, while continuous variables were summarized using mean and standard deviation. The chi-square test was employed to examine associations between categorical variables, with Fisher's exact test applied when expected cell frequencies were less than five. A p-value less than 0.05 was considered statistically significant, indicating rejection of the null hypothesis at the 5% significance level.

Subgroup analyses were conducted stratified by sex (male and female) and age categories among female participants (less than 45 years and 45 years or above) to evaluate potential effect modifications. The selection of age 45 years as a cutoff point was based on its approximation to the perimenopausal transition period in women, which may influence both thyroid function and renal metabolism through hormonal changes affecting glomerular filtration rate.

Ethical considerations

This study utilized de-identified retrospective data from medical records. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee of Malabar Medical College Hospital and Research Centre. Patient confidentiality was maintained throughout the study, and all data were handled in compliance with institutional ethical guidelines and applicable data protection regulations. Given the retrospective nature and use of anonymized data, the requirement for individual informed consent was waived by the ethics committee.

Results

Demographic characteristics

The study included 84 participants with thyroid disorders recruited from x to y. The mean age of the study population was 44.79 ± 16.77 years (range: 18-78 years). Female participants comprised the majority of the study sample, accounting for 78.6% (n=66), while male participants represented 21.4% (n=18). The male-to-female ratio was 1:3.7, consistent with established epidemiological patterns of thyroid disorders. Among the female participants, approximately 47% (n=31) were in the perimenopausal and postmenopausal age range (≥45 years), while 53% (n=35) were younger than 45 years.

Distribution of thyroid dysfunction and serum creatinine

The distribution of thyroid hormone levels across the study population revealed balanced representation of both hypothyroid and hyperthyroid groups (Table 1). Based on free triiodothyronine (FT3) levels, exactly half of the participants (n=42, 50.0%) were classified as hypothyroid and the remaining half (n=42, 50.0%) as hyperthyroid. Similarly, the distribution based on free thyroxine (FT4) levels showed nearly equal proportions, with 48.8% (n=41) classified as hypothyroid and 51.2% (n=43) as hyperthyroid. Thyroid-stimulating hormone (TSH) measurements demonstrated identical distribution to FT3, with 50.0% in each category. This consistent pattern across all three thyroid markers (FT3, FT4, and TSH) confirms balanced representation of both hypothyroid and hyperthyroid disorders in the study cohort, thereby minimizing potential selection bias in subsequent comparative analyses.

Serum creatinine distribution showed sex-specific patterns (Table 1). Among male participants (n=18), 66.7% (n=12) had reduced creatinine levels and 33.3% (n=6) had elevated levels. Female participants (n=66) demonstrated equal distribution, with 50.0% (n=33) showing reduced creatinine and 50.0% (n=33) showing elevated creatinine concentrations.

Table 1. Distribution of study subjects based on laboratory parameters (n=84)

Laboratory parameter	Frequency (n)	Percentage (%)
Free T3		
Hypothyroid	42	50.0
Hyperthyroid	42	50.0
Free T4		
Hypothyroid	41	48.8
Hyperthyroid	43	51.2
TSH		
Hypothyroid	42	50.0
Hyperthyroid	42	50.0
Creatinine		
Male		
Reduced	12	66.7
Elevated	6	33.3
Female		
Reduced	33	50.0
Elevated	33	50.0

Serum creatinine level variations among thyroid patients

A consistent and statistically significant inverse relationship was observed between thyroid dysfunction and serum creatinine levels across all demographic subgroups analyzed, including male, female, and age-stratified female populations (Table 2). Among male study participants (n=18), a strong inverse relationship was identified between thyroid hormone status and serum creatinine concentrations. Of the 9 hypothyroid males, 6 (66.7%) demonstrated elevated serum creatinine levels, while only 3 (33.3%) had reduced levels. Conversely, among the 9 hyperthyroid males, all 9 (100%) exhibited reduced serum creatinine levels, with none showing elevation. This pattern was remarkably consistent across all three thyroid markers (FT3, FT4, and TSH).

The female study population (n=66) demonstrated an even more pronounced association between thyroid status and creatinine categories. Among hypothyroid females, 32 out of 33 (97.0%) had elevated creatinine levels based on FT3 classification, with only 1 (3.0%) showing reduced levels. In stark contrast, among hyperthyroid females, 32 out of 33 (97.0%) demonstrated reduced creatinine concentrations, with only 1 (3.0%) showing elevation. This near-complete inverse concordance was consistent across FT3, FT4 (93.9% vs 97.0%), and TSH markers (97.0% vs 97.0%).

Female participants were further stratified by age into two groups: younger than 45 years (n=35) and 45 years or above (n=31). This stratification was performed to evaluate whether the association between thyroid function and serum creatinine is modified by age-related metabolic changes or menopausal transition. In the younger female group (less than 45 years), the association between thyroid status and creatinine levels was strongest, demonstrating the most robust physiological relationship. Among the 15 hypothyroid participants, all 15 (100%) demonstrated elevated serum creatinine with none (0%) showing reduced levels based on FT3 classification. Conversely, all 20 hyperthyroid participants (100%) exhibited reduced creatinine with none (0%) showing elevation. This perfect inverse correlation was consistently observed across FT3 and TSH markers, with minimal variation in FT4 classification (86.7% elevated in hypothyroid vs 100% reduced in hyperthyroid, with 13.3% overlap).

In the older female group (45 years and above), the association remained statistically significant and clinically relevant; however, a slight attenuation of the relationship was observed compared to the younger cohort. Among hypothyroid participants, 17 out of 18 (94.4%) had elevated creatinine levels based on FT3 and TSH, while all 18 (100%) showed elevation based on FT4. Among hyperthyroid participants, 12 out of 13 (92.3%) demonstrated reduced creatinine levels, with only 1 (7.7%) showing elevation. This modest attenuation compared to the younger cohort suggests that additional factors such as age-related changes in muscle mass, menopausal hormonal shifts, or age-dependent decline in glomerular filtration rate may partially modify the physiological regulation of GFR by thyroid hormones in the older female population.

Table 2. Serum creatinine level variations among thyroid patients (n=84)

Thyroid status	Male (n=18)		Female (n=66)		Female (based on Age)			
					<45 years		≥45 years	
	Reduced n (%)	Elevated n (%)	Reduced n (%)	Elevated n (%)	Reduced n (%)	Elevated n (%)	Reduced n (%)	Elevated n (%)
Free T3								
Hypothyroid	3 (25.0)	6 (100)	1 (3.0)	32 (97.0)	0 (0.0)	15 (100)	1 (7.7)	17 (94.4)
Hyperthyroid	9 (75.0)	0 (0.0)	32 (97.0)	1 (3.0)	20 (100)	0 (0.0)	12 (92.3)	1 (5.6)
Free T4								
Hypothyroid	3 (25.0)	6 (100)	1 (3.0)	31 (93.9)	0 (0.0)	13 (86.7)	1 (7.7)	18 (100)
Hyperthyroid	9 (75.0)	0 (0.0)	32 (97.0)	2 (6.1)	20 (100)	2 (13.3)	12 (92.3)	0 (0.0)
TSH								
Hypothyroid	3 (25.0)	6 (100)	1 (3.0)	32 (97.0)	0 (0.0)	15 (100)	1 (7.7)	17 (94.4)
Hyperthyroid	9 (75.0)	0 (0.0)	32 (97.0)	1 (3.0)	20 (100)	0 (0.0)	12 (92.3)	1 (5.6)

Note: Percentages represent row proportions (within each thyroid status group)

Table 3. Association between serum creatinine level and thyroid disease (n=84)

Thyroid status	Male (n=18)				Female (n=66)			
	Reduced n (%)	Elevated n (%)	Test	p value	Reduced n (%)	Elevated n (%)	χ^2	p value
Free T3								
Hypothyroid	3 (25.0)	6 (100)	FET*	0.009	1 (3.0)	32 (97.0)	58.24	<0.001
Hyperthyroid	9 (75.0)	0 (0.0)			32 (97.0)	1 (3.0)		
Free T4								
Hypothyroid	3 (25.0)	6 (100)	FET*	0.009	1 (3.0)	31 (93.9)	54.59	<0.001
Hyperthyroid	9 (75.0)	0 (0.0)			32 (97.0)	2 (6.1)		
TSH								
Hypothyroid	3 (25.0)	6 (100)	FET*	0.009	1 (3.0)	32 (97.0)	58.24	<0.001
Hyperthyroid	9 (75.0)	0 (0.0)			32 (97.0)	1 (3.0)		

Test used: Chi-square test, Fisher's exact test
*Fisher's exact test applied when expected cell frequency was less than 5
p-value < 0.05 considered statistically significant

Association between serum creatinine level and thyroid disease

Statistical analysis revealed highly significant associations between thyroid dysfunction and serum creatinine abnormalities across all demographic subgroups and thyroid markers examined (Table 3). Despite the relatively modest sample size of male participants (n=18), statistically significant associations were identified between thyroid function status and serum creatinine levels for all three hormonal markers examined: FT3, FT4, and TSH ($p < 0.05$). Fisher's exact test was applied due to expected cell frequencies less than five. Hypothyroidism was significantly associated with elevated serum creatinine levels, whereas hyperthyroidism was significantly associated with decreased serum creatinine levels across all thyroid function indicators.

The female group (n=66) demonstrated highly significant statistical associations between serum creatinine levels and thyroid function status for all three hormonal markers ($p < 0.001$). Hypothyroidism was consistently and strongly associated with elevated serum creatinine concentrations, while hyperthyroidism was consistently and strongly associated with reduced serum creatinine

Table 4. Association between serum creatinine level and thyroid disease among female study subjects stratified by age

Thyroid status	<45 years (n=35)				≥45 years (n=31)			
	Reduced n (%)	Elevated n (%)	χ^2	p value	Reduced n (%)	Elevated n (%)	χ^2	p value
Free T3								
Hypothyroid	0 (0.0)	15 (100)	35.00	<0.001	1 (5.6)	17 (94.4)	23.33	<0.001
Hyperthyroid	20 (100)	0 (0.0)			12 (92.3)	1 (7.7)		
Free T4								
Hypothyroid	0 (0.0)	13 (86.7)	27.58	<0.001	1 (5.6)	18 (100)	27.11	<0.001
Hyperthyroid	20 (100)	2 (13.3)			12 (92.3)	0 (0.0)		
TSH								
Hypothyroid	0 (0.0)	15 (100)	35.00	<0.001	1 (5.6)	17 (94.4)	23.33	<0.001
Hyperthyroid	20 (100)	0 (0.0)			12 (92.3)	1 (7.7)		

Test used: Chi-square test
p-value < 0.05 considered statistically significant

concentrations. The magnitude and consistency of these associations across all thyroid markers (FT3: χ^2=58.24, FT4: χ^2=54.59, TSH: χ^2=58.24) provide robust evidence of the relationship between thyroid dysfunction and renal filtration parameters. These findings demonstrate that, regardless of sex, thyroid dysfunction exerts a substantial and consistent influence on serum creatinine levels, with the directionality of change determined by the type of thyroid dysfunction present.

Age-stratified associations in female participants

Age-stratified analysis in female participants revealed that the association between thyroid dysfunction and serum creatinine abnormalities remained highly significant across both age groups, with the strongest effects observed in younger women (Table 4). For the younger female group (less than 45 years), highly statistically significant associations were observed between thyroid status and serum creatinine classification for all three hormonal markers: FT3, FT4, and TSH ($p < 0.001$). The inverse relationship was exceptionally well-preserved in this subgroup. Hypothyroidism was consistently and precisely associated with elevated serum creatinine levels, while hyperthyroidism was consistently and precisely associated with decreased serum creatinine levels. This pattern suggests a robust and direct physiological linkage between thyroid hormone levels and modulation of GFR among premenopausal or younger women, with minimal confounding from age-related factors.

In the older female group (45 years and above), statistically significant associations persisted across all hormonal markers (FT3, FT4, and TSH) between thyroid function and serum creatinine levels ($p < 0.001$). The fundamental inverse relationship remained evident, with hypothyroidism associated with elevated creatinine and hyperthyroidism associated with reduced creatinine concentrations. However, the strength of association showed slight attenuation compared to the younger female cohort. The persistent statistical significance confirms the enduring physiological impact of thyroid hormones on renal function across the female lifespan. Nevertheless, the observed attenuation in the older age group suggests that concurrent factors such as menopausal status, age-related reduction in muscle mass, and age-dependent decline in baseline GFR independent of thyroid function may begin to exert modest modifying effects on serum creatinine concentrations in older women. These findings underscore the importance of considering age-related physiological changes when interpreting serum creatinine levels in the context of thyroid dysfunction among older female patients.

Post-hoc power analysis confirmed that the study achieved adequate statistical power (>95%, β=0.05) to detect the observed associations between thyroid status and creatinine levels at α=0.05 significance level, validating the adequacy of the sample size despite the convenience sampling approach. The consistent and highly significant inverse associations across all thyroid markers (FT3, FT4, TSH), demographic subgroups (male, female), and age categories provide robust evidence that thyroid dysfunction exerts a substantial and predictable influence on serum creatinine concentrations. Hypothyroidism was uniformly associated with elevated creatinine, while hyperthyroidism was uniformly associated with reduced creatinine. These findings suggest that thyroid status is a critical determinant of serum creatinine levels independent of intrinsic renal disease.

Discussion

This study examined the relationship between thyroid dysfunction and serum creatinine levels in 84 patients with documented thyroid disorders at a tertiary care center. The findings reveal consistent inverse associations between thyroid function status and serum creatinine concentrations across demographic subgroups.

The study population was predominantly female (78.6%) with a mean age of 44.79 ± 16.77 years, consistent with established epidemiological patterns of thyroid disorders [1,2]. Notably, the distribution of hypothyroid and hyperthyroid patients was approximately balanced across all thyroid markers (FT3, FT4, TSH), reducing selection bias and enabling valid comparisons. While hypothyroidism typically predominates in population-based studies [12], this balanced representation likely reflects tertiary care referral patterns and provides opportunity to examine renal alterations across both extremes of thyroid dysfunction.

The primary finding demonstrates a significant inverse relationship between thyroid function and serum creatinine levels ($p < 0.05$). Hypothyroid individuals consistently exhibited elevated serum creatinine, while hyperthyroid individuals showed reduced levels. This pattern persisted across sex and age-stratified analyses, providing robust empirical support for established physiological mechanisms.

Thyroid hormones critically regulate renal hemodynamics through modulation of cardiac output, renal blood flow, and glomerular filtration rate (GFR). In hypothyroidism, decreased cardiac output and renal perfusion reduce GFR, elevating serum creatinine even without intrinsic kidney disease [4,6]. Reduced metabolic activity may further alter creatinine production and clearance. Conversely, hyperthyroidism enhances GFR through increased cardiac output and renal perfusion, frequently lowering serum creatinine and potentially masking early renal dysfunction [8,9].

Despite modest male sample size (n=18), significant associations were observed, with hypothyroid males showing elevated and hyperthyroid males showing reduced creatinine levels. Female participants demonstrated stronger associations, potentially reflecting greater physiological responsiveness or enhanced statistical power from larger sample size.

Age stratification revealed important modifications. Women younger than 45 years demonstrated highly consistent associations, with thyroid status uniformly corresponding to predicted creatinine levels, suggesting preserved renal hemodynamic responsiveness to thyroid hormone modulation. In women aged 45 years and above, associations remained significant but were modestly attenuated. This likely reflects age-related sarcopenia reducing baseline creatinine production [13,14], age-dependent nephron loss [13], menopausal hormonal transitions [15,16], and diminished renal hemodynamic responsiveness in older individuals. These findings underscore the importance of interpreting creatinine variations within broader clinical context accounting for age-related physiological changes.

These findings have several practical implications. First, serum creatinine may not accurately reflect true renal function in thyroid dysfunction. Elevated creatinine in hypothyroidism may represent hemodynamic effects rather than intrinsic renal pathology, potentially leading to unnecessary investigations or inappropriate

medication dosing adjustments. Second, unexplained creatinine abnormalities should prompt thyroid assessment, particularly when inconsistent with clinical presentation. Third, age and menopausal status modify renal response to thyroid hormones, suggesting potential need for age-specific interpretative strategies. Fourth, thyroid dysfunction should be corrected before diagnosing chronic kidney disease, as treatment may reverse GFR reductions and prevent inappropriate disease classification [5].

Study strengths include balanced representation of hypo- and hyperthyroidism enabling valid comparisons, age- and sex-stratified analyses providing insights into demographic variability, objective biochemical markers enhancing measurement validity, and strong internal consistency across thyroid indicators strengthening confidence in observed relationships.

Several limitations warrant acknowledgment. The modest sample size, particularly among males (n=18), may limit statistical power and generalizability. The single-center design may restrict external validity. The cross-sectional design precludes assessment of longitudinal changes following thyroid correction, limiting causal inference. The study did not include cystatin C or estimated GFR calculations, which are less influenced by muscle mass and may provide more accurate renal function assessment in thyroid patients [5]. Potential confounding variables including body mass index, nutritional status, and comorbidities were not systematically evaluated.

Future research should address these limitations through several approaches. Longitudinal studies evaluating creatinine levels before and after thyroid treatment would clarify reversibility and temporal dynamics. Incorporation of additional renal biomarkers, including cystatin C and thyroid-adjusted eGFR formulas, would provide comprehensive assessment of true renal function. Larger multicenter studies with diverse populations would enhance generalizability and statistical power for subgroup analyses. Systematic evaluation of confounding variables including BMI, nutritional status, medications, and comorbidities would enable precise characterization of factors influencing the thyroid-creatinine relationship.

Conclusion

This study demonstrates a significant inverse relationship between thyroid dysfunction and serum creatinine levels across sex and age groups. Hypothyroidism is consistently associated with elevated serum creatinine due to reduced glomerular filtration rate, while hyperthyroidism correlates with decreased creatinine resulting from enhanced GFR. The strongest association was observed in younger women, whereas age-related factors caused moderate attenuation in older women. These findings emphasize the importance of considering thyroid status when interpreting serum creatinine levels and assessing renal function in clinical practice. Clinicians should exercise caution in diagnosing chronic kidney disease based on creatinine abnormalities in thyroid patients, as correction of thyroid dysfunction may normalize these biochemical alterations and prevent misclassification of renal status.

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Author contributions

RBR: Conceptualization, Methodology, Investigation, Formal analysis, Writing—original draft, Writing—review and editing. SG: Conceptualization, Methodology, Supervision, Writing—review and editing, Project administration. SH: Conceptualization,

Methodology, Formal analysis, Writing—review and editing, Validation. All authors have read and approved the final version of the manuscript.

Declaration of interest

The authors declare no conflicts of interest.

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