Evaluation Of Thyroid Dysfunction In Children Of Different Stages Of CKD In A Tertiary Care Hospital

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KEYWORDS

CKD, Thyroid dysfunction, TSH, T3, T4, Pediatric nephrology

ABSTRACT:

Background: Thyroid dysfunction is a common yet often overlooked complication in children with chronic kidney disease (CKD). This study aimed to evaluate the pattern of thyroid abnormalities across different stages of CKD in pediatric patients at a tertiary care hospital. ***Methods:*** This cross-sectional analytic study was conducted in the Department of Paediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from February 2017 to January 2018. In this study, we included 60 pediatric patients with CKD, either newly diagnosed or previously diagnosed, who were admitted to the inpatient department or attended the outpatient department. ***Results:*** The mean age of participants was 12.02 ± 4.21 years, with a male predominance (63.3%). Most patients (78.3%) were from rural areas. The most common thyroid dysfunction was Low T3 Syndrome (58.3%), especially in Stage V (62.5%). Subclinical hypothyroidism was found in 8.3% of cases, all in Stage V, while hyperthyroidism was rare (1.7%). Euthyroidism was observed in 15% of patients. TSH levels were significantly higher in advanced CKD stages ($p = 0.031$), and a significant positive correlation was found between TSH and CKD stage ($r = +0.258$, $p = 0.046$). Conversely, T3 showed a significant negative correlation with CKD stage ($r = –0.254$, $p = 0.041$). T4 levels also decreased with disease progression, though not significantly ($r = –0.082$, $p = 0.533$). Anemia, respiratory distress, and edema were the most frequent clinical features. ***Conclusion:*** Thyroid dysfunction, particularly Low T3 Syndrome and subclinical hypothyroidism, is common in pediatric CKD, especially in advanced stages. Routine screening for thyroid function in children with CKD may enable early detection and management.

INTRODUCTION

Chronic Kidney Disease (CKD) is an emerging global health concern, particularly in children. According to the Kidney Disease Improving Global Outcomes (KDIGO, 2012), CKD is defined as structural or functional kidney abnormalities lasting more than three months. [1] It is classified into five stages based on glomerular filtration rate (GFR), with early stages (I–II) often being asymptomatic and difficult to detect, while advanced stages (III–V) present with more evident signs of kidney dysfunction. [2] As CKD progresses, complications such as cardiovascular disease, hyperlipidemia, anemia, endocrine disorders, and mineral and bone disorder (CKD-MBD)

are common. [3] Early recognition and management of these complications are vital to reducing morbidity and mortality.

Endocrine abnormalities, particularly thyroid dysfunction, are common in the later stages of CKD. These issues can involve disruptions in several hormones, including thyroid, gonadal, adrenal hormones, erythropoietin, and vitamin D. In CKD, thyroid dysfunction may result from abnormal circulating hormone levels or impaired hormone action at the tissue level. [4] Multiple mechanisms contribute to hypothyroidism in CKD. These include decreased levels of albumin and thyroid-binding pre-albumin, impaired secretion of pituitary thyrotropin (TSH) due to the uremic state, and iodide retention in the bloodstream. [5,6] Additionally, low T3 levels can arise from impaired peripheral conversion of thyroxine (T4) to triiodothyronine (T3), as elevated cytokines like TNF-alpha and interleukin suppress the enzyme responsible for this conversion. [7]

The kidney plays a key role in the metabolism, synthesis, secretion, and elimination of thyroid hormones. As kidney function declines, these processes are disturbed, leading to thyroid hormone imbalances. Thyroid hormones are essential for growth, development, and maintaining water and electrolyte balance. [6] These hormones also affect renal function both directly and indirectly: pre-renal effects are mediated through cardiovascular function and renal blood flow, while renal effects include modulation of GFR, tubular reabsorption and secretion, and overall renal physiology. [8]

In renal failure, decreased hormone clearance and reduced renal blood flow impair the transport and metabolism of hormones. As a result, serum hormone levels become unbalanced. [9]

Conversely, hyperthyroidism can worsen CKD through mechanisms such as intraglomerular hypertension, increased proteinuria (which causes direct kidney injury), oxidative stress, and elevated angiotensin levels—all contributing to disease progression. [8]

Thyroid hormones, particularly T3, have been identified as potential prognostic markers in CKD. Studies suggest that T3 levels may correlate with survival in patients with kidney disease. [6] However, data on thyroid hormone status in children with CKD remain limited. Early detection and treatment of thyroid dysfunction in these patients could delay CKD progression and improve outcomes. [10]

Clinically, hypothyroidism is difficult to recognize in CKD patients because many of its symptoms, such as dry skin, fatigue, edema, and poor growth, overlap with those of CKD itself. These overlapping features make diagnosis especially challenging in pediatric patients, where factors like malnutrition, anemia, and uremia further complicate clinical assessment. Uremia also interferes with thyroid hormone metabolism by reducing circulating hormone levels and altering hormone storage and content in the thyroid gland. Although various studies have examined thyroid function in uremic patients, results have been inconsistent. Some studies suggest that reduced T3 levels before renal transplantation are associated with a higher risk of graft failure. [11] Furthermore, subclinical hypothyroidism has been identified as an independent risk factor for rapid decline in renal function. Early screening and intervention may help preserve residual kidney function in children affected by this condition. [12]

Despite its significance, research on thyroid hormone levels in children with CKD remains limited. To date, there is a notable lack of data from Bangladesh, particularly at the tertiary care level. Therefore, this study aimed to evaluate the pattern of thyroid abnormalities across different stages of CKD in pediatric patients at a tertiary care hospital.

METHODOLOGY & MATERIALS

This cross-sectional analytic study was conducted in the Department of Paediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, from February 2017 to January 2018. In this study, we included 60 pediatric patients with CKD, either newly diagnosed or previously diagnosed, who were admitted to the inpatient department or attended the outpatient department.

These were the following criteria for eligibility as study participants:

Inclusion Criteria

- Children aged between 2 and 18 years.
- Diagnosed cases of chronic kidney disease (CKD Stage III to V), either newly diagnosed or previously diagnosed
- Patients who had not started thyroid hormone therapy before the study.

- Willingness of parents/guardians to provide informed consent.

Exclusion Criteria
- Patients with a known history of thyroid disorders before CKD diagnosis.
- Patients receiving thyroid hormone replacement or anti-thyroid medications.
- Patients with acute kidney injury (AKI) instead of CKD.
- Children with congenital anomalies unrelated to the urinary system that might affect thyroid function.
- Patients with critical illnesses or sepsis that could confound thyroid hormone levels (e.g., non-thyroidal illness syndrome).

Operational Definition:
a) **Subclinical Hypothyroidism**: A mild form of hypothyroidism where the serum Thyroid Stimulating Hormone (TSH) level is elevated, but free T3 and free T4 levels remain within the normal range. It often presents without clear clinical symptoms.
b) **Low T3 Syndrome**: Also known as Euthyroid Sick Syndrome, it is a condition seen in critically ill or chronically ill patients, characterized by low serum T3 levels with normal or low TSH and normal or low T4, without underlying thyroid disease.
c) **Hyperthyroidism**: A condition where the thyroid gland produces excessive amounts of thyroid hormones (T3 and/or T4), leading to suppressed TSH levels and symptoms such as weight loss, palpitations, anxiety, and heat intolerance.
d) **Euthyroidism**: A state of normal thyroid function, where levels of TSH, free T3, and free T4 fall within the standard reference ranges and there are no clinical signs or symptoms of thyroid dysfunction.

Data Collection Procedure: Legal guardians of children diagnosed with CKD were approached for inclusion in the study. After explaining the objectives and procedures of the research, informed written consent was obtained from each participant's guardian. A total of 60 children with CKD who met the inclusion criteria were enrolled from both the inpatient and outpatient units of the Pediatric Nephrology Department at Bangabandhu Sheikh Mujib Medical University (BSMMU). Diagnosis was established through a detailed medical history and clinical evaluation, and all findings were systematically recorded in a structured data collection form. Each patient underwent a thorough physical examination to assess signs and symptoms associated with CKD and its complications. Relevant clinical features such as anemia, edema, respiratory distress, and hypertension were documented. Demographic data, including age, sex, and place of residence, were also recorded. Laboratory investigations performed for all participants included measurement of TSH, T3, and T4, along with complete blood count, serum creatinine, and eGFR. CKD staging was done according to the KDIGO 2012 guidelines, classifying patients into Stage III, IV, or V based on their eGFR levels.

Statistical Analysis: All data were systematically recorded using a pre-formatted data collection form. Quantitative data were expressed as mean ± standard deviation, while qualitative data were presented as frequency distributions and percentages. Continuous variables were analyzed using Student's unpaired t-test; Kruskal Wallis test was used to compare hormone levels across CKD stages; and Spearman's rho was employed to assess the relationship between CKD stage and thyroid hormone levels (TSH, T3, T4). A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 22 (Statistical Package for the Social Sciences) for Windows. This study received ethical approval from the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University.

RESULTS

Table I: Demographic profile of the patients (n=60)

Age (years)	**Frequency (n)**	**Percentage (%)**
<5	2	3.3
5 - 9	14	23.3
10 - 14	21	35.0
15 - 20	23	38.3
Mean ± SD	12.02 ± 4.21	
Gender		
Male	38	63.3
Female	22	36.7
Residence		
Urban	13	21.7

Rural	47	78.3
Cause of CKD		
Hypoplastic kidney	22	36.7
Glomerulonephritis	13	21.7
Obstructive uropathy	16	26.7
Recurrent UTI	3	5.0
Wasp sting	1	1.7
Neurogenic bladder	3	5.0
Nephrolithiasis	1	1.7
Stone disease	1	1.7

Table I shows that the study included 60 patients, with a mean age of 12.02 ± 4.21 years. Most patients (38.3%) were aged between 15 and 20 years, followed by 35.0% in the 10–14 year age group, 23.3% in the 5–9 year age group, and only 3.3% were under 5 years old. In terms of gender distribution, males were predominant, accounting for 63.3% of the participants, while females made up 36.7%. Regarding their place of residence, a significant majority of the patients (78.3%) were from rural areas, whereas only 21.7% resided in urban locations. The most common etiology was hypoplastic kidney, accounting for 22 cases (36.7%), followed by obstructive uropathy in 16 cases (26.7%) and glomerulonephritis in 13 cases (21.7%). Less frequent causes included recurrent urinary tract infections (UTIs) and neurogenic bladder, each contributing to 3 cases (5.0%).

Table II: Thyroid dysfunction in different stages of CKD (n=60)

Thyroid dysfunction	Stage III	Stage IV	Stage V	Total
Subclinical Hypothyroidism	0 (0.0)	0 (0.0)	5 (12.5)	5 (8.3)
Low T3 Syndrome	5 (55.6)	5 (45.5)	25 (62.5)	35 (58.3)
Hyperthyroidism	0 (0.0)	0 (0.0)	1 (2.5)	1 (1.7)
Euthyroidism	3 (33.3)	2 (18.2)	4 (10.0)	9 (15.0)
Others	1 (11.1)	4 (36.4)	5 (12.5)	10 (16.7)
Total	9 (100.0)	11 (100.0)	40 (100.0)	60 (100.0)

Table II presents the distribution of thyroid dysfunction across various stages of CKD among 60 patients. The most common abnormality observed was Low T3 Syndrome, affecting 58.3% of the total population, with the highest prevalence in Stage V CKD (62.5%), followed by Stage III (55.6%) and Stage IV (45.5%). Subclinical hypothyroidism was observed only in Stage V patients, accounting for 12.5% in that group and 8.3% of the total population. Hyperthyroidism was rare, identified in only one patient (1.7%) in Stage V. Euthyroidism was present in 15% of the patients, with slightly higher proportions in Stage III (33.3%) and Stage IV (18.2%) compared to Stage V (10.0%).

Table III: Clinical presentation of study subjects (n=60)

Clinical presentation	Stage III (n=9)	Stage IV (n=11)	Stage V (n=40)
Anemia	9 (100.0)	11 (100.0)	39 (97.5)
Edema	1 (11.1)	2 (18.2)	12 (30.0)
Respiratory distress	5 (55.6)	6 (54.5)	26 (65.0)
Hypertension	1 (11.1)	3 (27.3)	7 (17.5)
Bony changes	0 (0.0)	0 (0.0)	5 (12.5)

Table III shows that anemia was the most common presentation, seen in nearly all patients—100% in both Stage III and IV, and 97.5% in Stage V. Respiratory distress was found 55.6% in Stage III, 54.5% in Stage IV, and increasing to 65.0% in Stage V. Edema was observed with increasing frequency in more advanced stages, ranging from 11.1% in Stage III to 30.0% in Stage V. Hypertension was reported in 11.1% of Stage III patients, 27.3% in Stage IV, and 17.5% in Stage V. Less common symptoms included bony changes, found exclusively in 12.5% of patients in Stage V.

Table IV: Thyroid hormone at different stages of CKD (n=60)

Thyroid hormone	CKD stages			p value
	Stage III	Stage IV	Stage V	
Serum TSH (mIU/L)	2.02 (0.88-3.55)	1.45 (0.05-3.57)	2.30 (0 – 9.39)	0.031
Serum T3 (nmol/L)	1.16	0.88	0.80	0.061

	(0.58-5.17)	(0.38-2.04)	(0.31-2.29)	
Serum T4 (nmol/L)	97.44 (10.66-139.67)	88.23 (45.80-179.11)	82.37 (36.54-209.30)	0.748

Kruskal-Wallis Test is done to measure the level of significance

Table IV shows that the Serum TSH level showed a statistically significant difference among the stages (p = 0.031). Median TSH was highest in Stage V (2.30 mIU/L; range: 0–9.39), followed by Stage III (2.02 mIU/L; range: 0.88–3.55), and lowest in Stage IV (1.45 mIU/L; range: 0.05–3.57). Serum T3 levels demonstrated median values of 1.16 nmol/L (Stage III), 0.88 nmol/L (Stage IV), and 0.80 nmol/L (Stage V). Median serum T4 levels were 97.44 nmol/L in Stage III, 88.23 nmol/L in Stage IV, and 82.37 nmol/L in Stage V. However, the difference in T4 levels among the stages was not statistically significant (p = 0.748).

Table V: Correlation of CKD stages with thyroid hormone (n=60)

	r value	p value
Serum TSH	+0.258	0.046
Serum T3	-0.254	0.041
Serum T4	-0.082	0.533

This table presents the correlation between CKD stages and thyroid hormone levels. A positive correlation was observed between CKD stage and Serum TSH level (r = +0.258), which was statistically significant (p = 0.046). In contrast, Serum T3 showed a significant negative correlation with CKD stage (r = –0.254, p = 0.041), suggesting that T3 levels decline with worsening kidney function. Serum T4 also showed a negative correlation (r = –0.082), but this was not statistically significant (p = 0.533).

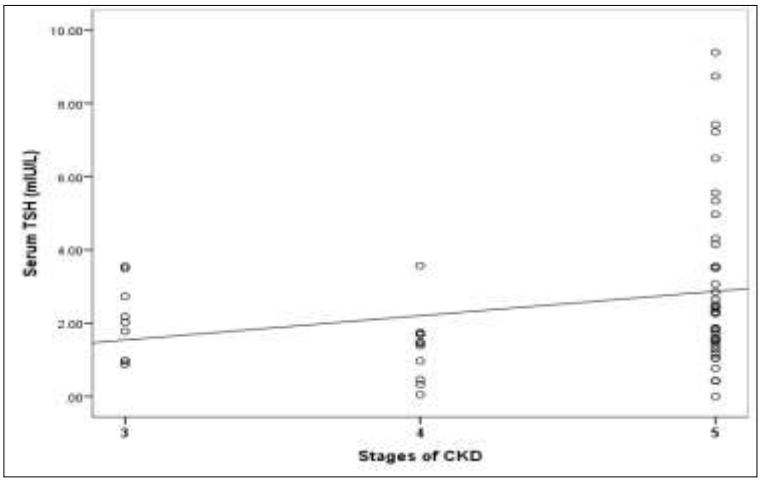

Figure 1: Correlation of CKD stages with serum TSH. Spearman's rho correlation is done. Here Spearman's rho correlation coefficient (r_s) is +0.258 (p=0.046).

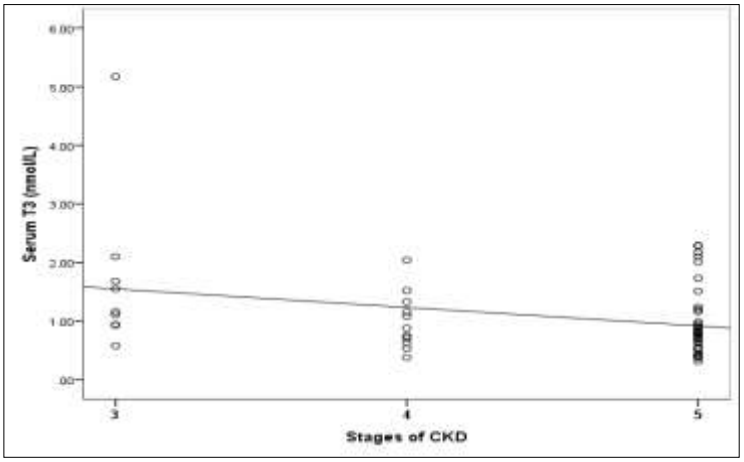

Figure 2: Correlation of CKD stages with serum T_3. Spearman's rho correlation is done. Here Spearman's rho correlation coefficient (r_s) is -0.264 (p=0.041).

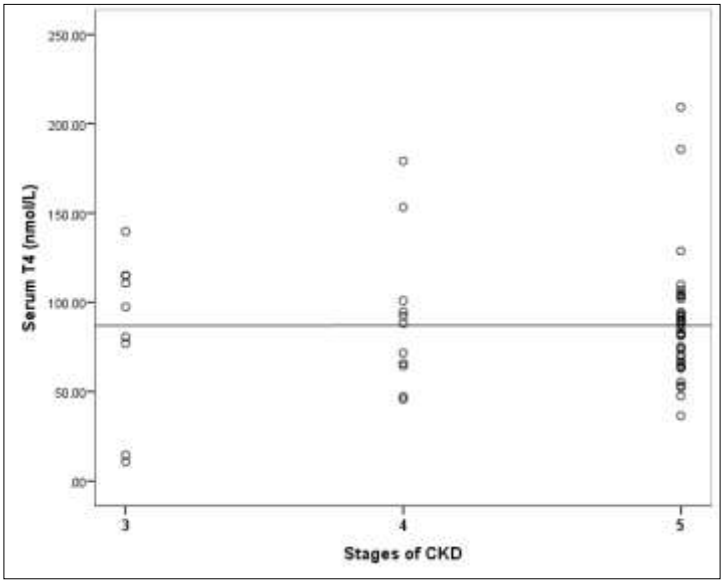

Figure 3: Correlation of CKD stages with serum T_4. Spearman's rho correlation is done. Here Spearman's rho correlation coefficient (r_s) is -0.082 (p=0.533)

DISCUSSION

In the present study, a total of 60 pediatric patients with chronic kidney disease (CKD) were evaluated, with a mean age of 12.02 ± 4.21 years. The largest proportion of patients (38.3%) belonged to the 15–20 years age group. Males were more frequently affected, comprising 63.3% of the study population, whereas females accounted for 36.7%. Although thyroid disorders are generally more common in females across all age groups [13], this male predominance may reflect population-based or referral bias. In this study, the male-to-female ratio was 1.73:1 in children with CKD. Singh *et al.* reported an overall male-to-female ratio of 1:1.2 in children with thyroid dysfunction, with a notable rise in female predominance in older age groups. In the 9–12 year age bracket, the ratio was 1:2.5. [14] Indian studies have reported male-to-female ratios ranging from 1:2.9 to 1:3.4, while a study from Scotland found a ratio of 1:2.8 in individuals under 22 years. [14-16]

In the current study, Low T3 Syndrome was the most prevalent thyroid abnormality, affecting 58.3% of patients. It was most frequent in Stage V CKD (62.5%), followed by Stage III (55.6%) and Stage IV (45.5%). Subclinical hypothyroidism (SCH) was observed exclusively in Stage V (12.5% of that group), accounting for 8.3% of the total population. Hyperthyroidism was rare, detected in only one patient (1.7%) with Stage V disease. Euthyroid status was present in 15% of the cohort, with relatively higher prevalence in earlier CKD stages. Chandra (2016) reported the presence of SCH in 40% and overt hypothyroidism in 16% of pediatric patients managed conservatively. [17] Similarly, Shakya *et al.* found a significant reduction in serum T3 and T4 levels, along with elevated TSH, among both male and female CKD patients. In their cohort, low T3 was observed in 38.54%, low T4 in 34.37%, SCH in 16.7%, and overt hypothyroidism in 7.29% of patients. Notably, SCH was more prevalent among females (29%) than males (9.6%), with a statistically significant p-value (0.035). [18] These results are consistent with findings by Chonchol *et al.* [19]

The current study observed no statistically significant gender-based differences in thyroid hormone levels. Mean serum TSH was slightly lower in males (2.44 ± 2.13 mIU/L) compared to females (2.73 ± 1.98 mIU/L), while T3 and T4 levels were also marginally lower in males. However, none of these differences reached statistical significance ($p > 0.05$).

In line with our findings, a study by Ansari *et al.* reported that 42.4% of their pediatric CKD patients had thyroid dysfunction, with subclinical and overt hypothyroidism present in 33.3% and 9.1% of cases, respectively. [20] These rates are similar to those found by El-Hana *et al.* [21] and Bajaj *et al.* [22]. Another hospital-based prospective study by Singh *et al.* documented 65 children with thyroid abnormalities, of which 61 had hypothyroidism and four had hyperthyroidism. [14]

Hasan *et al.* found that 15.7% of children with CKD had hypothyroidism, with a higher prevalence among girls. Interestingly, their study did not show significant variations in thyroid hormone levels across CKD stages. [23] This finding aligns with those of Yadav *et al.*, who observed a 26.2% prevalence of thyroid dysfunction in

pediatric CKD, with higher rates in advanced stages.[24] Similarly, Garrido-Magaña *et al.* reported a 28% incidence of thyroid dysfunction mostly subclinical hypothyroidism among children on dialysis. [7] Raj *et al.* also emphasized the high burden of thyroid abnormalities in this population. [25]

While some studies, such as that by Yadav *et al.*, have reported an increasing trend of hypothyroidism with CKD progression, our study did not find a statistically significant correlation between thyroid dysfunction and CKD stage. However, Serum TSH levels in our cohort did show a significant increase with disease progression ($p = 0.031$), being highest in Stage V. Although median serum T3 and T4 levels decreased with advancing CKD, these changes were not statistically significant ($p = 0.061$ and $p = 0.748$, respectively). [24]

Ansari *et al.* also noted increasing thyroid dysfunction with CKD severity. In their study, SCH and hypothyroidism increased from 33.3% in Stage III to 66.7% in Stage V. Their statistical analysis showed a significant correlation between CKD stage and thyroid function using the Chi-square test ($p < 0.05$). [20] Del Río-Camacho *et al.* similarly reported acquired hypothyroidism as a frequent comorbidity in pediatric CKD. [26]

The mechanisms underlying thyroid dysfunction in CKD are multifactorial. Reduced renal clearance, chronic inflammation, malnutrition, and non-thyroidal illness syndrome may all contribute to altered thyroid hormone metabolism and feedback regulation. [27] The predominance of Low T3 Syndrome in our study supports this, as also seen in the findings of Obeed *et al.* and Mohamed *et al.*, who reported decreasing FT3 and FT4 with declining estimated glomerular filtration rate (eGFR). [28,29]

Overall, these findings underscore the importance of monitoring thyroid function in pediatric CKD patients, especially those in advanced stages, even in the absence of overt clinical symptoms.

Limitations of the study

This study was conducted at a single center with a relatively small sample size due to a limited study period. After evaluating the patients, we did not conduct a long-term follow-up, so we could not assess any potential changes or interfering factors that may emerge over time in these patients.

CONCLUSION & RECOMMENDATIONS

This study found that thyroid dysfunction is common in pediatric patients with chronic kidney disease (CKD), with Low T3 Syndrome and subclinical hypothyroidism being the most frequently observed abnormalities. These dysfunctions were more prevalent in children with end-stage renal disease (Stage V CKD). Compared to Stage III and IV, Stage V patients had lower serum T3 and T4 levels and slightly elevated TSH levels, indicating a progressive decline in thyroid function with worsening renal status. These findings underscore the need for routine thyroid screening in children with CKD to enable early detection and management, which may help slow disease progression and improve clinical outcomes.

Further research using a prospective, longitudinal study design with a larger sample size is recommended to validate and expand upon these findings.

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