



## Association Between Thyroid Dysfunction and Serum Biochemical Abnormalities in Children with CKD at a Tertiary Care Center

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### ABSTRACT:

**Background:** Chronic kidney disease (CKD) in children is associated with multiple systemic complications including endocrine abnormalities such as thyroid dysfunction, which often remain underdiagnosed due to non-specific clinical manifestations. Thyroid hormones regulate calcium and phosphate metabolism, bone turnover, and protein synthesis, and their dysfunction can exacerbate biochemical derangements in CKD.

**Aim of the study:** The aim of this study was to assess the association between thyroid dysfunction and serum biochemical abnormalities in children with CKD.

**Methods:** This cross-sectional analytic study was conducted at the Department of Pediatric Nephrology, Bangladesh Medical University (BMU), which was formerly known as Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from February 2017 to January 2018. Total 60 children aged 2–18 years with CKD were included in this study.

**Result:** The mean age was 12 years (range 2–18) and 63.3% were male. Serum creatinine was highest in subclinical hypothyroidism (7.05 mg/dl) and lowest in hyperthyroidism (4.15 mg/dl). Biochemical parameters varied by thyroid dysfunction and CKD stage. Serum creatinine ranged from  $4.15 \pm 0.07$  mg/dl (hyperthyroidism) to  $7.05 \pm 4.11$  mg/dl (subclinical hypothyroidism). Calcium was lowest in hyperthyroidism ( $5.90 \pm 0.28$  mg/dl) and highest in euthyroid ( $8.35 \pm 1.45$  mg/dl). CKD stage-V showed highest creatinine ( $7.85 \pm 4.84$  mg/dl) and lowest TCO<sub>2</sub>



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( $17.24 \pm 6.02$  mmol/L). Phosphate increased and calcium decreased significantly with CKD stage. Electrolytes varied minimally; all p-values  $>0.05$  except for CKD trends.

Conclusion: This study found that while thyroid dysfunction showed non-significant variations in biochemical markers, CKD progression significantly affected creatinine, calcium, and phosphate levels. Electrolyte changes across CKD stages were minimal.

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## Introduction

Chronic kidney disease (CKD) in children remains a major cause of children's long-term morbidity and mortality, with an estimated incidence of 15-74 per million children globally, and rising detection rates over the last few years via improved diagnostic facilities and child nephrology outreach.<sup>1,2</sup> Although paediatric CKD epidemiology varies geographically and by socio-economic standing, its impact is underestimated in low- and middle-income countries due to limited registries and the lack of early detection schemes. Paediatric CKD leads to an array of systemic complications including growth retardation, mineral bone disease, cardiovascular complications, and endocrine dysfunction.<sup>3,4</sup> Of these, endocrine diseases such as thyroid dysfunction are oftentimes under-diagnosed due to coinciding non-specific manifestations such as fatigue, failure to grow, and delayed puberty, which are also features of CKD in itself.<sup>5,6</sup>

Thyroid dysfunction in children with CKD is a range of abnormalities that include subclinical hypothyroidism, euthyroid sick syndrome (low T3 syndrome), and overt hypothyroidism, whose prevalence rises progressively according to CKD severity.<sup>6,7</sup> In a study using the case-control approach in Iraq, significantly lower T3 and T4 levels and increased levels of TSH were observed in children with CKD compared to controls, and thyroid dysfunction was detected in all children with stage 5 CKD, reflecting the high association between renal impairment severity and thyroid abnormalities.<sup>5</sup> Also, an Indian observational study of undialysed CKD patients revealed subclinical hypothyroidism and low T3 syndrome to be the most prevalent abnormalities, which were correlated with declining glomerular filtration rate.<sup>7</sup> This reflects that thyroid dysfunction continues to remain uncorrected in children with CKD, which can postpone interventions that might improve growth, as well as metabolic function.

The pathophysiological bases for thyroid dysfunction in CKD are multicentric. The kidney plays a significant role in thyroid hormone metabolism and excretion, and nearly two-thirds of thyroid hormone degradation is via renal means.<sup>8</sup> CKD produces reduced renal clearance and tubular transport of iodine, reduced peripheral

conversion of thyroxine (T4) to triiodothyronine (T3) due to decreased deiodinase activity, and loss of thyroid-binding globulin and other carrier proteins through proteinuria, all resulting in reduced circulating thyroid hormone concentration and bioavailability.<sup>8,9</sup> Furthermore, the common chronic inflammation and malnutrition in advanced CKD impede thyroid hormone synthesis and feedback regulation changes, clinically manifesting as euthyroid sick syndrome or low T3 syndrome.

Thyroid hormones are key regulators of metabolic homeostasis, including calcium and phosphate homeostasis, bone turnover, and protein synthesis.<sup>9</sup> Hypothyroidism decreases bone turnover and mobilization of calcium, possibly exacerbating CKD-mineral bone disorder, and abnormal thyroid status also affects phosphate homeostasis and parathyroid hormone (PTH) regulation, further impairing mineral and bone health control in patients with CKD.<sup>9</sup> Hypoalbuminemia that is commonly seen with CKD is also exacerbated by thyroid derangement due to reduced protein synthesis, causing poor growth and nutrition in children.

Despite the proven mechanistic linkages between thyroid and kidney function, evidence investigating such correlations in children with CKD are limited in South Asia, particularly Bangladesh. Most of the existing data are derived from adult populations or consist of only general paediatric prevalence of thyroid disorders without clear evaluation of thyroid disturbances within CKD patients.<sup>7,10,11</sup>

Therefore, the present study aims to determine the prevalence of thyroid dysfunction and its relationship with serum biochemical abnormalities in children with CKD attending a tertiary care center in Bangladesh.

## Objectives

To assess the association between thyroid dysfunction and serum biochemical abnormalities in children with Chronic kidney disease (CKD).

## Methodology & Materials

This cross-sectional analytic study was conducted at the Department of Pediatric Nephrology, Bangladesh Medical University (BMU), which was formerly known



as Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from February 2017 to January 2018. Total 60 children aged 2–18 years with chronic kidney disease (CKD), both newly and previously diagnosed, attending inpatient or outpatient services, were included in this study. Patients with pre-existing thyroid disorders or who refused participation were excluded. CKD staging was categorised using eGFR calculated by the revised Schwartz formula:  $eGFR = 0.413 \times (\text{height in cm}/\text{serum creatinine in mg/dl})$ .

Stage	GFR (ml/min/1.73m <sup>2</sup> )	Terms
I	>90	Kidney damage with normal or increased GFR
II	60–89	Kidney damage with mild decrease in GFR
III	30–59	Moderately decreased GFR
IV	15–29	Severely decreased GFR
V	<15	Kidney failure

Clinical variables assessed included age, gender, anthropometry (weight, height, BMI), pallor, blood pressure, respiratory rate, bony changes, and skin condition. Height was measured using a stadiometer in children >2 years, while length was measured in younger children using an infantometer, and height standard deviation scores (SDS) were calculated using CDC data. Blood pressure was recorded using an aneroid sphygmomanometer by auscultatory method, averaging three readings at 15-minute intervals in the right arm. Laboratory variables included serum creatinine, electrolytes, calcium, phosphate, intact parathyroid hormone, albumin, TSH, total T3, total T4, complete blood count, and urine analysis including bedside albumin testing. Data were collected using a structured questionnaire, entered into SPSS version 22, and analysed using descriptive statistics, t-tests, Kruskal-Wallis test, ANOVA, Pearson's and Spearman's correlation, with  $p < 0.05$  considered significant. Ethical approval was obtained from the Institutional Review Board of BMU.

## Result

Table I shows the demographic characteristics of the study population. The mean age of participants was

12.02 ± 4.21 years, ranging from 2 to 18 years. The largest proportion of children belonged to the 15–20 years age group (38.3%), followed by 10–14 years (35%), 5–9 years (23.3%), and only 3.3% were under five years. Males comprised 63.3% of the cohort while females were 36.7%. The majority (78.3%) of children resided in rural areas, with only 21.7% from urban settings. Table II presents biochemical parameters according to thyroid dysfunction types. Mean serum creatinine was highest in children with subclinical hypothyroidism (7.05 ± 4.11 mg/dl) and lowest in hyperthyroidism (4.15 ± 0.07 mg/dl), though the difference was not statistically significant ( $p = 0.896$ ). Serum albumin levels were similar across groups, ranging from 31.60 ± 5.46 gm/L in subclinical hypothyroidism to 34.78 ± 7.07 gm/L in euthyroid children ( $p = 0.780$ ). Mean serum calcium was lowest in hyperthyroid children (5.90 ± 0.28 mg/dl) and highest in euthyroid children (8.35 ± 1.45 mg/dl), without significant difference ( $p = 0.147$ ). Serum inorganic phosphate ranged from 5.44 ± 1.55 mg/dl in low T3 syndrome to 7.56 ± 3.66 mg/dl in subclinical hypothyroidism ( $p = 0.147$ ). Table III shows biochemical parameters by CKD stage, demonstrating a significant increase in serum creatinine with advancing CKD stage, from 1.52 ± 0.64 mg/dl in stage III to 7.85 ± 4.84 mg/dl in stage V ( $p < 0.001$ ). Serum calcium decreased significantly with CKD progression ( $p = 0.005$ ), while serum inorganic phosphate increased significantly ( $p = 0.001$ ). Serum albumin levels decreased with stage but the difference was not significant ( $p = 0.328$ ). Table IV shows serum electrolyte levels across CKD stages in 60 patients. Sodium levels were similar in all stages (Stage III: 135.44 ± 3.05, Stage IV: 137.00 ± 3.41, Stage V: 135.72 ± 6.07 mmol/L;  $p = 0.749$ ). Potassium levels increased slightly from Stage III to Stage V (3.76 ± 0.45, 4.38 ± 0.97, and 4.34 ± 0.93 mmol/L respectively;  $p = 0.193$ ). Chloride levels remained stable across stages ( $p = 0.589$ ). TCO<sub>2</sub> levels showed a decreasing trend from Stage III (21.13 ± 4.33 mmol/L) to Stage V (17.24 ± 6.02 mmol/L), though not statistically significant ( $p = 0.165$ ).

Table-I: Demographic characteristics of the study people (N=60)

Variable	Frequency (n)	Percentage (%)
<b>Age (years)</b>		
<5	2	3.3
5 – 9	14	23.3
10 – 14	21	35.0
15 – 20	23	38.3



<b>Mean ± SD</b>	12.02 ± 4.21	
<b>Min – Max</b>	2 – 18	
<b>Gender</b>		
Male	38	63.3

Female	22	36.7
<b>Residence</b>		
Urban	13	21.7
Rural	47	78.3

Table-II: Biochemical parameters by thyroid dysfunction type (N=60)

Parameter	Subclinical Hypothyroidism	Low T3 Syndrome	Hyperthyroidism	Euthyroidism	p-value
Serum Creatinine (mg/dl)	7.05 ± 4.11	6.14 ± 4.85	4.15 ± 0.07	5.73 ± 4.78	0.896
Serum Albumin (gm/L)	31.60 ± 5.46	31.63 ± 8.80	33.00 ± 7.07	34.78 ± 7.07	0.780
Serum Calcium (mg/dl)	7.30 ± 2.19	7.77 ± 1.29	5.90 ± 0.28	8.35 ± 1.45	0.147
Serum Inorganic Phosphate (mg/dl)	7.56 ± 3.66	5.44 ± 1.55	6.85 ± 0.21	6.25 ± 2.66	0.147

Table-III: Biochemical parameters by CKD stage (N=60)

Parameter	Stage III	Stage IV	Stage V	p-value
Serum Creatinine (mg/dl)	1.52 ± 0.64	3.92 ± 3.30	7.85 ± 4.84	<0.001
Serum Albumin (gm/L)	36.00 ± 6.10	33.00 ± 8.22	31.70 ± 8.00	0.328
Serum Calcium (mg/dl)	8.86 ± 1.06	8.44 ± 1.45	7.39 ± 1.35	0.005
Serum Inorganic Phosphate (mg/dl)	3.74 ± 0.76	5.26 ± 2.13	6.28 ± 1.90	0.001

Table-IV: Serum electrolytes by CKD stage (N=60)

Electrolyte	Stage III	Stage IV	Stage V	p-value
Sodium (mmol/L)	135.44 ± 3.05	137.00 ± 3.41	135.72 ± 6.07	0.749
Potassium (mmol/L)	3.76 ± 0.45	4.38 ± 0.97	4.34 ± 0.93	0.193
Chloride (mmol/L)	106.67 ± 3.50	106.73 ± 4.65	104.52 ± 8.87	0.589
TCO <sub>2</sub> (mmol/L)	21.13 ± 4.33	19.25 ± 6.01	17.24 ± 6.02	0.165

## Discussion

In this cross-sectional study of thyroid dysfunction and serum biochemical derangement in Bangladeshi children with CKD, the mean age of participants was 12.02 years, and most children were aged 10–20 years with a male predominance of 63.3%. This trend by age mirrors that of Kim et al.<sup>12</sup> in South East England, which documented male predominance (58%) among paediatric CKD patients despite their younger median age of 6.7 years, postulated to be attributable to regional differences in

CKD aetiologies and detection timing. A further distinctive characteristic of this population was rural residence (78.3%), which was noted with regard to inequalities in early nephrology referral access in Bangladeshi rural settings.

Where biochemical parameters were analyzed according to types of thyroid dysfunction, serum creatinine was highest in subclinical hypothyroidism (7.05 mg/dl) and lowest in hyperthyroidism (4.15 mg/dl), even though the difference was non-significant. Srivastava et al.<sup>7</sup> also



found elevated creatinine in subclinical hypothyroid patients compared to euthyroid CKD patients, showing advanced renal impairment in hypothyroid subgroups.<sup>7</sup> Serum calcium was lowest in hyperthyroid children (5.90 mg/dl) and highest for euthyroid children (8.35 mg/dl), agreeing with Mohamed and Sayed<sup>6</sup> whose findings described lower serum calcium in thyroid dysfunction groups due to reduced bone turnover and impaired mobilization of calcium. Serum phosphate was also highest in subclinical hypothyroidism (7.56 mg/dl) and elevated in low T3 syndrome (5.44 mg/dl), supporting findings by Srivastava et al.<sup>7</sup> of elevated levels of phosphate among thyroid dysfunction patients due to reduced renal excretion and deranged hormonal regulation.<sup>7</sup> Serum albumin concentrations were similar between groups in the present study but lower among thyroid dysfunction patients, according to Mohamed and Sayed<sup>6</sup> who had previously reported hypoalbuminemia as another metabolic burden among these children.

Biochemical examination by CKD stage revealed a marked increase in serum creatinine with higher stage ( $p < 0.001$ ), and also significant decrease in serum calcium ( $p = 0.005$ ) and increase in serum phosphate ( $p = 0.001$ ). Trends are consistent with Gupta et al.<sup>13</sup> who reported worsening kidney function and calcium-phosphate imbalance with advanced CKD stage. Singh and Bhatta<sup>15</sup> also noted raised creatinine and phosphate and falling calcium and albumin at advancing stages, indicating mineral bone disorder risk. Wesseling-Perry et al.<sup>15</sup> depicted that even at early CKD, biochemical abnormalities in calcium and phosphate metabolism are likely, indicating the need for early biochemical monitoring.

Serum electrolyte analysis showed that sodium and chloride levels remained constant across CKD stages, while potassium levels increased slightly from stage III to V and  $\text{TCO}_2$  levels showed a declining trend. No significant change in sodium across CKD stages was also reported by Poudel et al.<sup>16</sup>, but there was a rising trend in potassium in severe CKD as a result of reduced tubular secretion. Dhondup and Qian<sup>17</sup> reported steady sodium and chloride levels, increasing potassium retention, and decreasing bicarbonate ( $\text{TCO}_2$ ) with CKD advancement, prone to metabolic acidosis. Brown et al.<sup>18</sup> reported low serum bicarbonate as a standalone predictor of CKD advancement among children, reaffirming the clinical importance of  $\text{TCO}_2$  measurement.

This study demonstrates that thyroid dysfunction, particularly low T3 syndrome and subclinical hypothyroidism, is highly prevalent among children with CKD, especially in advanced stages.

### Limitations of the study

In our study, there was small sample size and absence of control for comparison. Study population was selected from one center in Dhaka city, so may not represent wider population. The study was conducted at a short period of time.

### Conclusion and recommendations

This study highlights the association between thyroid dysfunction and biochemical abnormalities in children with CKD. While serum creatinine was highest in subclinical hypothyroidism, and calcium lowest in hyperthyroidism, these differences were not statistically significant. However, CKD progression was significantly associated with increased serum creatinine and phosphate, and decreased calcium. Electrolyte levels remained largely stable across CKD stages. These findings underscore the importance of monitoring thyroid and biochemical parameters in pediatric CKD to ensure timely intervention and management.

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