Original Article

DOI: 10.7860/JCDR/2026/82973.24506

Paediatrics Section

Thyroid Function and Serum Calcium Level in Children with Nephrotic Syndrome Attending a Tertiary Care Hospital in Kolkata, India: A Cross-sectional Study

RAKESH KUMAR MADDHESHIYA[1], SUDIP SAHA[2], MOUSUMI DAS[3], IRA DAS[4]

ABSTRACT

Introduction: Nephrotic Syndrome (NS) in children is a common renal disorder characterised by massive proteinuria, hypoalbuminaemia, and oedema. However, loss of thyroid-binding proteins and vitamin D metabolites in the urine may disrupt thyroid and calcium homeostasis.

Aim: To evaluate thyroid function and serum calcium levels in children with NS attending a tertiary care hospital in Kolkata, India.

Materials and Methods: The present cross-sectional study was conducted at the Department of Paediatrics in Chittaranjan Seva Sadan hospital of Obstetrics, Gynaecology and child health, Kolkata, India, from December 2022 to May 2024. Total 96 children aged 1-12 years diagnosed with NS (first episode or relapse) were enrolled in the study. Cases of thyroid disease, those on calcium supplementation within last 12 hours, blood/albumin transfusion within last four month, known cases of liver disease, acute renal failure, acid-base disorders, or steroid-resistant NS were excluded. Clinical data, thyroid profile {Triiodothyronine (T3), Thyroxine (T4), Thyroid-Stimulating Hormone (TSH)}, and serum calcium of those children who were included in the study were analysed. Continuous variables were expressed as mean±Standard Deviation (SD); categorical variables as percentages. Statistical comparisons were made using t-tests, Chi-square tests, and z-tests. In present study, significance was set at p-value <0.05.

Results: In present study, out of 96 patients, 76 (79.2%) were male while 20(20.8%) were female. A total of 65 patients (67.7%) were below seven years of age while 31 patients (32.3%) were between 7-12 years of age. Mean age±SD was 58.4±34.3 months. Forty children (41.7%) had first episode, while 56 (58.3%) were relapsed cases. Hypothyroidism was present in 9(9.4%) overall, rising from 2 in 40 patients (5%) in first episodes to 3 in 4 patients (75%) in fifth episodes (p=0.0002). Mean serum calcium declined from 9.66 mg/dL in first episodes to 8.65 mg/dL by the fifth episode (p=0.0004), with hypocalcaemia observed in 75% of fifth episode cases.

Conclusion: Thyroid dysfunction and hypocalcaemia are common metabolic complications in paediatric NS, particularly with recurrent episodes. Routine assessment of thyroid and calcium profiles is recommended to mitigate growth, metabolic, and bone health complications.

Keywords: Calcium metabolism, Hypocalcaemia, Hypothyroidism, Paediatric renal disorder, Proteinuria

INTRODUCTION

The NS is one of the most common renal disorders in children and is characterised by massive proteinuria, hypoalbuminaemia, oedema, and hyperlipidaemia [1]. In addition to these classical features, NS is now recognised as a systemic disease associated with multiple metabolic and endocrine abnormalities. Among these, disturbances in thyroid function and calcium metabolism are particularly important in the paediatric age group, as they may adversely affect growth, bone health, and overall development [2].

Several studies have reported an association between NS and thyroid dysfunction, especially hypothyroidism [3-5]. The underlying pathophysiology is attributed to urinary loss of thyroid hormones and thyroid-binding proteins such as thyroxine-binding globulin, transthyretin, and albumin due to increased glomerular permeability [6]. This leads to reduced circulating levels of total T3 and T4, with a compensatory rise in TSH [6]. Hajizadeh N et al., reported a significant prevalence of subclinical and overt hypothyroidism in children with active NS, which improved after remission [3]. Similar findings have been observed in other studies, suggesting that thyroid dysfunction is closely related to disease activity and severity [4,5].

Alterations in calcium metabolism are also commonly observed in children with NS. Hypocalcaemia may result from urinary loss of vitamin D-binding protein, leading to reduced serum vitamin D levels, along with hypoalbuminaemia affecting total serum calcium concentrations [7,8]. Additionally, prolonged steroid therapy and reduced intestinal calcium absorption may further contribute to disordered calcium homeostasis [9]. Previous studies have reported varying prevalence of hypocalcaemia in nephrotic children, indicating that this abnormality is often under recognised and undertreated [7-9].

Although thyroid dysfunction and hypocalcaemia have been individually studied in NS, there is limited literature evaluating both abnormalities concurrently in the paediatric population [3-7]. Some previous studies [5,7] have been limited by small sample sizes, heterogeneous study populations, or lack of standardised biochemical criteria. Moreover, data from Indian children, particularly from eastern India, remain scarce. Nutritional status, iodine intake, vitamin D deficiency, and socioeconomic factors may influence the prevalence and severity of these metabolic disturbances, highlighting the need for region-specific data [10].

Hence, present cross-sectional study was undertaken to assess thyroid function and calcium metabolism in children with NS using standardised diagnostic criteria and laboratory methods.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Department of Paediatrics, in Chittaranjan Seva Sadan Hospital of Obstetrics, Gynaecology and Child Health, Kolkata, India. The study was

conducted from December 2022 to May 2024, over a duration of 18 months. The study protocol was approved by the Institutional Ethics Committee (IEC 15/2022) and conducted in accordance with the Declaration of Helsinki. Informed consent in writing was obtained from parents or legal guardians of all participants.

Inclusion criteria: Children aged 1-12 years with a diagnosis of NS (first episode or relapse) were included, as the hospital admits paediatric patients only up to 12 years of age. Proteinuria of ≥3+ on dipstick or urinary protein >40 mg/m²/hour was considered significant for NS diagnosis [1].

Exclusion criteria: subjects with prior calcium supplementation within 12 hours, known thyroid disease, blood or albumin transfusion within four months, liver disease, acid-base disorders, acute renal failure, or steroid-resistant NS were excluded.

Sample size calculation: It was calculated by taking z^2PQ/D^2 formula.

Sample size= 87

Where, z= 1.96 at 95% level of confidence,

P= prevalence of thyroid dysfunction of 23%, as reported by Hajizadeh N et al., among children with NS [3].

Q=1-p , D=10% absolute error (0.1),

Taking additional 10% for non-response and those who drop out for unavoidable reasons,

Final Sample size=96

Study Procedure

Data were collected using a structured proforma that included clinical details-presence of fever, abdominal pain, abnormal chest findings, presence of hypertension, episode history and laboratory investigations. Urinary protein was assessed using a semi-quantitative urine dipstick method, where proteinuria of ≥3+ on dipstick or urinary protein >40 mg/m²/hour was considered significant for NS diagnosis [1]. A 5mL random venous blood samples were collected for biochemical analysis. Serum calcium was estimated using the Arsenazo III colorimetric method on an automated analyser. Serum calcium levels <8.5 mg/dL were considered indicative of hypocalcaemia [7].

Thyroid function tests including serum T3, T4, and TSH were measured using a Chemiluminescence Immunoassay (CLIA) method. Normal thyroid function was defined using laboratory reference ranges (T3: 0.8-2.0 ng/mL, T4: 5-12 µg/dL, TSH: 0.3-5.0 mIU/L), as described by Afroz S et al., [5]. Hypothyroidism was defined as elevated TSH levels with low or normal T4 values, as per standard paediatric reference ranges [5].

Episode history was recorded based on medical records and caregiver interviews, and patients were classified according to the number of NS relapses.

STATISTICAL ANALYSIS

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 26.0 and GraphPad Prism. Continuous variables were expressed as mean±SD, and categorical variables as percentages. Comparisons were performed using t-tests, Chi-square tests, and z-tests where appropriate. The p-values <0.05 were considered statistically significant.

RESULTS

The study population predominantly consisted of children below seven years of age with a marked male preponderance. Most children were in the first episode of NS, though a significant proportion had recurrent disease. Heavy proteinuria (≥3+) was observed in all participants. Overall, hypothyroidism was detected in 9.4% of cases [Table/Fig-1].

Children with NS demonstrated hypoalbuminaemia with preserved mean thyroid hormone levels and TSH values within the reference range in most cases. Mean serum calcium was within the lower normal range, suggesting early biochemical alteration in calcium metabolism [Table/Fig-2].

Variables	Category	n (%)
Age	Mean±SD	58.4±34.3
	<7 years	65 (67.7)
	7-12 years	31 (32.3)
Gender	Male	76 (79.2)
	Female	20 (20.8)
Clinical features	Fever	24 (25.0)
	Hypertension	11 (11.5)
	Abdominal tenderness	64 (66.7)
	Abnormal chest auscultation	3 (3.1)
	History of tuberculosis	0 (0)
Urine protein (dipstick)	3+	70 (72.9)
	4+	26 (27.1)
Nephrotic Syndrome (NS) episode	First episode	40 (41.7)
	Second episode	19 (19.8)
	Third episode	6 (6.3)
	Fourth episode	27 (28.1)
	Fifth episode	4 (4.2)
Thyroid status	Hypothyroid	9 (9.4)
	Euthyroid	87 (90.6)

[Table/Fig-1]: Demographic, clinical and disease profile of study participants (N=96).

Parameters	Mean±SD	Median	Range
Serum albumin (g/dL)	2.52±0.21	2.5	2.0 - 2.9
Urine protein/creatinine ratio	2.27±0.13	2.3	2.1 - 2.6
Serum calcium (mg/dL)	9.33±0.77	9.7	8.0 - 10.2
T3 (ng/mL)	1.54±0.40	1.55	0.46 - 2.10
T4 (µg/dL)	9.81±2.40	10.2	3.0 - 13.4
TSH (mIU/L)	2.70±1.62	1.9	1.2 - 8.4
Urine protein (mg/dL)	324.6±58.2	330	240 - 420
Urine creatinine (mg/dL)	142.8±21.4	145	110 - 190

[Table/Fig-2]: Biochemical parameters of study participants (N=96).

The prevalence of hypothyroidism increased progressively with the number of NS relapses. While hypothyroidism was uncommon during initial episodes, three-fourths of children with a fifth episode exhibited thyroid dysfunction, indicating a strong association with disease recurrence [Table/Fig-3].

Episodes	Total	Hypothyroid n (%)	Euthyroid n (%)
First	40	2 (5.0)	38 (95.0)
Second	19	1 (5.3)	18 (94.7)
Third	6	0 (0)	6 (100)
Fourth	27	3 (11.1)	24 (88.9)
Fifth	4	3 (75.0)	1 (25.0)

[Table/Fig-3]: Association between thyroid status and Nephrotic Syndrome (NS) episodes (N=96).
Chi square=22.27; df=4; p=0.0002

A gradual decline in mean serum calcium levels was observed with increasing disease episodes. Children with frequent relapses demonstrated lower calcium values compared to those experiencing a first episode, highlighting cumulative metabolic effects of recurrent proteinuria [Table/Fig-4].

Although most children maintained normal serum calcium levels, hypocalcaemia was detected in a subset of patients, predominantly

Episodes	n	Mean±SD (mg/dL)
First	40	9.66±0.56
Second	19	9.44±0.66
Third	6	9.00±0.86
Fourth	27	9.10±0.71
Fifth	4	8.65±0.61

[Table/Fig-4]: Mean serum calcium levels according to episode number of nephrotic syndrome.

among those with multiple relapses, underscoring the need for periodic biochemical monitoring. Out of total patients of NS 8.3% had hypocalcaemia [Table/Fig-5].

Serum Calcium Status	Total	Episodes				
		First	Second	Third	Fourth	Fifth
Hypocalcaemia	8 (8.3%)	0	0	1	4	3
Normal calcium	88 (91.7%)	40	19	5	23	1

[Table/Fig-5]: Distribution of patients based on serum calcium status.

DISCUSSION

The NS is a common paediatric renal disorder with important systemic metabolic consequences due to persistent proteinuria. The present study evaluated thyroid function and serum calcium levels in children with NS and demonstrated that both abnormalities are significantly associated with disease recurrence. The mean age of the study population was 58.4±34.3 months, with nearly two-thirds of children below seven years of age. This finding is consistent with the established epidemiology of childhood NS, which predominantly affects younger children [1]. A marked male predominance (79.2%) was observed, similar to previous Indian and international studies, supporting the known male preponderance in paediatric NS [11].

In the present study, hypothyroidism was detected in 9.4% of children. Importantly, the prevalence of hypothyroidism increased significantly with increasing number of NS episodes, reaching the highest proportion among children with multiple relapses (p=0.0002). This observation suggests a strong association between disease chronicity and thyroid dysfunction.

The mechanism of thyroid dysfunction in NS is primarily related to urinary loss of thyroid hormones and thyroid-binding proteins such as thyroxine binding globulin, albumin, and transthyretin [5]. In early or isolated episodes, compensatory mechanisms help maintain a euthyroid state; however, with persistent or recurrent proteinuria, these mechanisms become insufficient, leading to elevated TSH levels and subclinical or overt hypothyroidism [12].

Afroz S et al., reported elevated TSH levels during active nephrotic relapse that normalised following remission, suggesting a reversible hypothyroid state linked to proteinuria [5]. Similar findings were reported by Ito S et al., who observed significantly higher TSH levels during relapse compared with remission, without the need for routine thyroid hormone supplementation [13]. Hajizadeh N et al., further demonstrated a high prevalence of thyroid dysfunction in children with prolonged NS and emphasised the importance of screening in persistent cases [3]. The present study strengthens existing evidence by showing a graded increase in hypothyroidism with increasing number of disease episodes, highlighting the cumulative effect of recurrent protein loss.

Although the overall mean serum calcium level in the study population was within the lower normal range, a progressive decline in serum calcium levels was observed with increasing number of NS episodes, which was statistically significant (p=0.0004). Children with frequent relapses exhibited lower calcium levels compared to those with a first episode.

Hypocalcaemia in NS is attributed to urinary loss of vitamin D binding protein, resulting in reduced circulating levels of 25-hydroxyvitamin D and impaired calcium absorption [7]. In addition, prolonged corticosteroid therapy can negatively affect calcium metabolism by decreasing intestinal absorption and increasing renal excretion [14].

Hossain A et al., demonstrated a significant positive correlation between serum albumin and ionized calcium levels in children with NS, indicating that hypoalbuminaemia plays an important role in calcium imbalance [14]. Similar findings were reported by Thakor JM et al., who observed significantly lower serum calcium levels in both steroid sensitive and steroid-resistant NS compared to controls [15]. The present study adds to existing literature by demonstrating that calcium level worsens with increasing disease recurrence, even in the absence of overt hypocalcaemia.

The findings of the present study have important clinical implications. Routine thyroid function testing may not be required in children with a first episode of NS who achieve early remission. However, children with frequent relapses represent a high-risk group and should undergo periodic thyroid function screening to detect subclinical hypothyroidism early [5,13]. Similarly, declining serum calcium levels in recurrent NS raise concerns regarding bone health, growth, and neuromuscular function. Regular monitoring of serum calcium, along with consideration of vitamin D status, may help prevent long-term skeletal complications [7,15]. The strengths of the study include a well-defined paediatric cohort, standardised biochemical evaluation, and assessment of disease severity using number of episodes.

Limitation(s)

The current study was a single-center, cross-sectional study, limiting causal inference and generalisability. Vitamin D and ionised calcium levels were not assessed. The effect of cumulative steroid exposure was not evaluated.

CONCLUSION(S)

Thyroid dysfunction and reduced serum calcium levels are observed in children with recurrent NS. The prevalence of hypothyroidism and decline in calcium levels increase with repeated relapses. Regular monitoring of thyroid function and serum calcium, especially in frequently relapsing cases, may help prevent long-term complications. Prospective longitudinal studies including vitamin D status and treatment-related factors are recommended to better understand the long-term metabolic impact of recurrent NS.

Acknowledgement

The authors would like to acknowledge the cooperation of all the children and their parents/guardians who participated in the present study. The authors also thank the nursing staff and laboratory personnel of Chittaranjan Seva Sadan Hospital of Obstetrics, Gynaecology and Child Health, Kolkata, for their assistance in data collection and laboratory investigations.

Declaration regarding use of Artificial Intelligence (AI): The authors declare that AI- assisted tools were used only for language editing and grammatical refinement of the manuscript. No AI tool was used for data analysis, interpretation of results, or generation of scientific content. The authors take full responsibility for the accuracy, originality, and integrity of the work.

REFERENCES

[1] Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet. 2003;362(9384):629-39.
[2] Mizdrak M, Smajic B, Mizdrak I, Ticinovic Kurir T, Kumric M, Paladin I, et al. Endocrine disorders in nephrotic syndrome: A comprehensive review. Biomedicines. 2024;12(8):1860.
[3] Hajizadeh N, Marashi SM, Nabavizadeh B, Elhami E, Mohammadi T, Nobandegani NM, et al. Examine of thyroid function in pediatric nephrotic syndrome: Tehran-Iran. Int J Pediatr. 2015;3(Suppl 1):59-65.
[4] Kapoor K, Saha A, Dubey NK, Goyal P, Suresh CP, Batra V, Upadhayay AD. Subclinical non-autoimmune hypothyroidism in children with steroid-resistant nephrotic syndrome. Clin Exp Nephrol. 2014;18(1):113-17.

[5] Afroz S, Khan AH, Roy DK. Thyroid function in children with nephrotic syndrome. Mymensingh Med J. 2011;20(3):407-11.
[6] Singh S, Mishra OP, Mandal PP, Patel PS, Sharma SS, Saini H, et al. Thyroid function in patients with idiopathic nephrotic syndrome. Int Urol Nephrol. 2021;53:1859-64.
[7] Goldstein DA, Haldimann B, Sherman D, Norman AW, Massry SG. Vitamin D metabolites and calcium metabolism in patients with nephrotic syndrome and normal renal function. J Clin Endocrinol Metab. 1981;52(1):116-21.
[8] Sharawat IK, Dawman L, Kumkhaniya MV, Devpura K, Mehta A. Bone mineral density and its influencing factors in children with idiopathic nephrotic syndrome: A prospective observational study. Trop Doct. 2019;49(4):292-98.
[9] Gulati S, Godbole MM, Singh U, Gulati K, Srivastava AK. Are children with idiopathic nephrotic syndrome at risk for metabolic bone disease? Am J Kidney Dis. 2003;41(6):1163-9.
[10] Weng FL, Shults J, Leonard MB, Stallings VA, Zemel BS. Risk factors for low serum 25-hydroxyvitamin D concentrations in otherwise healthy children and adolescents. Am J Clin Nutr. 2007;86(1):150-58.
[11] Banh THM, Hussain-Shamsy N, Patel V, Vasilevska-Ristovska J, Borges K, et al. Ethnic differences in incidence and outcomes of childhood nephrotic syndrome. Clin J Am Soc Nephrol. 2016;11(10):1760-68.
[12] Gilles R, Heijer MD, Ross AH, Sweep FC, Hermus AR, Wetzels JF. Thyroid function in patients with proteinuria. Neth J Med. 2008;66(11):483-85.
[13] Ito S, Kano K, Ando T, Ichimura T. Thyroid function in children with nephrotic syndrome. Pediatr Nephrol. 1994;8(4):412-15.
[14] Hossain A, Mostafa G, Mannan KA, Deb KP, Hossain MM, Alam S. Correlation between serum albumin and ionized calcium in idiopathic nephrotic syndrome in children. Urol Nephrol Open Access J. 2016;3(2):44-47.
[15] Thakor JM, Mistry KN, Gang S. Association between serum calcium and biochemical parameters among nephrotic syndrome patients: A case-control study. Egyptian Pediatric Association Gazette. 2022;70:18:01-06.

PARTICULARS OF CONTRIBUTORS:
1. Senior Resident, Department of Paediatrics, R.G. Kar Medical College, Kolkata, West Bengal, India.
2. Associate Professor, Department of Paediatrics, Chittaranjan Seva Sadan Hospital, Kolkata, West Bengal, India.
3. Assistant Professor, Department of Paediatrics, Chittaranjan Seva Sadan Hospital, Kolkata, West Bengal, India.
4. Assistant Professor, Department of Paediatrics, Chittaranjan Seva Sadan Hospital, Kolkata, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Mousumi Das,
Skyline Lakeview Complex, H-Block, Flat-1B, Purbapara, Laskarpur,
Kolkata-700153, West Bengal, India.
E-mail: mousumids99@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Oct 11, 2025
- Manual Googling: Mar 21, 2026
- iThenticate Software: Mar 24, 2026 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 9

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Aug 31, 2025**
Date of Peer Review: **Dec 30, 2025**
Date of Acceptance: **Mar 26, 2026**
Date of Publishing: **Oct 01, 2026**