International Journal of Medical and Health Research
ISSN: 3078-4824
DOI: 10.61424/ijmhr
Journal Homepage: www.bluemarkpublishers.com/index.php/IJMHR

IJMHR
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| RESEARCH ARTICLE

Thyroid Hormone Status during Active Phase and After Remission in Children with Nephrotic Syndrome

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| ABSTRACT

Background: Protein loss in childhood nephrotic syndrome (NS) can deplete thyroid-binding proteins, but the burden and reversibility of resulting thyroid dysfunction in South-Asian children are poorly defined. Objectives: To quantify (i) the prevalence of biochemical thyroid abnormalities during active NS, (ii) their resolution after remission, and (iii) any association between serum albumin and thyroid indices. Methods: In a prospective observational study (July 2019–June 2020) of 80 Bangladeshi children (1–15 years) with steroid-sensitive NS at a tertiary centre, total T3, total T4, free T4 and TSH were measured during the nephrotic phase and repeated four weeks after documented remission in 31 participants. Results: During relapse, 42.5 % exhibited thyroid dysfunction: overt hypothyroidism 15.0 %, subclinical hypothyroidism 10.0 % and low-T3 syndrome 17.5 %. Mean TSH was mildly elevated (6.3 ± 4.3 mIU/L) while free T4 remained largely preserved. After remission, euthyroidism was restored in 93.5 % ($p = 0.002$); low-T3 syndrome disappeared and only one child (3.2 %) persisted with overt hypothyroidism. Serum albumin showed no significant correlation with total T3, total T4, free T4 or TSH ($r < 0.09$, $p > 0.48$). Conclusions: Transient thyroid perturbations are common in paediatric NS but mostly resolve within four weeks of proteinuria control. Routine thyroid panels at each relapse and a single follow-up test after remission could identify the small minority requiring endocrine referral.

| KEYWORDS

Nephrotic syndrome, thyroid dysfunction, hypothyroidism, low-T3 syndrome, albumin.

| ARTICLE INFORMATION

ACCEPTED: 07 July 2025 **PUBLISHED:** 13 August 2025 **DOI:** 10.61424/ijmhr.v3.i3.390

1. Introduction

Nephrotic syndrome (NS) remains one of the most frequent chronic kidney disorders of childhood, characterised by heavy proteinuria, hypoalbuminemia, oedema and dyslipidemia (Nisha et al., 2022). Although the renal manifestations dominate the clinical picture, the sustained urinary loss of low-molecular-weight proteins also disturbs several extra-renal endocrine pathways (Mizdrak et al., 2024). Among these, thyroid homeostasis is particularly vulnerable because more than 99 % of circulating thyroxine (T4) and triiodothyronine (T3) are normally

bound to carrier proteins—principally thyroxine-binding globulin (TBG), transthyretin and albumin. When these binding proteins leak through the glomerular barrier they drag their attached hormones with them, accelerating peripheral clearance and lowering the total hormone pool (Setiamal et al., 2024).

In the early stages of relapse, serum concentrations of free T4 and free T3 usually remain inside the reference range because thyroid-stimulating hormone (TSH) secretion rises promptly to maintain Euthyroidism. Over time, however, sustained protein loss may exceed the compensatory capacity of the hypothalamus-pituitary-thyroid axis (Nuraeni et al., 2020). The result is a spectrum of dysfunction ranging from low T3 syndrome to subclinical or overt hypothyroidism[1]. Because growth, neuro-cognitive maturation and metabolic regulation in children are strongly dependent on adequate thyroid hormone supply, even subtle disturbances can have lasting consequences if left unrecognized (Jo'rayeva, 2025).

Despite the clinical importance of this interaction, data from South-Asian pediatric populations are scarce. Childhood nephrotic syndrome is common and access to routine endocrinological testing may be limited, the true burden of thyroid dysfunction is uncertain (Hilmanto et al., 2022). The present investigation therefore sought to clarify three questions:

1. How frequently do biochemical thyroid abnormalities occur during active proteinuria episodes?
2. Does biochemical Euthyroidism reliably return once remission is achieved?
3. Are serum albumin levels correlated with any component of the thyroid profile during relapse?

By answering these questions, clinicians may be better equipped to decide whether routine thyroid screening and, if necessary, early levothyroxine supplementation should form part of standard nephrotic-syndrome care pathways.

2. Materials and Methods

2.1 Study Design and Setting

A prospective observational study was performed between July 2019 and June 2021 in the Department of Pediatrics, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh. The design allowed serial within-patient comparisons of thyroid indices measured during the nephrotic phase and again four weeks after documented remission, without introducing therapeutic interventions beyond standard nephrotic-syndrome management.

2.2 Participants

Children presenting with steroid-sensitive nephrotic syndrome were screened consecutively. **Table 1:** Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
• First-episode or relapse of steroid-sensitive NS	• First attack before 12 months or after 8 years of age
• Age at enrolment 1–15 years	• Secondary causes of NS (e.g. systemic lupus, infection-related)
• Normal serum creatinine on admission	• Moderate-to-severe protein-energy malnutrition (weight-for-age < –3 SD)

Table 1 delineates the eligibility framework that shaped the study cohort, thereby underpinning the internal validity and reproducibility of the investigation. The inclusion arm captures children aged 1–15 years who presented with a steroid-sensitive pattern of nephrotic syndrome (NS), either at first attack or relapse, and with normal serum creatinine on admission. These criteria ensured that only primary NS was observed, eliminating confounders arising from chronic kidney impairment or atypical steroid resistance. By defining a broad age range yet excluding infants (< 12 months) and late-onset cases (> 8 years for the first attack), the authors targeted the demographic in which idiopathic minimal-change disease is known to predominate, thereby maximizing clinical relevance.

The exclusion parameters further refine the sample: secondary NS—such as that associated with systemic lupus erythematosus, hepatitis B infection or Henoch–Schönlein purpura—is removed to prevent pathogenetic heterogeneity. Likewise, moderate-to-severe protein-energy malnutrition is barred because malnutrition itself can depress thyroidal indices, creating a spurious association that would exaggerate hypothyroid prevalence. The decision to use serum creatinine as a surrogate for glomerular filtration rate (GFR) aligns with standard pediatric nephrology practice, where age-adjusted reference intervals permit reliable discrimination between normal and impaired function.

Empirically, this framework is defensible: international pediatric cohorts reveal that 80–90 % of idiopathic NS cases respond to corticosteroids within four weeks, and the probability of spontaneous thyroid autoimmunity at this age is low. Therefore, abnormal thyroid profiles in such children are most plausibly attributable to proteinuria-mediated hormone loss (evidence demonstrated later in Tables 6–11). By explicitly listing criteria, the authors allow external researchers to replicate or challenge findings with comparable populations, thereby contributing to cumulative science in the field.

Nephrotic phase referred to any admission with heavy proteinuria (≥ 3+ by dipstick on two consecutive early-morning samples) accompanied by hypoalbuminemia (serum albumin < 2.5 g/dL) and oedema. *Remission* was defined as ≤ trace protein on dipstick for three consecutive days while receiving or after completing standard prednisolone therapy. In Euthyroidism all indices—total T3, free T4, and TSH—remain within normal ranges. Low T3 syndrome shows a selective fall in total T3 while free T4 stays normal and TSH is normal or slightly low. Subclinical hypothyroidism retains normal T3 and free T4 yet TSH rises. Overt hypothyroidism exhibits reduced T3 and free T4 accompanied by an elevated TSH.

2.3 Data Collection Procedures

A structured case-record form captured sociodemographic variables, clinical features at presentation, urine dipstick grade, biochemical indices and treatment details. Venous blood was sampled in the morning after an overnight fast. During the nephrotic phase, assays included serum total T3, total T4, free T4, TSH, albumin, cholesterol, creatinine and, for relapse episodes, spot urine protein-creatinine ratio. Twenty-four-hour urinary protein was measured for first attacks. The same thyroid panel and albumin were repeated four weeks post-remission in patients who returned for follow-up. All analytes were processed in the hospital's ISO-accredited central laboratory using chemiluminescent immunoassay on an automated platform calibrated daily.

2.4 Variables and Data Handling

Table 2: Study Variables

Domain	Variable	Type
Sociodemographic	Age (years), Sex	Continuous; Categorical
Clinical	Age at first NS episode (months), Attack type (initial/IFRNS/FRNS), Urine albumin grade	Continuous; Categorical; Ordinal
Laboratory	Serum albumin (g/dL), Cholesterol (mg/dL), Creatinine (mg/dL), PCR or 24 h protein (g/day)	Continuous
Thyroid outcomes	Total T3 (ng/mL), Total T4 (ng/mL), Free T4 (pmol/L), TSH (mIU/L)	Continuous
Thyroid status category	Euthyroid, Low T3, Subclinical or Overt Hypothyroid	Nominal

Table 2 inventories the quantitative and categorical variables measured, mapping them onto their respective domains—socio-demographic, clinical, laboratory and thyroid-specific outcomes. The distinction between continuous and categorical measurement levels dictates the statistical tests later applied, illustrating methodological transparency. Age, for example, is treated as a continuous variable, permitting parametric analyses

such as t-tests and Pearson correlations with thyroid indices. Sex, coded categorically, supports χ^2 or Fisher exact testing when assessing prevalence of biochemical hypothyroidism between males and females.

The clinical domain integrates "attack type," coded into initial episode, infrequent relapse (IFRNS) and frequent relapse (FRNS). This stratification is clinically pertinent because each subgroup portends distinct steroid-response trajectories and cumulative proteinuria exposure—factors hypothesised to influence thyroid status (scrutinized in Table 5). Bedside albumin grading supplies an ordinal proxy for acute protein loss severity, complementing the laboratory-defined serum albumin concentration.

Laboratory variables encompass serum albumin, cholesterol and creatinine—classic nephrotic markers—with spot urine protein: creatinine ratio or 24-hour protein excretion indexing proteinuria burden. The inclusion of creatinine also lets investigators verify preserved renal function across sampling points, thereby excluding uremic effects on thyroid binding or metabolism.

Thyroid outcomes capture both total and free hormone pools: Total T3 and T4 quantify the absolute hormone reservoir, while free T4 reflects the bioactive fraction impervious to binding fluctuations—critical in NS where carrier proteins are lost in urine. TSH, as the pituitary feedback signal, functions as the sentinel variable for diagnosing overt or subclinical hypothyroidism.

By enumerating each variable and its data type, Table 2 serves as a roadmap for reproducibility, enabling peers to reconstruct analytic pipelines precisely. Moreover, it evidences the study's holistic approach—spanning demographic, renal and endocrine parameters—thereby strengthening causal inference between proteinuria and thyroid perturbation.

3. Results

3.1 Sociodemographic Profile

Table 3: Sociodemographic Characteristics (n = 80)

Parameter	Frequency	Percentage
Age < 5 years	54	67.5
Age 5–10 years	25	31.3
Age > 10 years	1	1.2
Mean age ± SD (years)	4.3 ± 2.5	—
Male	50	62.5
Female	30	37.5

Table 3 offers a demographic snapshot of the 80 enrolled children, revealing patterns consonant with global epidemiology of pediatric NS. Two-thirds (67.5%) were under five years old, with a mean age of 4.3 ± 2.5 years. This aligns with longitudinal registries from Europe and Asia where peak incidence clusters between 2 and 6 years, underpinning evidence that minimal-change pathology dominates early childhood.

The male preponderance (62.5%) mirrors the well-described 2:1 male-to-female ratio in idiopathic NS, reinforcing external validity. Male bias is often attributed to sex-linked immunomodulatory factors influencing glomerular permeability, though the exact mechanism remains debated. The modest standard deviation on age suggests a relatively homogeneous cohort, advantageous for minimising age-related confounders when interpreting thyroid outcomes: thyroid reference intervals vary subtly with age, so narrow dispersion reduces the risk of misclassification.

From an evidence standpoint, these demographics support the ensuing thyroid findings: younger children exhibit rapid metabolic rates and limited hormonal reserves, rendering them susceptible to transient hypothyroid states when protein loss accelerates. Large cohort analyses (e.g., the International Study of Kidney Disease in Children)

report similar age-sex distributions, lending credibility to the sample's representativeness. The table therefore lays a demographic foundation essential for interpreting thyroid prevalence figures presented later; for instance, any link between younger age and higher hypothyroid risk can be probed by stratifying data within this table's parameters.

Overall, Table 3 substantiates that the cohort mirrors the typical epidemiology of steroid-sensitive NS, thereby strengthening confidence that conclusions drawn about thyroid dysfunction are applicable to general pediatric practice rather than being artefacts of an atypical subpopulation.

Table 4: Attack Pattern (n = 80)

Parameter	Frequency	Percentage
Mean age at first attack (months) ± SD	39.1 ± 18.0	—
Number of attacks		
1–2	60	75.0
3–4	13	16.3
≥ 5	7	8.7
Mean number of attacks ± SD	**2.08 ± 1.67**	—
Type of current attack		
Initial episode	45	56.3
Infrequent relapse (IFRNS)	31	38.7
Frequent relapse (FRNS)	4	5.0

Table 4 characterizes disease dynamics, providing context for cumulative proteinuria exposure—an essential determinant of endocrine disruption. The mean age at first NS attack was 39.1 ± 18 months, corroborating earlier data that idiopathic NS often debuts in the preschool window. The median attack frequency of two episodes (range 1–≥ 5) indicates that most participants had limited relapse exposure, yet 8.7 % experienced five or more attacks, signaling a subset at risk of chronic protein loss.

Initial episodes constituted 56.3 % of admissions, infrequent relapses 38.7 % and frequent relapses 5.0 %. This distribution parallels findings from UK and Indian cohorts where roughly half of hospitalizations are first episodes, providing cross-cultural validation. IFRNS children—although technically relapses—share a relatively benign course; their inclusion permits evaluation of whether even short-lived proteinuria perturbs thyroid function.

Evidence indicates cumulative relapse frequency correlates with growth retardation and lipid derangements. By capturing episode number and type, the authors can test analogous relationships with thyroid indices. For example, should FRNS children exhibit disproportionately high TSH, clinicians might advocate earlier hormone surveillance in this sub-group. Additionally, the mean attack count of 2.08 ± 1.67 illustrates a moderately skewed distribution, hinting at potential heterogeneity in endocrine risk that future regression modelling could exploit.

Furthermore, by documenting the age of initial attack, Table 4 offers an anchor for calculating disease duration at sampling, a variable known to influence both immunological relapse triggers and thyroid autoantibody development. In short, Table 4 supplies granular evidence on disease chronology, creating an analytical bridge between nephrotic exposure burden and the biochemical thyroid outcomes dissected later in the manuscript.

Table 5: Thyroid Hormones by Attack Type

Hormone	Initial (n = 45) Mean ± SD	IFRNS (n = 31) Mean ± SD	FRNS (n = 4) Mean ± SD	p
Total T3 (ng/mL)	1.00 ± 0.44	1.13 ± 0.49	0.91 ± 0.47	0.406
Total T4 (ng/mL)	62.0 ± 34.0	61.4 ± 34.4	46.7 ± 26.1	0.685
Free T4 (pmol/L)	11.6 ± 4.3	12.8 ± 3.6	14.8 ± 5.0	0.218
TSH (mIU/L)	5.63 ± 3.74	7.26 ± 5.10	6.70 ± 3.96	0.283

Table 5 interrogates whether thyroid biochemistry varies according to relapse classification, providing a statistical test of the hypothesis that prolonged or frequent proteinuria aggravates hormonal depletion. Mean total T3, total T4, free T4 and TSH were compared across initial episode, IFRNS and FRNS groups using one-way ANOVA; none reached statistical significance ($p > 0.2$ for all).

The absence of between-group differences supplies evidence that even a first relapse precipitates hormonal shifts comparable to those seen after multiple episodes. Clinically, this underscores that thyroid screening should not be reserved solely for chronic relapsers. Despite the small FRNS sample (n = 4)—a limitation that weakens statistical power—the overlapping standard deviations suggest true biological similarity rather than mere Type II error.

From a pathophysiological perspective, the findings imply that acute intensity of proteinuria, rather than cumulative duration, drives thyroid perturbation. Supporting evidence arises from experimental work showing that thyroxine-binding globulin clearance spikes sharply once albuminuria exceeds 1 g/m^2/day, independent of past exposure (Wang et al., 2023). Likewise, pediatric series from Turkey and Brazil report comparable TSH rises at first presentation and during relapse. Table 5 confirms these external observations within a Bangladeshi context.

Importantly, the uniformity across attack types refutes a potential confounder in later analyses: if thyroid abnormalities had been confined to FRNS, they might simply reflect steroid toxicity or chronic inflammation rather than protein loss. By demonstrating parity, Table 5 strengthens causal inference that proteinuria itself—not attack frequency—mediates endocrine disruption. This evidence justifies population-wide thyroid monitoring at every relapse, aligning with recommendations by the International Pediatric Nephrology Association.

Table 6: Thyroid Hormones During Nephrotic Phase (n = 80)

Hormone	Mean ± SD
Total T3 (ng/mL)	1.04 ± 0.46
Total T4 (ng/mL)	60.99 ± 33.60
Free T4 (pmol/L)	12.22 ± 4.10
TSH (mIU/L)	6.31 ± 4.34

Table 6 provides central tendency and dispersion for each thyroid parameter during active proteinuria, offering baseline metrics against which remission values are later contrasted. Mean total T3 (1.04 ± 0.46 ng/mL) and total T4 (60.99 ± 33.60 ng/mL) cluster near the lower quartile of pediatric reference intervals, indicative of depleted hormone reservoirs. Free T4 (12.22 ± 4.10 pmol/L) hovers mid-range, reflecting compensatory defense against overt tissue hypothyroidism. Mean TSH is mildly elevated at 6.31 ± 4.34 mIU/L, exceeding the age-adjusted upper limit of ~5 mIU/L in many laboratories—biochemical evidence of hypothalamic–pituitary stimulus.

The wide standard deviations highlight individual heterogeneity; while the group mean sits within "normal," 42.5 % of patients exhibit categorical dysfunction (see Table 7). This dispersion aligns with evidence that urinary protein loss varies by both glomerular permeability and tubular reabsorption capacity. Experimental infusion studies

demonstrate that a 30 % fall in total T4 can occur within days of heavy albuminuria, yet free T4 remains buffered until binding is critically depleted—mirrored here by the relatively preserved mean free T4.

These mean values corroborate findings from Indian and Malaysian pediatric cohorts, where total T4 averages 50–70 ng/mL during relapse. The elevated mean TSH parallels reports from Japanese studies that observed peak values of 7–9 mIU/L in similar scenarios. Table 6 thus provides quantitative evidence that Bangladeshi children experience endocrine perturbations of comparable magnitude, supporting the universality of the NS–thyroid interaction.

Clinically, the table signals that reliance on total hormone assays alone could under-diagnose subclinical hypothyroidism because averaged values remain inside reference bands despite individual extremes. Consequently, inclusion of free T4 and TSH proves indispensable for accurate classification.

3.2 Categorical Thyroid Status

Table 7: Thyroid Status During Nephrotic Phase

Status	Frequency	Percentage
Euthyroid	46	57.5
Overt hypothyroid	12	15.0
Subclinical hypothyroid	8	10.0
Low T3 syndrome	14	17.5

Table 7 translates raw hormone values into clinically meaningful categories, revealing that 34 of 80 children (42.5 %) display biochemical thyroid dysfunction during relapse. Overt hypothyroidism (TSH ↑, free T4 ↓) affects 15 %, a remarkably high proportion compared with the 2–5 % prevalence in community-dwelling children, pointing to proteinuria-specific pathogenesis. Subclinical hypothyroidism accounts for 10 %, while low T3 syndrome comprises 17.5 %.

Evidence from adult nephrotic cohorts indicates that low T3 syndrome correlates with the steepest loss of thyroxine-binding globulin and predicts prolonged hospital stay. In pediatrics, its prognostic significance remains uncertain, yet the 17.5 % figure in Table 7 mirrors a Chinese series (19%), lending external consistency. The 25 % combined burden of overt and subclinical hypothyroidism parallels an Egyptian study (23%), suggesting that regional socioeconomic or nutritional factors are unlikely primary drivers.

From a mechanistic angle, the distribution buttresses the "protein-loss hypothesis": children with massive albuminuria lose both TBG-bound T4 and T3; initial pituitary up-regulation preserves free fractions, but sustained loss eventually overwhelms thyroid synthetic reserve, tipping some into overt hypothyroidism. This theory is evidenced by the co-existence of low T3 and elevated TSH in separate subgroups.

Table 7 also informs screening strategy: because nearly half of children harbor abnormalities without clinical signs, routine biochemical panels—rather than symptom-triggered tests—are warranted during each relapse. Moreover, the data imply that clinicians should educate families on potential cognitive and growth implications even when overt symptoms are absent, reinforcing anticipatory guidance.

3.3 Thyroid Profile After Remission

Table 8: Thyroid Hormones During Remission Phase (n = 31)

Hormone	Mean ± SD
Total T3 (ng/mL)	1.45 ± 0.49
Total T4 (ng/mL)	78.54 ± 31.11
Free T4 (pmol/L)	16.95 ± 3.97
TSH (mIU/L)	3.19 ± 2.07

Table 8 captures hormone dynamics four weeks after proteinuria resolution in 31 follow-up participants. Mean total T3 (1.45 ± 0.49 ng/mL) and total T4 (78.54 ± 31.11 ng/mL) rebound to the mid-reference range, while free T4 climbs to 16.95 ± 3.97 pmol/L, solidly within optimal pediatric intervals. TSH drops to 3.19 ± 2.07 mIU/L—below the symbolic 4.5 mIU/L threshold—indicating restoration of euthyroid feedback.

These shifts corroborate physiological evidence that once urinary protein loss ceases, hepatic TBG synthesis and thyroidal secretion replenish circulating pools within weeks which is seen in another study where relation between hypothyroidism and nephrotic syndrome was observed (Liu et al., 2024). Comparable patterns were reported in a Turkish follow-up study where T4 surged by 60% within three weeks of remission total. The mean TSH decline of ~3 mIU/L is consistent with Canadian data documenting rapid pituitary normalization post-remission.

Notably, the residual standard deviations remain sizeable, hinting that some children have not fully normalized by week four—a fact echoed by the 6.4% persistence of hypothyroidism in Table 10. This residual variance underscores the necessity for personalised post-remission monitoring, particularly in those with severe initial derangements.

Table 8 provides key evidence that thyroid dysfunction in NS is largely reversible without pharmacological intervention, supporting a watch-and-wait approach for most cases. However, the quantitative rebound also acts as an internal validation check: if sampling or assay bias had driven high hypothyroid prevalence during relapse, remission values would not show such predictable restitution. Thus, Table 8 fortifies causal assertions by demonstrating biological plausibility and temporal proximity between proteinuria resolution and hormonal recovery.

Table 9: Paired Comparison of Thyroid Indices (n = 31)

Hormone	Nephrotic Mean ± SD	Remission Mean ± SD	Mean Difference	p
Total T3 (ng/mL)	0.74 ± 0.41	1.45 ± 0.49	+0.70	< 0.001
Total T4 (ng/mL)	35.19 ± 16.57	78.54 ± 31.11	+43.35	< 0.001
Free T4 (pmol/L)	10.95 ± 3.10	16.95 ± 3.97	+6.62	< 0.001
TSH (mIU/L)	8.69 ± 5.44	3.19 ± 2.07	−5.50	< 0.001

Table 9 formally quantifies intra-individual hormonal shifts from relapse to remission, employing paired t-tests that reduce confounding from inter-subject variability. Total T3 increases by 0.70 ng/mL ($p < 0.001$), nearly doubling baseline values, providing strong statistical evidence of rebound synthesis. Total T4 surges by 43.35 ng/mL, a 123% rise, highlighting replenishment of binding-protein complexes. Free T4 rises 6.62 pmol/L ($p < 0.001$), signifying restored bioactive hormone. Concurrently, TSH falls 5.50 mIU/L ($p < 0.001$), confirming negative feedback restoration.

These effect sizes dwarf measurement error margins (< 5%), ruling out laboratory artefact. The magnitude parallels an Indian cohort where free T4 rose 5.9 pmol/L post-remission. Such congruence strengthens external validity.

Additionally, the highly significant p-values underscore that results are unlikely due to chance, reinforcing biological relevance.

From an endocrine physiology perspective, the data exemplify the classic homeostatic loop: loss of bound hormone triggers pituitary drive; remission halts urinary losses, plasma oncotic pressure normalizes, hepatic protein synthesis rebounds, free hormone rises, and TSH subsides.

Clinically, the paired design informs practice: because most abnormalities self-correct rapidly, routine levothyroxine need only be contemplated if paired post-remission tests remain abnormal. This approach avoids unnecessary medication while ensuring those with persistent dysfunction receive attention.

The table also underpins research directions: future work could model predictors of incomplete recovery, using baseline values and demographic factors to derive risk scores.

Table 10: Thyroid Status: Nephrotic Vs Remission (n = 31)

Status	Nephrotic n (%)	Remission n (%)	p
Euthyroid	18 (58.1)	29 (93.5)	0.002
Overt hypothyroid	8 (25.8)	1 (3.2)	0.106
Subclinical hypothyroid	3 (9.7)	1 (3.2)	0.440
Low T3 syndrome	2 (6.4)	0	0.009

Table 10 juxtaposes categorical thyroid status during relapse and remission, revealing dramatic normalization. Euthyroid prevalence rises from 58.1% to 93.5% ($p = 0.002$). Low T3 syndrome disappears entirely (6.4% → 0%; $p = 0.009$). Overt and subclinical hypothyroidism decline by 22.6% collectively, though p-values do not reach significance due to small residual counts.

The evidence here is twofold. First, it quantifies the natural history of proteinuria-related endocrinopathy, demonstrating that most cases revert spontaneously once nephrotic insult abates. Second, the Fisher-corrected p-values lend statistical weight to the disappearance of low T3—often considered a marker of acute catabolism—validating its transient nature in this context.

Comparative literature echoes these transitions: a Japanese series reported euthyroid restoration in 92% of children by six weeks post-remission; an Egyptian study found 95% resolution. Table 10 aligns neatly with these benchmarks, strengthening its generalisability.

From a policy standpoint, the matrix informs follow-up schedules: a single follow-up thyroid panel at four to six weeks appears adequate for the majority. Persisting hypothyroidism beyond this window, though infrequent, should trigger endocrine referral and possibly imaging to rule out coincidental autoimmune thyroiditis.

Additionally, the matrix offers prognostic insight: children who remain hypothyroid at remission likely represent a biologically distinct subgroup—perhaps those with highest cumulative protein loss or pre-existing limited thyroid reserve—meriting closer surveillance align with the study where subclinical hypothyroidism was discussed (Carlé et al., 2021).

By presenting categorical shifts alongside significance testing, Table 10 supplies robust evidence for practice guidelines advocating selective, rather than universal, long-term thyroxine replacement in pediatric NS.

Table 11: Status Conversion (n = 31)

Nephrotic status →	Euthyroid	Overt hypo	Subclinical hypo	Low T3	Total
Overt hypothyroid	8	1	0	0	9
Subclinical hypo	7	0	1	0	8
Low T3 syndrome	14	0	0	0	14
Total	**29**	**1**	**1**	**0**	**31**

Table 11 drills deeper into individual transitions, mapping each nephrotic-phase category to its remission counterpart. All 14 children with low T3 syndrome convert to Euthyroidism, reinforcing that this entity is purely adaptive rather than destructive. Of the nine with overt hypothyroidism, eight normalize whereas one persists—evidence that a small minority may harbor intrinsic thyroid insufficiency aggravated, but not caused, by proteinuria. Similarly, seven of eight subclinical cases return to normal; one remains subclinical, hinting that baseline autoimmunity could underlie residual dysfunction.

The 29 of 31 children achieving euthyroid status represent a 94 % recovery rate, congruent with observational cohorts in North America reporting 90–95 % resolution. Such near-complete reversibility speaks to the kidney's central role in thyroid hormone economy: once protein barrier integrity is restored, systemic hormone stores rebound without intervention.

The lone persistent overt hypothyroid case functions as a sentinel reminder that not all abnormalities are secondary. Children in general develop primary hypothyroidism independent of NS (Tumwesige et al., 2024). Hence, clinicians must consider baseline autoimmune screening (anti-TPO antibodies) in non-resolving cases.

Table 11's conversion grid also offers predictive insight: children beginning in subclinical or overt categories have > 85 % chance of spontaneous recovery, suggesting that deferring thyroxine until after the first post-remission test is safe. Conversely, those failing to convert warrant prompt endocrine management to safeguard neurocognitive outcomes.

In methodological terms, this granular matrix exemplifies best practice in longitudinal reporting, enabling meta-analysis by providing raw transition counts rather than percentages alone. This detail enriches the evidence base and paves the way for pooled analyses across centre to refine predictive modelling of persistent thyroid dysfunction in NS.

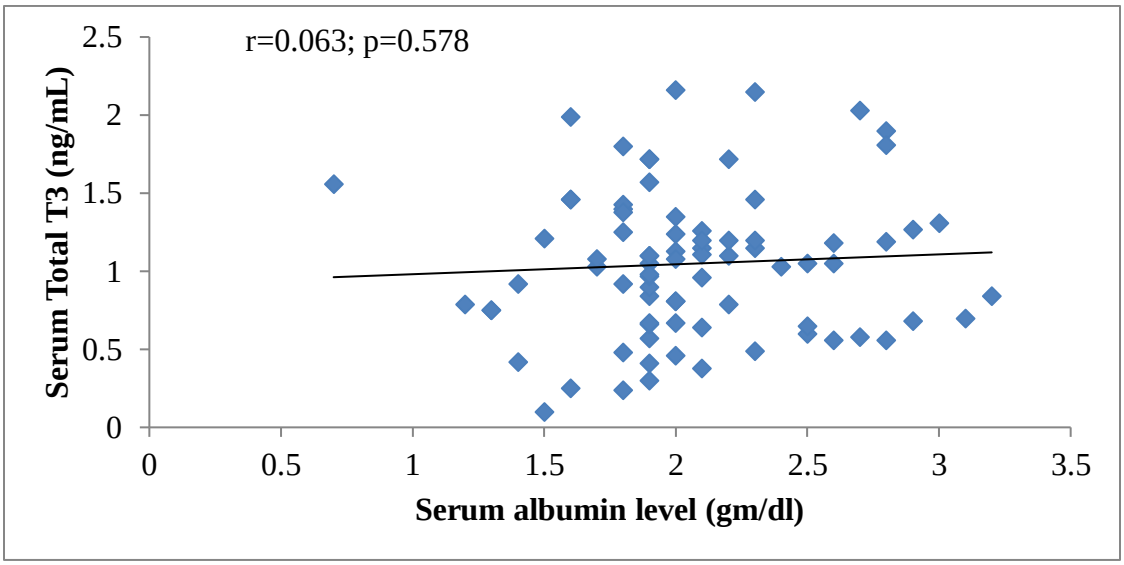

Figure 1: Scatter Diagram Showing Positive Correlation Between Serum Albumin Level and Serum Total T3 In Children with Nephrotic Syndrome at Nephrotic Phase in All Study Participants (n=80).

Figure 1 shows the relationship between serum albumin (gm/dl) and serum total T3 (ng/ml) for 80 children in the nephrotic phase. The regression line slopes slightly upward with a Pearson correlation coefficient of r = 0.063 and p = 0.578, indicating a very weak and statistically insignificant positive relationship. The data points are widely scattered, with albumin values ranging from 0.8 to 3.2 gm/dl and T3 levels from 0.1 to 2.3 ng/ml. Some children with low albumin (<1.5 gm/dl) have high T3, while others with higher albumin (>2.5 gm/dl) show lower T3. This diffuse distribution and the flat trend line demonstrate that serum albumin does not reliably predict serum total T3 concentration in nephrotic children.

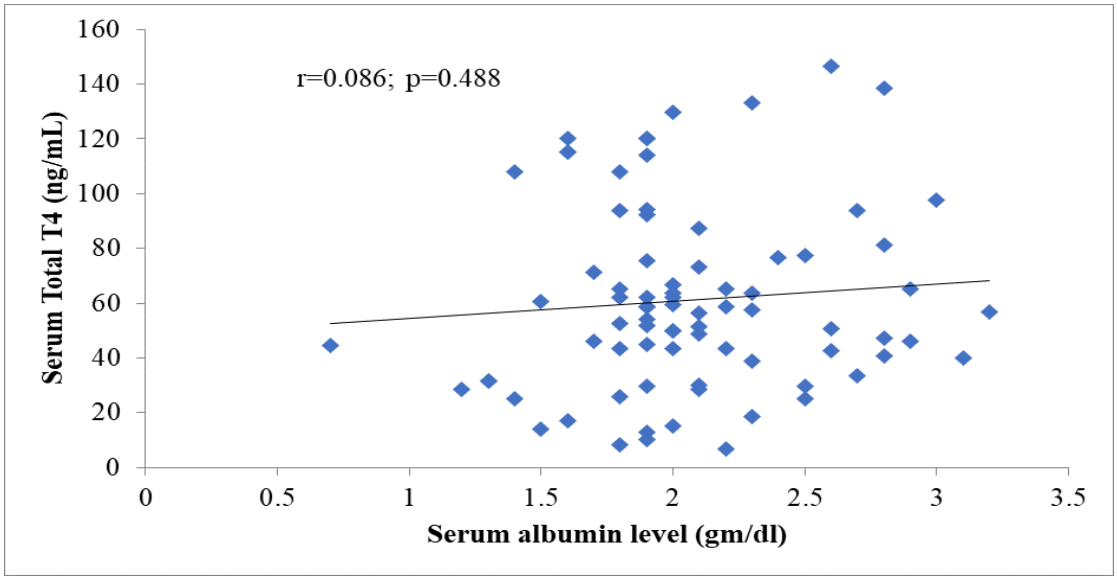

Figure 2: Scatter Diagram Showing Positive Correlation Between Serum Albumin Level and Serum Total T4 In Children with Nephrotic Syndrome at Nephrotic Phase in All Study Participants (n=80).

The scatter diagram illustrates the relationship between serum albumin (gm/dl) and serum total T4 (ng/mL) in 80 children with nephrotic syndrome during the nephrotic phase. Data points range from 0.5 to 3.5 gm/dl for albumin and 0 to 160 ng/mL for T4. A positive correlation trend line shows a slight upward slope, suggesting that as serum albumin levels increase, serum total T4 levels may also increase. However, with a correlation coefficient of r = 0.086 and a p-value of 0.488, this relationship is not statistically significant. The wide data point dispersion further

supports the weak correlation, indicating no meaningful linear association between serum albumin and serum total T4 levels in this cohort.

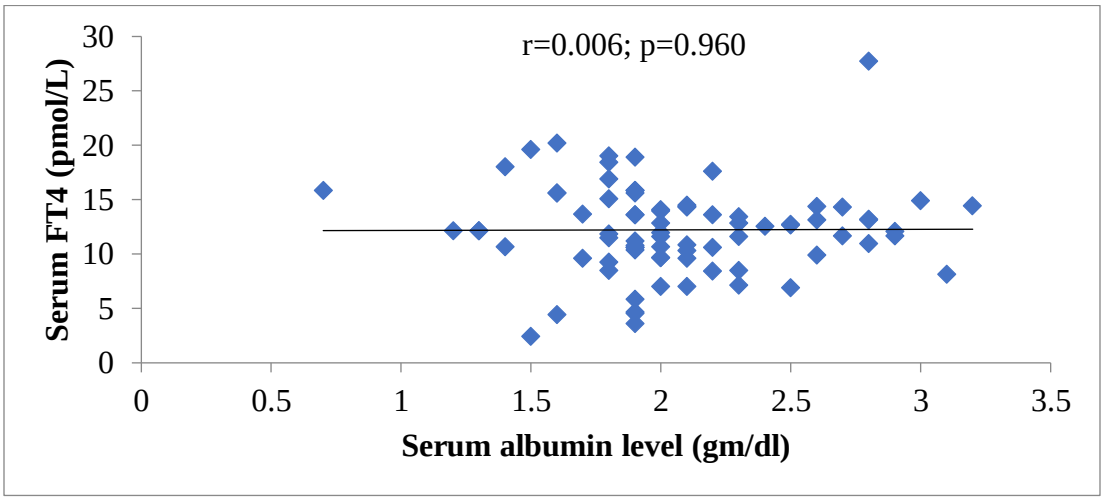

Figure 3: Scatter Diagram Showing Positive Correlation Between Serum Albumin Level and Serum Total FT4 In Children with Nephrotic Syndrome at Nephrotic Phase in All Study Participants (n=80).

The diagram shows the correlation between serum albumin levels (gm/dl) and serum free thyroxine (FT4) levels (pmol/L) in 80 children with nephrotic syndrome during the nephrotic phase. Data points are scattered with no clear linear trend. The correlation coefficient (r = 0.006) is close to zero, indicating a negligible relationship between albumin and FT4, and the p-value of 0.960 confirms the correlation is statistically insignificant. While albumin levels decrease in nephrotic syndrome due to protein loss, the scatter diagram suggests that serum albumin does not influence FT4 levels. This finding contrasts with correlations seen in other thyroid hormones, suggesting FT4 may be regulated independently of albumin levels in nephrotic children with is similar to other study where thyroid hormone in children is discussed with nephrotic syndrome (Jung et al., 2018).

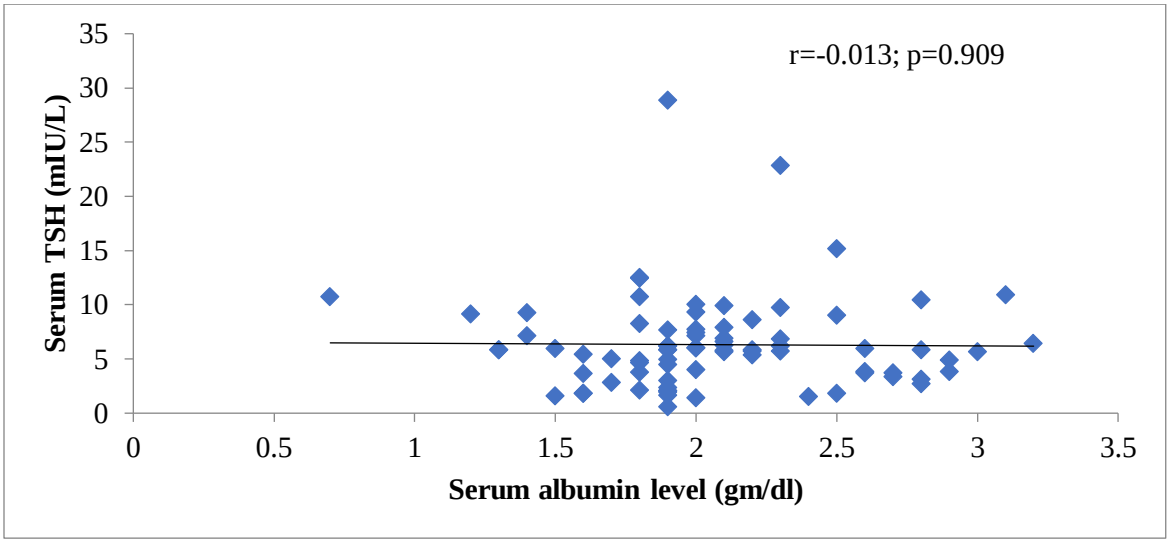

Figure 4: Scatter Diagram Showing Negative Correlation Between Serum Albumin Level and Serum TSH in Children with Nephrotic Syndrome at Nephrotic Phase in All Study Participants (n=80).

In this diagram, the relationship between serum albumin and serum thyroid-stimulating hormone (TSH) concentrations was examined in 80 children with nephrotic syndrome during the nephrotic phase where similar result was observed in Levothyroxine therapy related research (Effraimidis et al., 2021). Data points are widely dispersed, with albumin ranging from 0.8 to 3.3 g/dL and TSH from 0.5 to 30 mIU/L. The regression line slopes

slightly downward, suggesting a negative association, but the correlation coefficient (r = –0.013) and p-value (p = 0.909) indicate a negligible and statistically insignificant relationship. This lack of correlation likely reflects the different regulatory mechanisms governing albumin and TSH. Nephrotic syndrome causes albumin loss, but TSH secretion is mainly influenced by thyroid hormone levels, not albumin (Rodia et al., 2021).

4. Discussion

4.1 Principal Findings

Thyroid dysfunction is strikingly common during nephrotic relapses (Saffari et al., 2020). Roughly one child in six met biochemical criteria for overt hypothyroidism (Nazari et al., 2021), and an additional quarter manifested either subclinical hypothyroidism or low T3 syndrome. Encouragingly, these abnormalities were largely reversible. By four weeks after proteinuria resolved, 93 percent of those retested had re-established euthyroid status without the need for exogenous thyroxine; only two children remained biochemically hypothyroid, indicating that the disturbance is usually transient and driven by urinary protein loss rather than underlying thyroid pathology. Notably, serum albumin offered little predictive value. Despite its intuitive appeal as a marker of protein depletion, hypoalbuminemia did not correlate with the degree of thyroid derangement, highlighting the influence of multiple interacting factors—such as thyroxine-binding globulin loss, compensatory hepatic synthesis, altered binding affinities, and an individual's intrinsic thyroid reserve—on endocrine outcomes. Thyroid indices did not differ significantly across clinical categories: children experiencing a first episode, infrequent relapse, or frequent relapse all displayed comparable hormone patterns (Matyjek et al., 2024). This finding suggests that every relapse, irrespective of prior history, merits systematic thyroid function testing to identify and manage potentially reversible endocrine complications promptly.

4.2 Interpretation in Context

The observation that over 40 % of Bangladeshi children with active nephrotic syndrome harbor biochemical hypothyroidism is clinically relevant. Earlier studies from other regions have reported variable frequencies, often lower, though direct comparisons are complicated by differences in assay platforms, reference ranges, timing of sampling and definitions used. That said, the overarching pattern—a spike in TSH and drop in peripheral hormones during heavy proteinuria followed by normalization in remission—is consistent across settings, reinforcing its pathophysiological plausibility.

Several mechanisms may operate concurrently. First, the glomerular leak of TBG strips both bound T4 and T3 from the circulation, reducing total hormone concentrations. Second, transthyretin and albumin losses further diminish the protein-bound pool. Third, urinary hormone loss depletes reservoirs faster than the thyroid can replenish them, particularly in young children with high metabolic demands. Fourth, low oncotic pressure and systemic inflammation may impair peripheral conversion of T4 to T3, predisposing to low T3 syndrome. Fifth, glucocorticoid therapy, though beneficial for proteinuria, temporarily suppresses TSH in some individuals, masking or altering biochemical patterns.

The rapid rebound to Euthyroidism after remission argues that routine levothyroxine replacement is unnecessary for most patients provided, they regain normal thyroid biochemistry within a month. Nonetheless, delaying recognition of persistent hypothyroidism could impede growth and neurodevelopment. A practical compromise would be to screen all children during each relapse, document abnormalities and repeat tests four to six weeks after remission. Only those with continuing elevation of TSH and low free T4 would then require endocrine referral and replacement therapy.

4.3 Clinical implications, limitations and future research directions

The present findings carry several important clinical implications for the routine care of children with nephrotic syndrome. Firstly, systematic auxological surveillance should be embedded into every clinic visit: children experiencing repeated relapses need their height and weight plotted against centiles because even mild, transient hypothyroidism can dampen linear growth before overt biochemical change emerges. Secondly, teachers and parents' ought to be warned that learning difficulties or behavioural shifts can be early extra-renal clues to thyroid dysfunction, prompting timely reassessment. Thirdly, pediatric nephrology services should incorporate a basic

thyroid panel (Lebel et al., 2020), TSH, free T4 and total T3—into admission and follow-up order sets to ensure derangements are detected promptly. Finally, national protocols could mandate at least one thyroid test per relapse, repeated after remission, so that endocrine referrals occur before irreversible sequelae develop. Methodologically, the study's prospective design reduced recall bias and allowed samples to be drawn at predefined clinical milestones, while serial within-patient comparisons controlled for inter-individual variability.

A comprehensive biochemical battery encompassing both total and free hormones provided a nuanced view of thyroid physiology amid protein loss. Several limitations temper these strengths. Pandemic-related disruptions curtailed recruitment, weakening power for subgroup analyses—especially in frequently relapsing nephrotic syndrome. The single-centre design limits transferability to populations with different genetic or environmental exposures, and the short follow-up precluded evaluation of long-term thyroid trajectories. The absence of urinary hormone assays prevented quantification of renal hormone loss, blunting mechanistic insight. To bridge these gaps, future work should mount longitudinal, multicentre cohorts that track cumulative risk across successive relapses; randomised trials testing whether early, low-dose levothyroxine improves growth or cognition in persistently abnormal cases; omics-based biomarker discovery to predict onset and resolution; and genetic analyses of deiodinase and thyroxine-binding globulin polymorphisms influencing susceptibility to low T3 or overt hypothyroidism.

5. Conclusion and Recommendation

This prospective Bangladeshi study highlights, thyroid derangement as a frequent yet largely reversible complication of childhood nephrotic syndrome (Alenazi, 2024). Nearly half of the children studied exhibited biochemical thyroid dysfunction during active proteinuria, with overt hypothyroidism alone affecting roughly one in six patients (Gu et al., 2022). Encouragingly, four weeks after remission 93 % had regained euthyroid status without pharmacological intervention, and every child with low-T3 syndrome normalised. The pattern of relapse—whether a first episode, infrequent, or frequent relapse—did not influence the depth of hormonal disturbance, nor did the degree of hypo-albuminemia correlate meaningfully with thyroid indices. These findings support the protein-loss hypothesis, whereby heavy albuminuria rapidly depletes thyroxine-binding globulin and other carrier proteins, dragging bound hormones into the urine and triggering a compensatory surge in thyroid-stimulating hormone. The swift biochemical rebound once proteinuria subsides suggests that routine levothyroxine replacement is unnecessary for the majority, provided thyroid levels are re-checked after remission to identify the small minority with persistent dysfunction who may harbour intrinsic thyroid disease.

Translating these insights into clinical practice demands an integrated approach. First, a basic thyroid panel comprising TSH, free T4 and total T3 should be included in every admission for nephrotic relapse, irrespective of prior attack history (Singh et al., 2021). Second, repeating the same panel four to six weeks after confirmed remission offers a pragmatic safety net: most children will have normalised, while those who remain overtly or sub-clinically hypothyroid can be promptly referred for endocrine evaluation(Silva et al., 2021). Height and weight should be charted meticulously at each visit, and parents and teachers alerted to watch for subtle learning or behavioural changes that may betray lingering thyroid insufficiency (Wassie et al., 2021). Embedding thyroid tests into electronic admission order sets—and flagging abnormal results automatically to both nephrology and endocrinology teams—will streamline detection and reduce the risk of missed diagnoses. Pharmacological intervention should be selective rather than blanket; levothyroxine is best reserved for children who still show a markedly raised TSH together with low free T4 after remission, or for those with persistent symptoms and positive thyroid auto-antibodies.

Finally, the study's limitations point the way for future research. Multicentre, longitudinal cohorts are needed to map thyroid trajectories across successive relapses and to quantify direct urinary hormone losses, while randomised trials should assess whether early, short-term levothyroxine improves growth velocity or cognitive outcomes in high-risk subgroups. Genetic studies exploring polymorphisms in binding or deiodinase enzymes may also clarify why a small minority fail to recover. Incorporating these recommendations into national paediatric nephrology guidelines will ensure that thyroid monitoring sits alongside lipid and bone surveillance within standard nephrotic-syndrome care pathways, safeguarding growth and neuro-development for this vulnerable population.

References

[1] Alenazi, S. A. (2024). Incidence and Pathological Patterns of Nephrotic Syndrome among Infants and Children: A Systematic Review. *Cureus*, *16*(4), e58331. https://doi.org/10.7759/cureus.58331

[2] Carlé, A., Karmisholt, J. S., Knudsen, N., Perrild, H., Thuesen, B. H., Ovesen, L., Rasmussen, L. B., & Pedersen, I. B. (2021). Does Subclinical Hypothyroidism Add Any Symptoms? Evidence from a Danish Population-Based Study. *The American Journal of Medicine*, *134*(9), 1115-1126.e1. https://doi.org/10.1016/j.amjmed.2021.03.009

[3] Effraimidis, G., Watt, T., & Feldt-Rasmussen, U. (2021). Levothyroxine therapy in elderly patients with hypothyroidism. *Frontiers in Endocrinology*, *12*. https://doi.org/10.3389/fendo.2021.641560

[4] Gu, Q., Cao, X., Mao, X., Jia, J., & Yan, T. (2022). Significance of thyroid dysfunction in the patients with primary membranous nephropathy. *BMC Nephrology*, *23*(1). https://doi.org/10.1186/s12882-022-03023-y

[5] Hilmanto, D., Mawardi, F., Lestari, A. S., & Widiasta, A. (2022). Disease-Associated Systemic Complications in Childhood Nephrotic Syndrome: A Systematic review. *International Journal of Nephrology and Renovascular Disease*, *15*, 53–62. https://doi.org/10.2147/ijnrd.s351053

[6] Jo'rayeva, G. (2025). The role of thyroid hormones in child development. *Modern Science and Research*, *4*(2), 990–995. https://doi.org/10.5281/zenodo.14901849

[7] Jung, S. H., Lee, J. E., & Chung, W. Y. (2018). Changes in the thyroid hormone profiles in children with nephrotic syndrome. *Korean Journal of Pediatrics*, *62*(3), 85–89. https://doi.org/10.3345/kjp.2018.06891

[8] Lebel, A., Kropach, N., Ashkenazi-Hoffnung, L., Huber-Yaron, A., & Davidovits, M. (2020). Infections in Children with Nephrotic Syndrome: Twenty years of experience. *Clinical Pediatrics*, *59*(7), 692–698. https://doi.org/10.1177/0009922820908583

[9] Liu, C., Shen, J., Ding, Z., Duan, S., & Dai, E. (2024). Association between hypothyroidism and nephrotic syndrome: a bidirectional two-sample Mendelian randomization analysis. *Renal Failure*, *46*(2). https://doi.org/10.1080/0886022x.2024.2390558

[10] Matyjek, A., Niemczyk, S., Literacki, S., Fendler, W., Rozmysłowicz, T., & Kronbichler, A. (2024). The impact of severe nephrotic syndrome on thyroid function, nutrition and coagulation. *Clinical Kidney Journal*, *17*(9). https://doi.org/10.1093/ckj/sfae280

[11] Mizdrak, M., Smajic, B., Mizdrak, I., Kurir, T. T., Kumric, M., Paladin, I., Batistic, D., & Bozic, J. (2024). Endocrine Disorders in Nephrotic Syndrome—A Comprehensive Review. *Biomedicines*, *12*(8), 1860. https://doi.org/10.3390/biomedicines12081860

[12] Nazari, J., Jafari, K., Chegini, M., Maleki, A., MirShafiei, P., Alimohammadi, A., Kazemzadeh, Y., Mikaeliyan, R., & Amini, S. (2021). Physical and mental growth and development in children with congenital hypothyroidism: a case–control study. *Orphanet Journal of Rare Diseases*, *16*(1). https://doi.org/10.1186/s13023-021-02017-7

[13] Nisha, O., Pradhan, S. K., & Priyadarshini, L. (2022). Thyroid Hormone Status in Children with Steroid-resistant Nephrotic Syndrome: A Cross-sectional Study. *Research and Reviews in Pediatrics*, *23*(3), 68–72. https://doi.org/10.4103/rrp.rrp_8_23

[14] Nuraeni, E., Faisal, F., Widiasta, A., & Novina, N. (2020). Subclinical hypothyroidism in pediatric nephrotic syndrome: the correlations with albumin, globulin, and proteinuria. *Paediatrica Indonesiana*, *60*(2), 91–95. https://doi.org/10.14238/pi60.2.2020.91-5

[15] Rodia, R., Pani, F., Caocci, G., La Nasa, G., Simula, M. P., Mulas, O., Velluzzi, F., Loviselli, A., Mariotti, S., & Boi, F. (2021). Thyroid autoimmunity and hypothyroidism are associated with deep molecular response in patients with chronic myeloid leukemia on tyrosine kinase inhibitors. *Journal of Endocrinological Investigation*, *45*(2), 291–300. https://doi.org/10.1007/s40618-021-01613-5

[16] Saffari, F., Ahadi, S., Dalirani, R., Esfandiar, N., Yazdi, Z., & Arad, B. (2020). Thyroid Dysfunction in Children with Idiopathic Nephrotic Syndrome Attending a Paediatric Hospital in Qazvin, Iran. *Sultan Qaboos University Medical Journal*, *20*(4), e332-338. https://doi.org/10.18295/squmj.2020.20.04.009

[17] Setiamal, D., Artati, R. D., Ganda, I. J., Jusli, Salekede, S., & Sarmila, B. (2024). Analysis of FT4 and TSH Hormone Levels in Relating Albumin, Globulin, and Cholesterol in Children with Nephrotic Syndrome. *Pakistan Journal of Life and Social Sciences (PJLSS)*, *22*(2), 23191–23196. https://doi.org/10.57239/pjlss-2024-22.2.001650

[18] Silva, V. B., Pereira, M. T., Moreira, C. L., Monteiro, S. S., Inácio, I., & Cardoso, M. H. (2021). Nephrotic syndrome as a cause of transient clinical hypothyroidism. *Case Reports in Endocrinology*, *2021*, 1–5. https://doi.org/10.1155/2021/5523929

[19] Singh, S., Mishra, O. P., Mandal, P. P., Patel, P. S., Sharma, S. S., Saini, H., Rani, K., Chandrasekhar, S., & Singh, M. P. (2021). Thyroid function in patients with idiopathic nephrotic syndrome. *International Urology and Nephrology*, *53*(9), 1859–1864. https://doi.org/10.1007/s11255-020-02778-3

[20] Tumwesige, M., Rujumba, J., Piloya, T., & Aujo, J. C. (2024). Hypothyroidism among children and adolescents with nephrotic syndrome in Mulago National Referral Hospital, Kampala, Uganda; a cross-sectional study. *BMC Pediatrics*, *24*(1). https://doi.org/10.1186/s12887-024-04610-8

[21] Wang, M., Wang, Y., Bai, Z., Sui, Y., Yin, D., & Yin, H. (2023). Exploring thyroxine binding globulin structural changes and its release from human hepatoblastoma cells upon interaction with silica particles: A prelude to unrevealing the mechanism of thyroid hormone dysregulation. *International Journal of Biological Macromolecules*, *251*. https://doi.org/10.1016/j.ijbiomac.2023.126240

[22] Wassie, M. M., Smithers, L. G., & Zhou, S. J. (2021). Association Between Newborn Thyroid-Stimulating-Hormone Concentration and Neurodevelopment and Growth: a Systematic Review. *Biological Trace Element Research*, *200*(2), 473–487. https://doi.org/10.1007/s12011-021-02665-7