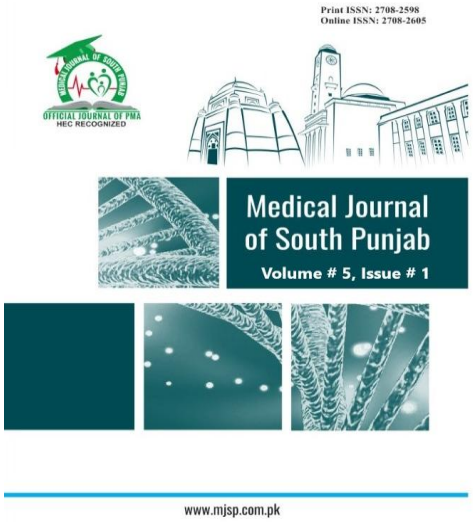
ISSN (E): 2708-2601
ISSN (P): 2708-2598

Medical Journal of South Punjab
Article DOI:10.61581/MJSP.VOL05/02/14
Volume 5, Issue 2, 2024



Hypothyroidism among children and adolescents with nephrotic syndrome

Publication History

Received: Jan, 28, 2024 Revised: May 13, 2024
Accepted: June 01, 2024 Published: June 30, 2024

Authors and Affiliation:

Kamran Ali[1], Abdul Samad[2], Salauddin Ali Khan[3]
[1]Khairpur Medical college and Teaching hospital (city branch) khairpur mirs, Pakistan,[2]Akhtar saeed trust Hospital Lahore, Pakistan
[3]AlphaMed Hospital Karachi, Pakistan
[*]**Corresponding Author Email**: ga.shahani@gmail.com

Conflict of Interest:

Author(s) declared no conflict of interest.

Acknowledgment:

No Funding received.

Citation: Ali K, Sama A , Khan SA. Hypothyroidism among children and adolescents with nephrotic syndrome. Medical Journal of South Punjab. 2024 June 30; 5(2):75-81.

Please scan me to access online.

An official publication of
Medteach Private Limited, Multan, Pakistan.
Email: farman@mjsp.com.pk, Website: https://mjsp.com.pk/index.php/mjsp

Medical Journal of South Punjab
Volume 5, Issue 2, 2024; pp: 75-81
Original Article

Hypothyroidism among children and adolescents with nephrotic syndrome

Kamran Ali[1], Abdul Samad[2], Salauddin Ali Khan[3]
[1]Khairpur Medical college and Teaching hospital (city branch) khairpur mirs, Pakistan,[2]Akhtar saeed trust Hospital Lahore, Pakistan
[3]AlphaMed Hospital Karachi, Pakistan
[*]**Corresponding Author Email**: ga.shahani@gmail.com

ABSTRACT

Objective: *to establish the prevalence of hypothyroidism and identify the factors associated with its occurrence among children and adolescents diagnosed with nephrotic syndrome (NS).*

Methods: *The study took place in the nephrology department of Khairpur Medical College and Teaching hospital (city branch) Khairpur Mirs Pakistan from February 2023 and January 2024. Data were collected through interviewer questions and patient information regarding their signs and symptoms of NS, other causes of hypothyroidism, and use of iodized salt and other study variables.*

Results: *Regarding proteinuria at the time of enrollment, 60.0% had nil or trace proteinuria, 27.5% had proteinuria levels of +1 to +2, and 12.5% had proteinuria levels ranging from +3 to +4. The mean estimated glomerular filtration rate (GFR) of the patients was 104.22 ± 19.62 mL/min/1.73m², with 30.0% showing a GFR of less than 90 mL/min/1.73m². The mean serum albumin level was 3.81 ± 2.07 g/dL, and 42.5% had serum albumin levels of ≤2.5 g/dL. Additionally, 27.5% were in remission at the time of enrollment.*

Conclusion: *The prevalence of hypothyroidism among children and adolescents with nephrotic syndrome (NS) is high. Hypoalbuminemia is a key factor associated with hypothyroidism in these patients. Children with NS and hypoalbuminemia should be screened for hypothyroidism, and clinicians should aim to maintain normal albumin levels.*

Keywords: *Hypothyroidism, Nephrotic syndrome, Hypoalbuminemia, Children, Adolescent*

1. INTRODUCTION

Nephrotic syndrome (NS) is the most frequent type of renal glomerular disease in a child. The prevalence for idiopathic NS in children varies within ethnic groups as well as geographic location[1]. The disease is characterized by severe initial proteinuria (≥40 mg/m²/hour with urine protein/creatinine ratio ≥200 mg/mL or 3+ on urine dipstick) to maintain massive urinary protein excretion, and less than normal circulating albumin levels, manifesting as edema. NS has been a known risk factor for hypothyroidism since its introduction in the 1950s, due not only to the process of disease but also treatment of NS[2,3].

It also results in significant protein loss into the urine, mostly through glomerular damage[4]. This also loses other proteins like thyroxine-binding globulin, albumin and thyroxine. Hence, the serum FT4 levels fall in response[5]. This triggers the production of TSH by the anterior pituitary gland. Proliferation in production of thyroid hormones by the thyroid gland because of TSH stimulation, could be continuously lost in urine secondary to chronic nephrotic state[6].

TBG and albumin are of particular prominence because as they conduct almost the entire thyroxine in serum, blood levels fall only after hypothyroidism has been present for a while[7]. This leads to loss of these proteins in the urine and as a consequence decreased serum levels of thyroid hormones in children with NS[8]. Prednisolone, a steroid used during treatment of NS, also suppresses release of TSH from the pituitary gland; this may lead to development of central hypothyroidism[9].

Thyroid hormones play a very important role in maintaining normal physiologic functions. Undetected and untreated overt hypothyroidism leads to abnormal growth in the pediatric and adolescent population in both physical and mental response[10].

This study aims to explore the prevalence of hypothyroidism among children and adolescents with nephrotic syndrome. By identifying the magnitude of thyroid dysfunction in this population, the study intends to provide local data that could inform clinical protocols, including whether routine screening for hypothyroidism should be integrated into the management of nephrotic syndrome in pediatric patients.

2. METHODOLOGY

The study took place in the nephrology department of Khairpur Medical College and Teaching hospital (city branch) Khairpur Mirs Pakistan from February 2023 and January 2024. Study was started after approval from hospital ethical board and consent from patients or their parents. All children and adolescents having age 1 to 20 years, diagnosed with disease of nephritic syndrome were included in the study. Sampling technique was non probability consecutive sampling. NS is established if at least two of the following, without consent, are present: edema; hypoalbuminemia ≤2.5 g/dL; and proteinuria ≥ + 3 or on dipstick. While treatment to these children and young adults is based on KDIGO criteria for NS, none of them has even one procedure nor any routine testing to check for hypothyroidism. On the other hand, all patients have growth management that is established in the hospital.

Data were collected through interviewer questions and patient information regarding their signs and symptoms of NS, other causes of hypothyroidism, and use of iodized salt and other study variables. They also examined clinical symptoms that indicate hypothyroidism, such as feeling cold, fatigue, tiredness, obesity. Anthropometric measurements are made clinically using measuring scales and stadiometers, such as weight in kilograms and height/height in centimeters. Disease information, including NS type, steroid dose, age at NS disease, and duration of NS disease, was collected from patient.

In this study, hypothyroidism included both overt and subclinical forms. Overt hypothyroidism was defined as a TSH level greater than 10 mU/L and an FT4 level below 10 pmol/L, or an FT4 level below 10 pmol/L with either a normal TSH level or a TSH level less than 0.5 mU/L. Subclinical hypothyroidism was defined as a TSH level between 5 and 10 mU/L, with normal age-appropriate FT4 levels: 10–23.2 pmol/L for children aged 1–5 years, 10–28 pmol/L for ages 6–10 years, and 10–30 pmol/L for ages 11–19 years.

Frequencies and percentages were calculated for categorical variables, and chi-square test of significance was applied to check the categorical variables, whereas mean and standard deviation was calculated for numeric variables, and independent samples t test was applied to check the significance and difference between two means. P-value ≤0.050 considered significant.

3. RESULTS

A total of 40 patients were included in this study, comprising 26 males (65.0%) and 14 females (35.0%). The mean age of the patients was 14.95 ± 3.79 years. Out of the total, 22 patients (55.0%) reported using iodized salt, while 7 patients (17.5%) used local salt. Hypothyroidism was found in 22.7% of participants. In terms of nephrotic syndrome type, 21 patients (52.5%) presented with steroid-sensitive nephrotic syndrome, 12 patients (30.0%) with steroid-resistant nephrotic syndrome, and 7 patients (17.5%) were newly diagnosed.

Regarding proteinuria at the time of enrollment, 24 patients (60.0%) had nil or trace proteinuria, 11 patients (27.5%) had proteinuria levels of +1 to +2, and 5 patients (12.5%) had proteinuria levels ranging from +3 to +4. The mean estimated glomerular filtration rate (GFR) of the patients was 104.22 ± 19.62 mL/min/1.73m², with 12 patients (30.0%) showing a GFR of less than 90 mL/min/1.73m². The mean serum albumin level was 3.81 ± 2.07 g/dL, and 17 patients (42.5%) had serum albumin levels of ≤2.5 g/dL. Additionally, 11 patients (27.5%) were in remission at the time of enrollment.

Prednisolone was used as medication in 27 patients (67.5%). There was no statistically significant association found between the medications used and any effect modifiers (p > 0.050).

Figure. No. 1
Distribution of medication in the study cases

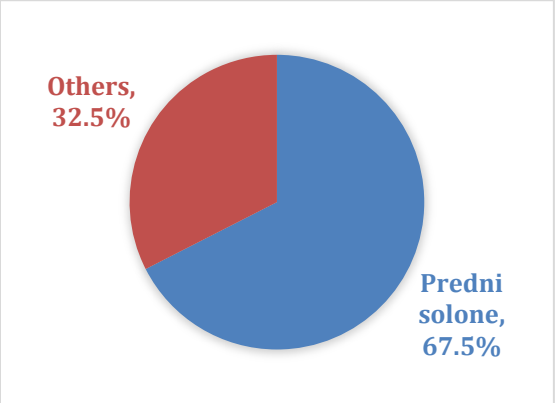


Table. No. 1
Demographic and baseline characteristics of the study cases

Variable	Frequency (Percentage)	Mean±S.D
Gender		
Male	26 (65.0%)	
Female	14 (35.0%)	
Age (years)	14.95±3.79	
Salt used		
Iodized salt	22 (55.0%)	
Local and iodized salt	10 (25.0%)	
Local salt	7 (17.5%)	
No salt	1 (2.5%)	
Type of nephrotic syndrome		
Steroid sensitive NS	21 (52.5%)	
Steroid resistant NS	12 (30.0%)	
Diagnosed newly	7 (17.5%)	
Degree of proteinuria on urine dipstick at enrollment		
Nil and Trace	24 (60.0%)	
+1 to +2	11 (27.5%)	
+3 to +4	5 (12.5%)	
Presence of edema		
Yes	6 (15.0%)	
No	34 (85.0%)	
Results of laboratory		
Estimated GFR		104.22±19.62
<90mL/min /1.73m^2	12 (30.0%)	
≥90mL/min /1.73m^2	28 (70.0%)	
Serum albumin		3.81±2.07
≤ 2.5 g/dL	17 (42.5%)	
>2.5 g/dL	23 (57.5%)	
Remission status at enrollment		
Yes	11 (27.5%)	
No	29 (72.5%)	

Table. No. 2
Association of medication with effect modifiers

Effect modifier	Medication		P-value
	Prednisolone 27 (67.5%)	Others 13 (32.5%)	
Estimated GFR			
<90mL/min /1.73m^2	9 (75.0%)	3 (25.0%)	0.507
≥90mL/min /1.73m^2	18 (64.3%)	10 (35.7%)	
Serum albumin			
≤ 2.5 g/dL	10 (58.8%)	7 (41.2%)	0.314
>2.5 g/dL	17 (73.9%)	6 (26.1%)	
Presence of edema			
Yes	6 (100.0)	0 (0.0%)	0.065
No	21 (61.8%)	13 (38.2%)	
Remission status at enrollment			
Yes	9 (81.8%)	2 (18.2%)	0.234
No	18 (62.1%)	11 (37.9%)	

4. DISCUSSION

It is important to note that although sudden remission is a sign of subclinical hypothyroidism, the problem persists and transitions into hypothyroidism[11]. In this study hypothyroidism was found in 22.7% of participants.

A prevalence study by Galukande et al[12] conducted within young, apparently healthy people who were undergraduate students from Makerere University in Uganda, showed that the prevalence of thyroid

dysfunction which was half comprised of hyperthyroidism and half hypothyroidism was 3.6%.

In a country like India, it is lower than the 33.3 % reported among the children and adolescents with nephrotic syndrome (NS) between 1-18 years of age. By the cross-sectional study conducted by Marimuthu et al[13] in India, Although the ages of the children who took part in the Marimuthu study were similar, with a mean age of 7.2 years (SD 3.9), the data may have been larger because they were limited to children with teenagers using steroids.

In a study Li et al[14] reported prevalence rates of autoimmune thyroid disease were reported to be higher among Asian populations, so perhaps that is the reason for the high incidence recorded in Indian studies. The most common form of hypothyroidism in the NS population is, therefore, subclinical.

Similar findings of the current study were reported in a case-control study performed at Pediatric Hospital Qazvin-Iran by Saffari et al[15] The authors detected an association of hypoalbuminemia with hypothyroidism. In another study, a significant negative correlation was noted between serum albumin and TSH levels. Since the protein loss in urine lowers the serum level of thyroid hormones in children and adolescents with NS, hence weighing the TSH levels will increase as compensatory effect. El-Aal et al[16] —50 children aged 1–12—prospective one year follow up, Sohag University Hospital/ Egypt During the study, a correlation of low serum albumin with low levels of thyroid hormones and high TSH (hypothyroidism) was found to be considerable. Although a more limited effect most of the studies concur that they are.

Jung et al[17] conducted a study at Inje University Busan Paik Hospital, Korea, enrolling 31 children with nephrotic syndrome (NS) between January 2001 and December 2017. They compared thyroid status during active nephrosis and in remission. Contrary to most studies, they found no significant correlations between serum albumin and T4, TSH, or Free T4 levels. Dagan et al[18] conducted a study suggesting that non-autoimmune hypothyroidism may be a significant complication of steroid-resistant nephrotic syndrome (SRNS) and should be actively monitored, especially in cases where there is renal function deterioration. They observed that hypothyroidism typically resolves when patients reach end-stage renal disease (ESRD). The study emphasizes the need for further research to understand the incidence and pathogenesis of this condition.

Akhter et al[19] reported that Hypothyroidism was found in nearly one-third of children with steroid-resistant nephrotic syndrome. Persistent proteinuria may cause subclinical or overt hypothyroidism, requiring regular monitoring of thyroid function tests. Lazar et al[20] studied 3,510 patients with subclinical hypothyroidism over a period of 5 years and concluded that, in children, initial normal or slightly elevated serum TSH levels are likely to remain stable or normalize spontaneously without the need for specific treatment.

5. CONCLUSION

The prevalence of hypothyroidism among children and adolescents with nephrotic syndrome (NS) is high. Hypoalbuminemia is a key factor associated with hypothyroidism in these patients. Children with NS and hypoalbuminemia should be screened for hypothyroidism, and clinicians should aim to maintain normal albumin levels.

6. REFERENCES

1. Singh S, Mishra OP, Mandal PP, Patel PS, Sharma SS, Saini H, Rani K, Chandrasekhar S, Singh MP. Thyroid function in patients with idiopathic nephrotic syndrome. International urology and nephrology. 2021 Sep 1:1-6.
2. Karki ST, Khatun N, Chapagain RH, Shrestha NJ, Agrawal S. Hypothyroidism among Children with Nephrotic Syndrome Admitted to a Tertiary Care Centre. JNMA: Journal of the Nepal Medical Association. 2024 Feb;62(270):110.
3. Tumwesige M, Rujumba J, Piloya T, Aujo JC. Hypothyroidism among children and adolescents with nephrotic syndrome in Mulago National Referral Hospital, Kampala, Uganda; a cross-sectional study. BMC pediatrics. 2024 Feb 19;24(1):132.
4. Solarin AU, Dada AO, Akinyosoye G, Oladimeji AB, Akinola IJ, Njokanma FO. Subclinical hypothyroidism in children with idiopathic childhood nephrotic syndrome at a tertiary institution in South West Nigeria. Nigerian Journal of Clinical Practice. 2022 Oct 26;25(10):1731-5.
5. Fukata S, Ito M, Nishikawa M, Kasahara T, Nishihara E, Akamiuzu T, Miyauchi A. Hypothyroidism due to nephrotic syndrome: a notable clinical entity. Endocrine Journal. 2022;69(3):307-11.
6. Das AK, Barua T, Dey D, Roy M, Choudhury Z, Karim MR. Thyroid function in children with idiopathic nephrotic syndrome. Chattagram Maa-O-Shishu Hospital Medical College Journal. 2020 Aug 28;19(1):51-4.
7. Hilmanto D, Mawardi F, Lestari AS, Widiasta A. Disease-associated systemic complications in childhood nephrotic syndrome: a systematic review. International Journal of Nephrology and Renovascular Disease. 2022 Feb 25:53-62.
8. Solarin A, Dada A, Akinyosoye G, Oladimeji A, Akinola I, Njokanma F. POS-463 Subclinical hypothyroidism in children with nephrotic syndrome attending Lagos State University Teaching Hospital, Ikeja. Kidney International Reports. 2022 Feb 1;7(2):S206.
9. Nuraeni E, Faisal F, Widiasta A, Novina N. Subclinical hypothyroidism in pediatric nephrotic syndrome: the correlations with albumin, globulin, and proteinuria. Paediatrica Indonesiana. 2020 Apr 17;60(2):91-5.
10. Vivarelli M, Gibson K, Sinha A, Boyer O. Childhood nephrotic syndrome. The Lancet. 2023 Sep 2;402(10404):809-24.
11. Reiners C. Factors interfering with and influencing the measurement of direct and indirect parameters of free thyroxine. Dtsch Med Wochenschr. 1986;111(34):1292–9.
12. Galukande M, Jombwe J, Fualal JO, Gakwaya A. Thyroid dysfunction among young adults in Uganda. East Cent Afr J Surg. 2010;15:76–9.
13. Marimuthu V, Krishnamurthy S, Rajappa M. Non-autoimmune subclinical and overt hypothyroidism in idiopathic steroid-resistant nephrotic syndrome in children. Indian Pediatr. 2017;54(11):925–9.
14. Li Y, Inomata K, Nishihara E, Kakudo K. IgG4 thyroiditis in the Asian population. Gland Surg. 2020;9(5):1838–46.

15. Saffari F, Ahadi S, Dalirani R, Esfandiar N, Yazdi Z, Arad B. Thyroid dysfunction in children with idiopathic nephrotic syndrome attending a Paediatric Hospital in Qazvin, Iran. Sultan Qaboos Univ Med J. 2020;20(4):e332–e8.
16. El-aal MA, Hegab AM, Elsayed E. Thyroid function in children with nephrotic syndrome: a prospective hospital-based study. Sohag Med J. 2020;24(2).
17. Jung SH, Lee JE, Chung WY. Changes in the thyroid hormone profiles in children with nephrotic syndrome. Korean J Pediatr. 2019;62(3):85–9.
18. Dagan A, Cleper R, Krause I, Blumenthal D, Davidovits M. Hypothyroidism in children with steroid-resistant nephrotic syndrome. Nephrology Dialysis Transplantation. 2012 Jun 1;27(6):2171-5.
19. Akhtar N, Aziz M, Aman L, Mubarak M, Lanewala AA, Hashmi S. Hypothyroidism in Children with Steroid-Resistant Nephrotic Syndrome and its Correlation with Clinicopathological Parameters at a Tertiary Care Center in Pakistan. Annals of King Edward Medical University. 2021 Nov 4;27(Special Issue (Jul-Sep)):423-8.
20. Lazar L, Frumkin RB, Battat E, Lebenthal Y, Phillip M, Meyerovitch J. Natural history of thyroid function tests over 5 years in a large pediatric cohort. J Clin Endocrinol Metab. 2009;94:1678-82.