RESEARCH

A STUDY ON THYROID FUNCTION IN CHILDREN WITH NEPHROTIC SYNDROME

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Abstract

Background: A reduction in albumin and high-molecular-weight proteins such as thyroxine-binding globulin and thyroid hormones is a characteristic of nephrotic syndrome, a glomerular illness that may produce subclinical or even overt hypothyroidism. The aim is to evaluate thyroid function test findings in children with nephrotic syndrome, as well as the association between the thyroid profile and different manifestations of the ailment. **Materials and Methods:** The Department of Paediatrics performed a cross-sectional research on 100 children under the age of 12 with nephrotic syndrome who were hospitalised and were in remission, relapse, SDNS, or SRNS. **Result:** The most frequent age range for presentations is 3 to 6 years, with 68 cases (68%), and 7 to 9 years, with 26 cases (26%). A presentation's median age is 5.7 years. More men (55%) are impacted than women (45%), although there is no discernible gender difference across other criteria. The levels of serum T3, T4, and TSH were determined to be normal. However, the initial episode's TSH readings were significantly higher than in remission. Serum albumin and TSH have a negative relationship that is statistically significant (p=0.003). **Conclusion:** Subclinical hypothyroidism is more common in patients with nephrotic syndrome. Proteinuria is most likely caused by the loss of thyroxine-binding globulin and the T4 that is attached to it, which also increases TSH production.

INTRODUCTION

Massive proteinuria, a symptom of the nephrotic syndrome, results in hypoproteinemia, extensive edoema, and hyperlipidemia.[1] The prevalence of nephrotic syndrome in children aged 1 to 10 years is 16/100000. The vast majority of them are primary or idiopathic in nature. Idiopathic minimalchange disease is the most common kind. One of the characteristics of nephrotic syndrome is that 80% of patients respond to corticosteroid therapy.

Children with the Nephrotic syndrome are at risk of life-threatening infections, while adults are at risk of thromboembolic complications. Chronic renal failure, starvation, a negative nitrogen balance, and accelerated atherosclerosis due to severe hyperlipidemia may all result from nephrotic syndrome. Additionally, the absence of the plasma-binding proteins may result in heightened sensitivity to various protein-bound compounds, including medications and endogenous hormones. The growth and development of the kidney as well as the preservation of water and electrolyte equilibrium depend on thyroid hormones (TH). Thyroxine (T4) and triiodothyronine (T3), thyroid hormones that influence endochondral calcification and the whole process of cartilage formation, are crucial for the maturation and development of the skeleton. On the other hand, thyroid hormone is metabolised and eliminated by the kidney. Proteins, primarily thyroid binding globulin, prealbumin, and albumin, bind thyroid hormone in the blood.[2] The thyroid hormones are reduced as a consequence of urine loss of intermediate-sized plasma proteins (40–200 kDa) and hormone-binding proteins such thyroxine binding globulin (TBG), transthyretin, and albumin.

Thyroid hormone levels in the blood decrease during nephrosis, but TSH production increases.[3]

Despite urinary thyroid hormone losses, T3 and T4 levels were normal, according to the scientists, who also reported a surge in TSH levels as a compensatory mechanism.[4] As a result, there will be mild to moderate hypothyroidism during the proteinuria period. Because thyroid is essential for a child's physical and mental development and is a curable ailment, there is a need to examine hypothyroidism and offer thyroid hormone replacement to individuals who show signs of hypothyroidism. Thyroid function tests were done in 100 cases of nephrotic syndrome over an 18-month period to look for evidence of hypothyroidism in different kinds of nephrotic syndrome and to look for a link between blood albumin and TSH.

MATERIALS AND METHODS

The cross-sectional study was conducted out by the Department of Paediatrics at Niloufer Hospital, which is part of Osmania Medical College. It will be one of India's key tertiary care centres from October 2018 to August 2020. 100 children with nephrotic syndrome were admitted to the paediatrics section at Niloufer Hospital, Osmania Medical College. 100 patients in all were included in the trial after meeting the inclusion criteria.

Inclusion Criteria

Children under the age of 12 with remission, recurrence, SDNS, or SRNS from Nephrotic syndrome.

Exclusion Criteria

Children with thyroid illness, those receiving thyroid-impairing drugs, and those who have hypoalbuminemia owing to other disorders such as liver disease or malnutrition.

The Institutional Ethical Committee of Osmania Medical College in Hyderabad gave its clearance.

Informed permission was gained after properly describing the nature of the research to the study participants' parents. The individual's information was captured using a pre-structured proforma. After obtaining parental permission, clinical data such as age, gender, presenting symptoms, pharmacological history, and type of nephrotic syndrome were obtained.

Blood samples from the patients were taken for thyroid function and albumin testing after the clinical examination and taking of their medical history. For measuring serum albumin, a photometric method is used. ELISA is used to measure T3, T4, and TSH levels.

Statistical Analysis

The patient data was gathered, recorded, and analysed on a Microsoft Excel sheet. For continuous variables, the mean and standard deviation were calculated. A student test was utilised to compare the statistically significant connection between the means of the two groups. To express categorical information, percentages or proportions were utilised. For categorical variables, the Chi square test was used. P value of < .05considered as statistically significant.

RESULTS

100 patients ranging in age from 1 to 12 years were included in this research. The age range with the most cases is 3 to 6 years old (68%), followed by 7 to 9 years old (26%). A presentation's median age is 5.7 years. More men (55%) than women (45%) were impacted. Eighty-two percent of the children who were seen had puffy faces, while 25 had decreased urine output and 40 had abdominal distention. The most frequent presenting complaint in this study is facial puffiness.

Table 1: Frequency Of cases.

Diagnosis	Frequency	Percentage
First Episode	48	48
Relapse	25	25
Remission	15	15
SDNS	6	6
SRNS	6	6
Total	100	100

A total of 100 cases between the ages of 1 and 12 years were included in this study, of which 48 cases (48%) were first episodes, 25 cases (25%) were relapses, including both frequent and infrequent relapses, 6 cases (6% each of SDNS and SRNS), and 15 cases (15%) were included at the time of remission.

Table 2: Distributions of Parameters

Parameter	N	Minimum	Maximum	Mean	Std Deviation
Age	100	2	11	5.72	2.01
Protein	100	3.6	6.6	4.607	0.73
Albumin	100	1.5	4	2.224	0.65
T3	100	0.9	1.8	1.263	0.23
T4	100	5.2	10.4	7.072	1.28
TSH	100	0.2	8.2	5.93	1.63

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The study's 100 patients had low median blood albumin levels (mean = 2.224 gm%), normal median T3 and T4 levels (mean = 1.263 ng/ml and 7.072 microg/dl, respectively), and slightly increased median TSH levels (mean = 5.93 iu/ml).

Table 3: Statistics by Gender

Parameter	Sex	N	Mean	Std Deviation	Std Err Mean	Student's t test P value
Age	Male	56	5.96	2.01	0.26	0.17
	Female	44	5.40	1.98	0.29	
Protein	Male	56	4.56	0.67	0.08	0.52
	Female	44	4.65	0.80	0.12	
Albumin	Male	56	2.17	0.60	0.08	0.40
	Female	44	2.28	0.71	0.10	
T3	Male	56	1.26	0.24	0.03	0.88
	Female	44	1.25	0.23	0.03	
T4	Male	56	7.05	1.24	0.16	0.90
	Female	44	7.08	1.34	0.20	
TSH	Male	56	6.01	1.59	0.21	0.56
	Female	44	5.82	1.68	0.25	

No significant gender variation of all parameters. p value >0.05insignificant.

Table 4: Mean Protein level in different types of nephrotic syndrome.

Protein	Mean	STDEV
First Episode	4.3	0.337
Relapse	4.29	0.302
SDNS	4.66	0.294
SRNS	4.45	0.361
Remission	6.15	0.282

The mean protein level is lower during a relapse (mean=4.29gm%) than it was during the first episode (mean=4.3gm%), although the difference in the mean is statistically insignificant. [p value > 0.05] The mean protein content in SRNS is lower than that in SDNS (mean=4.66mg%), at 4.45gm on average. However, the change is not statistically noteworthy. Protein levels in remission were (mean=6.15gm%), which was significantly different from all other groups.

Table 5: Mean Albumin level in different types of nephrotic syndrome.

Albumin	Mean	STDEV
First Episode	1.96	0.181
Relapse	1.92	0.226
SDNS	2.08	0.213
SRNS	2.01	0.147
Remission	3.7	0.290

The mean albumin level is lower during relapse (mean=1.92gm%) than it was during the first episode (mean=1.96gm%) and SRNS (mean=2.01gm%), although the difference in the mean is statistically insignificant. [p value > 0.05] Compared to SDNS, where the mean albumin level was 2.08 mg, SRNS had a mean albumin level of 2.01 gm. However, the change is not statistically noteworthy. Albumin levels (mean=3.7gm%) in remission patients were substantially different from all other types (p value < 0.05).

Table 6: Mean T3 and T4 level in different types of nephrotic syndrome.

T3	Mean	STDEV
First Episode	1.21	0.203
Relapse	1.24	0.234
SDNS	1.36	0.332
SRNS	1.23	0.216
Remission	1.42	0.268
T4		
First Episode	6.63	1.127
Relapse	6.74	0.747
SDNS	6.56	0.595
SRNS	7.4	1.058
Remission	9.07	0.792

In each of the 100 patients that were a part of this investigation, the serum T3 level was within the normal range. Mean serum T3 levels were 1.21ng/ml in instances of a single episode, 1.24ng/ml in situations of relapse, 1.36ng/ml in cases of SDNS, 1.23ng/ml in cases of SRNS, and 1.42ng/ml in cases of remission. A single episode's mean serum T4 level (mean=6.63microgr/dl) is

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lower than relapse patients' (mean=6.74microgr/dl) and higher than cases of SDNS (mean=6.56microgr/dl). The mean T4 level in instances of remission (mean=9.07microgr/dl) is greater than in all other categories, although the difference is statistically insignificant (P > 0.05)

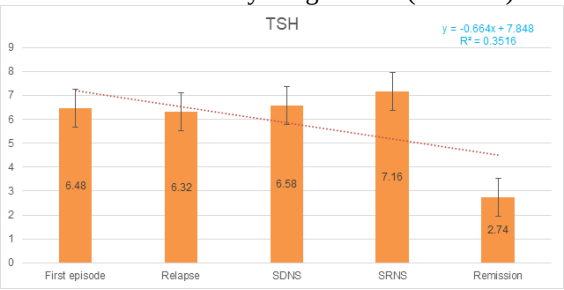

Figure 1: Mean TSH level in different types of nephrotic syndrome.

The mean serum TSH level during a single episode was greater than the mean during a relapse (mean =6.32 iu/ml), although the difference was statistically insignificant. When compared to other forms of nephrotic syndrome, the mean serum TSH level in SRNS patients was higher (mean=7.16 iu/ml), although it was not statistically significant (P value >0.05). TSH levels were significantly increased in one episode compared to remission instances. (P value = 0.018)

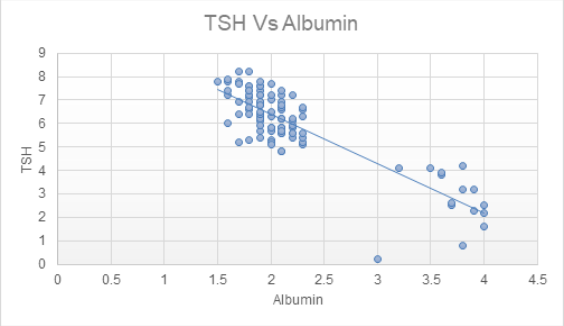

Figure 2: Scatter plot showing relationship between TSH and albumin

TSH and serum albumin have a negative relationship that is statistically significant. (p=0.003).

DISCUSSION

The most frequent age group of presentation in our research, which included 100 kids between the ages of 1 and 12, was between 3 and 6 years (68%) and 7 to 9 years (26%). Age of presentation is 5.7 years on average. 20 instances of nephrotic syndrome were included in a research by Hara M et al., of which 12 cases ranged in age from 1 to 4 years, 5 cases ranged from 5 to 9 years, and the mean age at presentation was 5.85 years. In this research, out of the 100 patients, 55 cases (or 55%) were male and 45 cases (or 45%) were female. All metrics show no discernible gender difference. Imran gatto et al.[4] study included 208 cases, of whom 62.5% (130) were men and 37.5% (75) were women (78).

82 children with nephrotic syndrome (out of 100 cases) had face puffiness (82%), 25 had reduced urine production (25%) and 40 had abdominal distention (40%). The most frequent presenting issue in this research is face puffiness. In their research of 35 kids aged 1 to 8 years, Vidhisahni et al. found that face puffiness is the most typical manifestation (80%), followed by reduced urine production (61.8%) and abdominal distention (31.42%). In their investigation of 40 patients with nephrotic syndrome, Rukmani et al.[5] found that 32 of the infants had face puffiness (80%), 26 had reduced urine production (65%), and 22 had abdominal distention (45%).

In this study, serum T3, T4 levels were found to be within normal limits. TSH levels were substantially greater in the first episode than after remission. TSH and serum albumin show a statistically significant negative connection (p=0.003). According to Pelletier J et al,[6] the present study's findings are compared to those of earlier investigations. Thyroid stimulating hormone (TSH) levels were higher than usual in 85 nephrotic children between the ages of 2 and 12. TSH levels increased significantly during nephrosis. The lack of a noticeable difference between T3 and T4 levels indicates that proteinuria is often associated with mild or subclinical hypothyroidism in children with nephrotic syndrome. Serum T3 and T4 levels in the 100 participants in this investigation are within normal limits. However, the TSH value of the first episode is substantially higher than that of the remission.

T3 and T4 readings are normal both during active illness and remission, according to Sharma M et al,[7] research's on hypothyroidism in nephrotic syndrome, although TSH values were greater in active disease. TSH returned to normal levels throughout remission, resulting in a period of subclinical hypothyroidism with proteinuria that didn't need thyroxine therapy. They also clarified why albumin and TSH had a bad connection. These findings are comparable to and comparable to those of the current investigation.

This study found a link between an increase in blood TSH levels and protein excretion in the urine. Numerous studies have shown a link between serum TSH levels and proteinuria. Gilles,[8] discovered that people with poor renal protein excretion had greater TSH levels than the control group in his study. Ito S et al,[9] found that the daily excretion of proteins in the urine correlates strongly with the excretion of T3, T4, and TBG in the urine. This research suggests that severe nephrosis may have higher TSH levels due to significant proteinuria. According to Afroz et al,[10] urine losses of many binding proteins in nephrotic syndrome produce transitory subclinical hypothyroidism. Although serum TSH levels increased after an attack, serum T3, T4, and other readings were normal both during and after the event. We identified analogous results in our study,

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such as normal blood T3, T4 levels, and higher TSH levels after an assault.

In this study, the average TSH level was 5.93 1.68 Iu/ml, the average T3 level was 1.263 0.23 ng/ml, and the average T4 level was 7.072 1.28 microg/dl. According to Sheehan MT et al,[11] the average and maximum measured TSH levels were both lower than our patients' findings, at 5.26 and 10.38 Iu/ml, respectively. According to Harton et al,[12] T3 and T4 levels in those with primary glomerular nephropathy were 12454 and 4.842.11, respectively. Although the average T4 levels in the two trials are similar, they are lower than the average T4 levels in this study.

Usberti M et al,[13] discovered that persons with nephrotic syndrome are more likely to have subclinical hypothyroidism. The thyroid profile returns to normal once the non-thyroid condition is addressed. According to Van den Born J et al. [14], who reported that abnormalities in thyroid function were observed in patients at the proteinuria stage, TSH levels were higher in patients with active disease than in controls when there was proteinuria and hypoalbuminemia. Previous research supports these results, and there is a statistically significant negative relationship between serum albumin and TSH.

Limitations

1. One hundred patients of nephrotic syndrome were the subject of this investigation. Therefore, because of the tiny sample size, we were unable to provide specific suggestions.
2. This study may not fully reflect data from the whole neighbourhood since it was confined to children admitted as patients to our tertiary care referral hospital.
3. There were no controls employed in this research.
4. Urine T3, T4, TSH, and urinary thyroid binding globulin measurements were not possible after 24 hours.

CONCLUSION

People with nephrotic syndrome are more likely to develop subclinical hypothyroidism, according to new study. Proteinuria is most likely caused by the loss of thyroxine-binding globulin and the T4 that is connected to it, which also increases TSH production. As soon as the nonthyroid ailment is treated, thyroid function returns to normal.

In some instances with proteinuria-stage subclinical hypothyroidism after remission, TSH returned to normal and prevented the need for thyroxine therapy. This explains why albumin and TSH have a negative relationship. Once the non-thyroid ailment has been treated, thyroid function has returned to normal. Every child with nephrotic syndrome should be evaluated for the potential of hypothyroidism. TSH and free T4 levels should be routinely checked for hypothyroidism in these individuals, especially if proteinuria is persistent.

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