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Original Research Article

Thyroid function test in nephrotic syndrome children who are admitted in emergency ward of Government Tirunelveli Medical College and Hospital, India

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ABSTRACT

Background: Nephrotic syndrome in childhood is largely primary or idiopathic, although a small proportion of cases are secondary to infectious agents and other glomerular and systemic diseases. The etiology of nephrotic syndrome is age-dependent. Most cases appearing in the first 3 months of life are referred as congenital nephrotic syndrome (CNS) and are due to genetic diseases. The objective of this study is to study the correlation between thyroid profile and different types of nephrotic syndrome.
Methods: This cross-sectional study was done between March 2017 to October 2017 in the Department of Pediatrics Tirunelveli Government Medical College. 40 cases of nephrotic syndrome between 1 to12 years, which include all types of nephrotic syndrome. After history taking and clinical examination, blood samples were collected from the patients for thyroid function test and analyzed with standard techniques.
Results: Serum T3, T4, TSH were found to be within normal limits. But TSH values in remission were significantly elevated compared to the first episode.
Conclusions: Thyroid profiles in control were within normal range. The T4 and T3 levels in nephrotic syndrome were low and TSH was high. Hypothyroidism was more common in children less than 6 years.

Keywords: Nephrotic syndrome, Steroid-Resistant Nephrotic Syndrome (SRNS), Steroid-Dependent Nephrotic Syndrome (SDNS), Thyroid function test.

INTRODUCTION

The interactions between kidney and thyroid functions are known for years. Thyroid hormones (TH) are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. Thyroid hormones, thyroxine (T4) and triiodothyronine (T3) play important roles in the maturation and development of the skeleton and affect enchondral calcification and the entire process of cartilage growth[1].On the other hand, the kidney is involved in the metabolism and elimination of thyroid hormone. Thyroid hormone in the circulation is bound to proteins, mainly thyroid binding globulin, prealbumin,and albumin. Nephrotic syndrome results in urinary loss of intermediate-sized plasma proteins (40-200 kDa) and hormone binding proteins such as thyroxine-binding globulin (TBG), transthyretin and albumin leading to a reduction in thyroid hormones. Many of physiologically important molecules which bind to plasma proteins also are losing in urine.[2] Children with the Nephrotic syndrome may face life-threatening infections, while adults are endangered by thromboembolic complications.[3] Nephrotic syndrome may lead to negative nitrogen balance, malnutrition, accelerated atherosclerosis because of severe hyperlipidemia and

cause chronic renal failure. In addition, losing the plasma binding proteins may lead to increased sensitivity to some protein-bound substances such as drugs and endogenous hormones.[4] Thyroid hormones almost affect every organ of the body and the anterior pituitary hormone affects production and secretion of thyroid hormones by releasing thyroid stimulating hormone (TSH) and this hormone itself is controlled by hypothalamic thyrotropin-releasing hormone.[5] Thyroidal status affects the kidney function during embryonic development and maturation indirectly by the cardiovascular system by its effect on renal blood flow (RBF), and directly by affecting glomerular function, the tubular secretory and absorptive capacities, electrolyte pumps and kidney structure.[6]

Because of the normal free T4 (FT4) and free T3 (FT3) levels it was thought that patients are metabolically euthyroid. Loss of Thyroid Binding Globulin (TBG) causes decreased total T4 leading to increase in the unboundhormone. When the thyroid is hyper or hypofunctioning there will be changes in clinical parameters such as glomerular filtration rate (GFR), urine specific gravity, urinary protein/creatinine ratio and markers of tubular function. In almost half of the nephrotic syndrome patients, spontaneous healing occurs and the others may suffer from infections, hypertension and uremia.[7,8]

METHODS

This cross-sectional study was done between March 2017 to October 2017 in the Department of Pediatrics Tirunelveli Government Medical College. 40 cases of nephrotic syndrome between 1 to12 years, which include all types of nephrotic syndrome were included in the study.

Inclusion criteria

- All cases of nephrotic syndrome between 1 to12 years.
- New and old cases which include relapses, SDNS, SRNS and on remission.

Exclusion criteria

- Children with a family history of hyperlipidemia
- Children with the previous history of thyroid dysfunction
- Children with other causes of hypoproteinemia like liver disease and malnutrition
- Age less than 1yr and more than 12 year.

Pre-structured proforma was used to record the information from the individual. After getting the consent from the parents clinical data were collected and entered in the proforma, which include age, sex, presenting complaints, drug history, and type of nephrotic syndrome (1sttepisode/relapse/SDNS/SRNS/remission). After history taking and clinical examination, blood samples were collected from the patients for thyroid function.

The photometric method used for measuring serum albumin. T3, T4 and TSH level measured by ELISA (Enzyme-Linked Immunosorbent Assay). For categorical variable chi-square test was used. P value of <.05 considered as statistically significant.

RESULTS

During relapse mean albumin (mean = 1.96 gm%) level less than that of first episode (mean = 2.08 gm%) and SRNS (mean 2.03 gm%) but the mean difference is statistically insignificant (p value >0.05). In SRNS mean albumin level, (mean = 2.03 gm%) lower than that of SDNS (mean = 2.23 mg%) and 1st episode (mean = 2.08 gm%). But the difference statistically insignificant. In remission albumin level (mean = 3.65 gm%) was statistically significant from all other types (p value less than <0.05).

Table 1: Mean albumin level in different types of nephrotic syndrome.

Serum albumin	Mean	SD
First episode	2.08	0.33
Relapse	1.96	0.29
SDNS	2.23	0.29
SRNS	2.03	0.21
Remission	3.65	0.25

Serum T3 level was with in normal limits in all of the 40 cases included in the present study. Mean serum T3 level in 1st episode (mean = 0.89 ng/ml), relapse (mean = 0.93 ng/ml) cases, SDNS (mean = 0.87 ng/ml) cases, SRNS cases (mean = 0.83 ng/ml) and in remission cases (mean 1.15 ng/ml).

Table 2: Mean variation of serum T3 in all types of nephrotic syndrome.

T3	Mean	SD
First episode	0.89	0.29
Relapse	0.93	0.35
SDNS	0.87	0.15
SRNS	0.83	0.32
Remission	1.15	0.49

Table 3: T4 in all types of nephrotic syndrome.

T4	Mean	SD
First episode	5.73	1.66
Relapse	6.71	2.21
SDNS	5.33	0.23
SRNS	6.87	2.47
Remission	6.25	2.68

Mean serum T4 in 1st episode (mean = 5.73 mg/dl) less than that of relapse (mean = 6.71 mg /dl) cases and higher than SDNS (mean = 5.33 mg/dl) cases. Mean T4 in SRNS (mean = 6.87 mg/dl) cases. Compared to all other types shows statistically insignificant elevation (P value .0.05).

Mean serum TSH level in 1st episode (mean = 4.90 IU/ml) higher than that of relapse (mean 4.12 IU/ml) and SDNS (mean = 3.77 IU/ml) cases but statistically insignificant. Mean serum TSH level in SRNS cases (mean = 5.00 IU/ml) elevated when compared to other types of nephrotic syndrome, but statistically insignificant (P value >0.05). Compared to remission cases TSH level in 1st episode significantly elevated. (P value 0.018).

DISCUSSION

In our study among 40 children between 1 to 12 yrs, the most common age group of presentation is 6 to 10yrs (24/40) followed by 1 to 5 yrs (12/40). Mean age of presentation is 6.9 yrs. In a study done by Hara M et al among 20 cases of nephrotic syndrome 12 cases were between 1 to 4 years, 5 cases were between 5 to 9 years and mean age of presentation was 5.85yrs.[9]

In the present study among the 40 cases 27 cases were male (68%) and13 cases were female (32%). Study done by Kaplan JM et al among 208 cases 62.5% were males (130) and 37.5% were females (78). Among 40 cases of nephrotic syndrome 32 children presented with facial Puffiness (80%), 26 children presented with decreased urine output (65%) and 22 cases with abdominal distention (45%)[10] Kestila M et al in their study among 35 children of 1 to 8yrs showed that most common presentation is facial puffiness (80%) followed by decreased urine output (62.85%) and followed by abdominal distention (31.42%).[11] They have studied children with nephrotic syndrome by checking Serum levels of FT3, FT4 and TSH in 20 children aged 1-16 years with the steroid-resistant nephrotic syndrome (SRNS) and a similar number of controls. They found an overt hypothyroidism with low FT4 (normal values: 0.7-2.0 ng/mL) and elevated serum TSH above reference values (0.45-4.5 mIU/L).[12]

Niaudet P et al, have studied 164 patients and they were divided into three groups according to the levels of thyroid hormone and treatment. The thyroid status, efficacy, and adverse reactions of thyroid treatment were observed in each group. Thyroid dysfunction was found in 73 patients. thyroid-stimulating hormone (TSH) levels were significantly higher in patients with thyroid dysfunction, whereas serum albumin and free and total T3 and T4 levels were lower than those of euthyroid patients.[13] Pelletier J et al have studied A total of 85 nephrotic children Aged from 2-12 years the mean value of thyroid stimulating hormone (TSH) was higher than normal level. A significant increase in TSH level during nephrosis was found. No significant difference between T3 and the T4 level was observed suggests that children with nephrotic syndrome commonly have a state of mild or subclinical hypothyroidism during proteinuria.In our study among 40 case serum T3 ,T4 and TSH all with in normal limits. But TSH value in first episode significantly higher than remission.[14]

Sharma M et al in their study on hypothyroidism in nephroticsyndrome showed that T3 and T4 values normal both during active disease and remission, but TSH values were higher in active disease. During remission, TSH became normal and producing a state of Subclinical hypothyroidism in proteinuria stage that didn't need treatment with thyroxine. They also explained the negative correlation between albumin and TSH.[15]

Reddy SR et al in their study they have compared thyroid profile of 30 controls with 30 children with nephrotic syndrome. Thyroid profiles in control were in normal range. The T4 and T3 levels in nephrotic syndrome were low and TSH was high. Hypothyroidism was more common in children less than 6 years.[16] Usberti M et al in their study showed that nephrotic syndrome patients have more risk of subclinical hypothyroidism. Thyroid profile becomes normal when the non-thyroid illness is resolved.[17]

Van den Born J et al told that abnormalities in thyroid function were seen in patients in proteinuria stage, Specifically, TSH levels were higher in patients with active disease than with controls when there were proteinuria and hypoalbuminemia. In our study negative correlation between serum albumin and TSH and that is statistically significant.[18]

Present findings suggest that nephrotic syndrome patients have an increased risk of subclinical hypothyroidism. Thyroid hormones accelerate the basal metabolic rate. Thyroid function returns to normal when the nonthyroid illness is resolved. Proteinuria results in loss of thyroid hormones, most probably caused by loss of thyroxine-binding globulin along with T4 bound to it, thus stimulating TSH production.[19,20]

CONCLUSION

We concluded from this study that nephrotic syndrome commonly has a state of mild or subclinical hypothyroidism during proteinuria although they are clinically euthyroid. This temporary hypothyroid state improves with remission and needs no treatment in older children, but early treatment may be considered in younger children to prevent physical and mental subnormality.

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