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Research Article

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Evaluating the Thyroid Function in Pediatric Nephrotic Syndrome: A study conducted in Ahvaz, Iran

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ABSTRACT

Nephrotic syndrome is a nonspecific kidney disorder, characterized by a number of signs of disease including proteinuria, hypoalbuminemia and edema and also an increase in permeability of the capillary walls of the glomerulus leading to the presence of high levels of protein passing from the blood into the urine. Nephrotic syndrome causes lose of plasma proteins and macromolecules leading to their deficiencies and heavy proteinuria. Nephrotic syndrome patients show different thyroid hormone profile although total T4 and T3 may be low due to urine loss of thyroxine-binding globulin. This was a clinical trial study conducted on 20 children with Nephrotic syndrome. The serum T3, T4 and TSH levels of the patients were measured with ELIZA method and then compared with the data of 20 healthy children who were matched by age, gender and other main demographic data to the patients. The T_4 and T_3 levels in nephrotic syndrome patients were low and TSH levels were high showing a hypothyroidism profile. However, the T_4 levels were significantly low in Nephrotic syndrome compared to the healthy group. Due to proteinuria because of nephrotic syndrome and lose of TBG and albumin (the proteins that thyroid hormones bind to) the levels of T3 and T4 in the blood were low and of TSH were high showing a hypothyroidism profile in nephrotic syndrome children.

Keywords: Thyroid function, Nephrotic syndrome, T3, T4 and TSH

INTRODUCTION

Nephrotic syndrome is a disorder that mostly appears in young children who are newly born but may occur in any age too, and it usually extends over many months or years (1) Congenital nephrotic syndrome (CNS) appears during the first three months of life but it may appears during the first year of life too and it is defined infantile and the nephrotic syndrome that appears after the first year of life is defined childhood nephrotic syndrome (2). Nephrotic syndrome causes lose of plasma proteins and macromolecules leading to their deficiencies and heavy proteinuria (exceeding 3.5 g/1.73 m^2 of body surface area in adults, or 40 mg/hr/m^2in children), hypoalbuminaemia, hypercholesterolemia, lipiduria, vitamin D deficiency (by losing vitamin-D-binding globulin), iron deficiency (by losing transferrin) and edema. Many of physiologically important molecules which bind to plasma proteins also are losing in urine. Children with Nephrotic syndrome may face life-threatening infections, while adults are endangered by thromboembolic complications. Nephrotic syndrome may lead to negative nitrogen balance, malnutrition, accelerated atherosclerosis because of severe hyperlipidemia and cause chronic renal failure (3-5). In addition, losing the plasma binding proteins may leads to increased sensitivity to some protein-bound substances such as drugs and endogenous hormones (5). Thyroid hormones almost affect every organ of the body

and the anterior pituitary hormone affects producing and secreting of the thyroid hormones by releasing thyroid stimulating hormone (TSH) that this hormone itself is controlled by hypothalamic thyrotropin-releasing hormone (6). Thyroidal status affects the kidney function during embryonic development and maturation indirectly by 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 (7). Because of the normal free T_4 (FT_4) and free T_3 (FT_3) levels it was thought that patients are metabolically euthyroid. Losing of Thyroid Binding Globulin (TBG) causes decreased total T4 leading to increase in unbound hormone (4). When the thyroid is hyper or hypofunctioning changes in clinical parameters such as glomerular filtration rate (GFR), urine specific gravity (USG), urinary protein/ creatinine ratio (UPC) and markers of tubular function may occur (7). In almost half of the nephrotic syndrome patients spontaneous healing occurs and the others may suffer of infections or hypertension and uremia (1). Thyroid hormones affects kidneys growth and development and also sodium and water homeostasis and Renal plasma flow (RPF).Hyponatremia, reduced RPF and GFR, and elevated serum creatinine concentrations are observed in patients with primary hypothyroidism, but these changes get normal by thyroid hormone replacement therapy (THRT) (8). Reducing in kidneys function leads to changes in synthesis, secretion, metabolism, and elimination of thyroid hormones (9). Nephrotic syndrome patients show different thyroid hormone profile although total T_4 and T_3 may be low due to urine loss of thyroxine-binding globulin, serum levels of free thyroxine (FT_4) and thyroid-stimulating hormone (TSH) are usually normal, so patients are considered to be euthyroid. A study was shown that two of four adult patients with hypothyroidism requiring thyroxine replacement therapy they relieved of the hypothyroidism when the nephrotic syndrome remitted (10). Anemia of persistent nephrotic syndrome appears before the kidney dysfunction, however, in a study was found that in nephrotic syndrome patients anemia was very common (11). Thyroxine replacement therapy has proven to have beneficial effects on the adjustment of thyroid hormones levels (12). According to our previous studies on hormonal changes (13) and renal complications (14) in diseases this study is designed. Therefore, according to the information above we decided to make a study to discover the way to organs affects each other in reality by checking hormones and molecules related to kidney and thyroid gland to give the exact amounts of them in order to discover the way they affecting each other.

MATERIALS AND METHODS

The current study was done in hospitals in Ahvaz and 20 children with Nephrotic syndrome were randomly enrolled in the study to check their thyroid markers levels, we choose two groups of children; a normal group and a group of nephrotic syndrome patients. we took blood samples and let it clot, then collect the serum to follow their serum T_3, T_4 and TSH levels by checking them every week by ELISA (Enzyme Linked Immunosorbent Assay) for screening and to know the real situation of their thyroid function and also their urine protein to know if they develop Nephrotic syndrome or not.

Statistical Analysis for each subgroup was done by (Two ways –ANOVA or HSD Tuckey (t-test) One way – ANOVA) and represented as mean (±standard deviation). Data were analyzed using SPSS Statistical Software.

RESULTS

The T_4 and T_3 levels in nephrotic syndrome patients were low and TSH levels were high showing a hypothyroidism profile but the T4 levels were significantly low in nephrotic syndrome compared to normal group (Table 1).

Table 1. Comparison of hormones levels of healthy and children with Nephrotic syndrome

Variable	Group	Mean±SD	pv
T_3*	A	1.53±0.61	0.12
	B	1.72±0.42	
T_4^+	A	5.82±2.65	0.01
	B	8.46±1.87	
TSH^+	A	3.45±3.23	0.38
	B	3.74±2.52	

A: Nephrotic syndrome
B: Healthy
+: Independent sample t-test
**: Mann-whitney*

DISCUSSION AND CONCLUSION

Nephrotic syndrome causes changes in the concentrations of thyroid hormones due primarily to loss of protein in the urine. Acute kidney injury and chronic kidney disease have notable effects on the hypothalamus-pituitary-thyroid axis (4).In nephrotic syndrome, thyroid hormone levels decrease while serum thyroid stimulating hormone (TSH) levels increase. Several studies have found a correlation between proteinuria and serum TSH and urinary T_4 levels.

Congenital nephrotic syndrome is commonly associated with hypothyroidism due to chronic massive proteinuria (12).

Kapoorand et al. have studied children with nephrotic syndrome by checking Serum levels of FT_3, FT_4 and TSH in 20 children aged 1-16 years with steroid resistant nephrotic syndrome (SRNS) and similar number of controls. they found an overt hypothyroidism with low FT_4 (normal values: 0.7–2.0 ng/mL) and elevated serum TSH above reference values (0.45–4.5 mIU/L) (12).

Guoand 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 T_3 and T_4 levels were lower than those of euthyroid patients (13).

Afrozand 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 T_3 and T_4 level was observed suggests that children with nephrotic syndrome commonly have a state of mild or subclinical hypothyroidism during proteinuria(14).

Ito et al. have studied seven children with untreated nephrotic syndrome was compared with that of the same patients in remission and age-matched controls. They found massive urinary losses of T_4, T_3, TBG, free T_4 and free T_3 in the untreated nephrotic children compared with the same patients in remission and age-matched controls. the mean serum free T_4 and free T_3 concentrations were significantly lower in the untreated patients than in the same patients in remission, and the mean serum TSH levels were significantly higher in the untreated patients than in the same patients in remission. These findings provide evidence of mild hypothyroidism in children with untreated nephrotic syndrome because of losses of T_4, T_3, free T_4, free T_3 and TBG into the urine(15).

Sawantand et al. have studied 60 patients with nephrotic syndrome and 20 healthy non-proteinuric individuals as control subjects. They measured their serum tri-iodothyronine, thyroxine and thyroid-stimulating hormone. TSH was elevated in the nephrotic patients compared to controls, while TT_4 and TT_3 were significantly lower in the patients than in controls(4).

While thyroid function tests are in the normal range in most nephrotic patients, the mean values for triiodothyronine (T3) and thyroid-binding globulin (TBG) are lower than those in non-nephrotic syndrome children because of a significant increase in urinary excretion of T3, T4 and thyroid binding globoline TBG (16).Thyroid hormones bind to thyroid binding Globulin (TBG), albumin and prealbumin do to lose of these proteins in urine in nephrotic syndrome, thyroid hormones levels decrease. In our study the levels of T3 and T4 were lower than the normal ranges and the TSH levels were significantly higher than the normal ranges specially the T_4 levels were significantly low pointing to hypothyroidism due to lose of TBG and albumin in urine because of nephrotic syndrome.

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