

Thyroid Function in Children with Idiopathic Nephrotic Syndrome

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Abstract

Background: The underlying abnormality in nephrotic syndrome is an increase in permeability of the glomerular membrane. Urinary losses of binding proteins such as Thyroxine Binding Globulin (TBG) albumin results in a reduction in serum thyroxine (T_4) and sometimes in total T_3 levels. The study was done to assess thyroid hormone status of idiopathic nephrotic syndrome patients at diagnosis, compare the thyroid function after treatment with steroid, correlate with serum albumin and compare the thyroid function with control group.

Materials and methods: It was an analytic type of cross sectional study, done in Paediatric ward, Chittagong Medical College Hospital, Chattogram from 01.05.11 to 30.11.11. Total 58 patients in two groups were included. In group A 32 cases of idiopathic nephrotic syndrome patients and in group B 26 control cases of same age and sex were taken. In group A thyroid function was done at initial diagnosis and in hypothyroid patients in this group again thyroid function was done after treatment with steroid. Data was collected through interviewing with pre-designed questionnaire, physical examination and investigation techniques.

Results: Thyroid hormone level of nephrotic children were significantly lower than that of control group. Nephrotic children with thyroid hypofunction were found euthyroid after initial treatment with steroid that was statistically significant and there was positive correlation between serum albumin and thyroid hormone level. □

Conclusion: Children suffering from nephrotic syndrome had significant thyroid hypofunction because of low serum albumin level and after treatment with steroid they became euthyroid.

Key words: Nephrotic syndrome; Thyroid function; Hypothyroid.

INTRODUCTION

Nephrotic syndrome is primarily a pediatric kidney disorder characterized by massive proteinuria, hypoalbuminemia, edema and hyperlipidemia with an incidence in Paediatric population is 2-3/100,000 children per year¹. Most common form of nephrotic syndrome in pediatric age group is idiopathic nephrotic syndrome.

We know that kidney is involved in the metabolism and elimination of thyroid hormone. The interactions between kidney and thyroid functions are known for years²⁻⁵. From a clinical practice viewpoint, it should be mentioned that both hypothyroidism and hyperthyroidism are accompanied by remarkable alterations in the metabolism of water and electrolyte^{6,7}. The decline in kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of TH⁸.

Nephrotic syndrome is also associated with changes in serum thyroid hormone levels⁹⁻¹². Urinary losses of binding proteins, such as Thyroxine Binding Globulin

(TBG) transthyretin or prealbumin, albumin and TH binded to them, result in a reduction in serum total thyroxine (T_4) and sometimes, in total T_3 levels. These hormonal changes are related both to the degree of proteinuria and to serum albumin levels. However patients often remain euthyroid, because free T_4 and T_3 levels are usually normal. This suggests that thyroid is able to compensate for hormonal urinary losses keeping the patient euthyroid. However, in patients with low thyroid reserve overt hypothyroidism can develop. Nephrotic syndrome may increase the exogenous levothyroxine needs in patients with hypothyroidism^{13,14}.

This study is to find out thyroid hormone status of idiopathic nephrotic syndrome patients at diagnosis, compare the thyroid function after treatment with steroid, correlate with serum albumin and compare the thyroid function with control group.

MATERIALS AND METHODS

This was analytic type cross sectional study conducted from May, 2011 to November, 2011 at the Paediatric Ward, Chattogram Medical College Hospital, Chattogram. Idiopathic nephrotic syndrome cases aged 2-6 years with typical presentation, diagnosed by positive heat coagulation test, low serum albumin (<2.5g/dl) and high serum cholesterol (>250 mg/dl) first morning protein creatinine ratio (>2 mg protein/mg creatinine) or 24 hours total urinary protein (>40mg/m²/hr) were included in this study. Children less than 2 yrs of age and more than 6 yrs of age, nephrotic syndrome due to secondary causes and nephrotic syndrome with atypical presentation like hypertension, gross haematuria were excluded. Informed written consent was taken from parents or legal guardian of these patients for serum T_3 , T_4 , TSH test to be done. Heat coagulation test was done and interpretation was recorded in every patients. After confirmation of diagnosis, blood was sent for serum T_3 , T_4 , TSH and results were recorded in data collection sheet and steroid started according to standard regimen. For initial attack – 60 mg/m²/day in two divided dose for 6 weeks followed by 40mg/m²/day single morning dose alternate day for 6 weeks. These patients were categorized as Group A. 1 case in group A dropped out from the study who was found hypothyroid. After completion of 3 months treatment again serum T_3 , T_4 , TSH was done only in those patients who were found hypothyroid. For control group cases were taken from NMC, Chattogram of same age group who came to do thyroid screening during study period. These patients were categorized as Group B. Data were analyze by IBM SPSS v.18.0. Z test, χ^2 test, student t test and Mann-Whitney U test and other test of significance was done where applicable to compose data. $p < 0.05$ was used as the minimum level of significance.

RESULTS

Total 32 nephrotic patients were included in Group A (Nephrotic children) and 26 cases in Group B (Control group). Mean age of our nephrotic children (Group A) and control group (Group B) was 4.53 (± 1.34) years and 4.04 (± 1.15) years that was not statistically significant ($p > 0.05$). Gender was matched in study subjects and control group (71.9% vs 53.8%, $p > 0.05$) (Table I).

Table I : Distribution of sex in both the study groups

SEX	Study Groups						χ^2 value	p value
	Group A		Group B		Total			
	n	%	n	%	n	%		
Male	23	71.9	14	53.8	37	63.8	2.019	$p > 0.05$
Female	9	28.1	12	46.2	21	36.2		
Total	32	100.0	26	100.0	58	100.0		

Mean serum albumin was 1.81 (± 0.44) gm/l and mean protein creatinine ratio was 4.85 (± 0.81). More than half (53.1%) of Group A (Nephrotic children) patients was found hypothyroid whereas only 19.2% of Group B (Control group) patients was hypothyroid that was statistically significant (p value = 0.008) (Table II). 1 case in Group A dropped out from the study who was found hypothyroid. Mean Serum T_3 , Serum T_4 , Serum TSH of Group A ($n = 32$) were 1.21 (± 0.63) nmol/L, 58.25 (± 35.39) nmol/L, 5.55 (± 3.20) nIU/L respectively whereas mean Serum T_3 , Serum T_4 and Serum TSH of Group B (Control group) were 2.11 (± 0.57) nmol/L, 114.56 (± 36.45) nmol/L, 3.08 (± 1.68) nIU/L respectively. Comparison between two groups was statistically significant ($p < 0.001$) (Table III).

Table II : Thyroid status on admission among the study groups

	Study Groups						χ^2 value	p value
	Group A		Group B		Total			
	n	%	n	%	n	%		
Euthyroid	15	46.9	21	80.8	36	62.1	7.000	Significant (< 0.01)
Hypothyroid	17	53.1	5	19.2	22	37.9		
Total	32	100.0	26	100.0	58	100.0		

Table III : Thyroid hormone assay on admission among the study groups

Thyroid Status on Admission	Study Groups	n	MEAN	\pm SD	MEDIAN	RANGE	SIGN.
Serum T_3 (nmol/L)	Group A	32	1.21	0.63	1.20	0.16 – 2.44	$t = 4.648$ $p < 0.001$
	Group B	15	2.11	0.57	1.90	1.38 – 3.06	
Serum T_4 (nmol/L)	Group A	32	58.25	35.39	55.00	12 – 150	$t = 5.343$ $p < 0.001$
	Group B	18	114.56	36.45	119.00	66 – 163	
Serum TSH (nIU/L)	Group A	32	5.55	3.20	4.68	0.47 – 12.03	$t = 3.781$ $p < 0.001$
	Group B	26	3.08	1.68	2.76	0.48 – 6.25	

Among hypothyroid cases ($n = 16$) before treatment mean Serum T_3 , mean Serum T_4 and mean Serum TSH were 0.76 (± 0.28) nmol/L, 32.87 (± 18.84) nmol/L and 7.55 (± 2.49) nIU/L respectively. After treatment with steroid, mean Serum T_3 , mean Serum T_4 level significantly increased and mean Serum TSH significantly reduced that became 2.32 (± 0.71) nmol/L, 124.06 (± 40.62) nmol/L and 2.45 (± 1.36) nIU/L respectively ($p < 0.001$ in comparison with group B. (Table IV).

Table IV : Thyroid hormone assay before and after treatment in hypothyroid cases

Thyroid Status in group A	n	MEAN	± SD	t value	p value	
Serum T ₃	Before Treatment	16	0.76	0.28	8.677	p< 0.001
	After Treatment		2.32	0.71		
Serum T ₄	Before Treatment	16	32.87	18.84	9.015	p< 0.001
	After Treatment		124.06	40.62		
Serum TSH	Before Treatment	16	7.55	2.49	8.351	p< 0.001
	After Treatment		2.45	1.36		

There was significant correlation between serum albumin (1.81±0.44 gm/l) and thyroid hormone (T₃ 1.21 ±0.63 nmol/L, T₄ 58.25 ±35.39 nmol/L, 5.55 ±3.20 mIU/L) of Group A (Nephrotic children) on admission (For T₃=p<0.05, T₄=p<0.01, TSH=p<0.001). (Table V, Figure 1, 2, 3).

Table V : Correlations between serum albumin and thyroid hormones in the study groups A

Correlations Between	n	Pearson's Coefficient (r)	p
Serum Albumin Serum T ₃ on Admission	32	0.415	p<0.05
Serum Albumin Serum T ₄ on Admission	32	0.519	p<0.01
Serum Albumin Serum TSH on Admission	32	-0.610	p<0.001

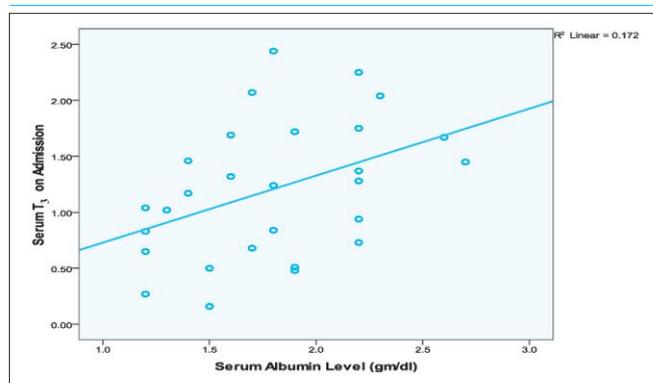


Figure 1 : Scatter plots showing correlation between serum albumin and serum T₃ in the study groups A

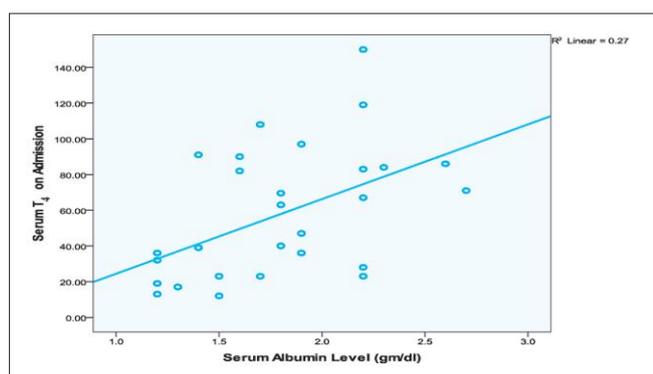


Figure 2 : Scatter plots showing correlation between serum albumin with serum T₄ in the study Group A

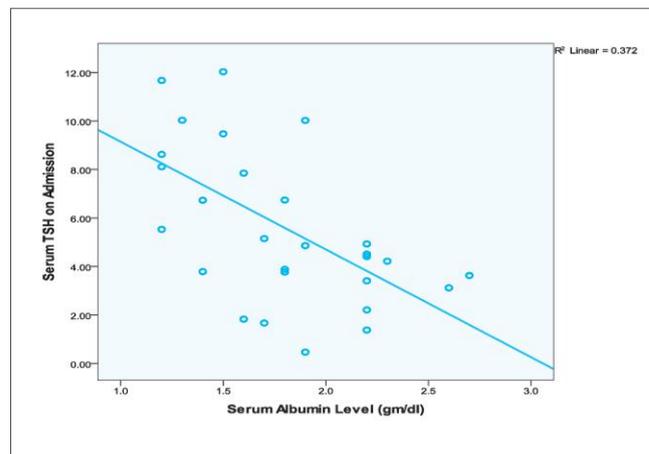


Figure 3 : Scatter plots showing correlation between serum albumin with serum TSH in the study Group A

DISCUSSION

Nephrotic syndrome is associated with changes in serum thyroid hormone levels. Urinary losses of binding protein and thyroid hormone bind to them, result in a reduction in serum total Thyroxine (T₄) and total T₃ levels. These hormonal changes are related both to the degree of proteinuria and to serum albumin levels. However patient often remain euthyroid, because free T₄ and T₃ levels are usually normal. In this study we have observed this status of thyroid function with idiopathic nephrotic syndrome at initial diagnosis, compare the thyroid function after treatment with control group, compare the thyroid function after treatment with steroid and correlate with serum albumin level.

In this study, male preponderance was noted like many other studies¹⁵. More than half (53.1%) of nephrotic children were hypothyroid similar to Nuhad Ismail¹⁶. Due to urinary losses of Thyroxine Binding Globulin (TBG) and other thyroid binding protein (transthyretin and albumin) and thyroid hormone bound to them result in a low total concentrations.

After treatment with steroid, nephrotic children with hypothyroid state became euthyroid. This findings is consistent with the results of RD Utigel¹⁷. This may be due to the repaired glomerular filtration barrier after treatment that results in reduced proteinuria and so increased serum protein binding of thyroid hormone after the rise of protein level.

We found a positive correlation between serum albumin and serum T₃, T₄, TSH. RD Utigel in his study conducted in England found decreased serum T₃, T₄ and increased serum TSH in relation to serum albumin which is consistent with this study¹⁷.

As it has been stated earlier the research hypothesis, children suffering from nephrotic syndrome have significant thyroid hypofunction due to low serum albumin level because of massive proteinuria has been established with the study.

CONCLUSION

Considering all above finding it may be concluded that children suffering from idiopathic nephrotic syndrome have significant thyroid hypofunction because of low serum albumin. This hypofunction is transient as treatment with steroid thyroid function becomes normal.

RECOMMENDATIONS

Though significant thyroid hypofunction was found in idiopathic nephrotic syndrome patients on initial diagnosis, when proteinuria resolved they became euthyroid. As in the present study sample size small, larger further study is recommended to find out the clinical correlation of nephrotic syndrome patient with thyroid function.

DISCLOSURE

All the authors declared no competing interest.

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