
Nephrotic Syndrome and Hypertension

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Abstract:

Background: Primary nephrotic syndrome (NS) is characterized by massive proteinuria and hypoalbuminemia leading to edema. Hyperlipidemia, hypercholesterolemias are usually associated. Minimal change disease accounts for approximately 85% of cases less than seven years of age. This condition is characterized by a predictable and gratifying response to steroids and an excellent long-term prognosis.

Aims of study: To study the relative frequency of hypertension in children with NS, and determine the complication rates.

Methods: This prospective study was carried out in Nephrology Department at central pediatric teaching hospital and a total of (71) patients with nephrotic syndrome diagnosed and/ or treated and followed up in the pediatric nephrology consultation clinic through, clinical examination and investigation (GUE, CBP and others) that was carried out over 7 months period from 15th of Jan. 2008 to 15th of July 2008. Patients with congenital nephrotic syndrome were excluded from the study.

Results: The total number of patients enrolled during the study period was 71. Males (46) and females (25) with male to female ratio 1.8:1. Age range between 1-18 years. A total of 50 patients (70%) (Male and female) were in the age group 1-5 years, followed by 17(23.9%) in the age group (6-10) and 4(5.6%) in age group > 10 years. According to sex distribution of the patients with nephrotic syndrome in relation to hypertension in which it presented in 18 males, 4 patients (5.6%) developed HT at initial attack and 14 patients (19.7%) later on, while in females 10 patients developed HT, 1 patient (1.4%) initially and 9 patients (12.7%) later on. The numbers of patients presented with initial attack 9(12.7%), infrequent relapses were present in 20(28.2%), while frequent relapses presented in 42 patients (59.2%). Steroid therapy was given to all patients with initial attack and relapses. Steroid sensitive nephrotic syndrome was found in 33 (46.5%), steroid dependent nephrotic syndrome and steroid resistant nephrotic syndrome in 28 (39.4%) and 10(14.1%) respectively. Hypertension was presented in 5 patients (7%) with initial attack, 23 patients (32.4%) developed hypertension later. While in later hypertension, 4 patients (5.6%) with infrequent relapses found to be hypertensive and 16 patients (22.5%) with frequent relapses had hypertension, and only 3(4.2%) with no relapse had hypertension. Hypertension was found in 5 patients (7%) with steroid sensitive nephrotic syndrome, 9 patients (12.6%) with steroid resistant nephrotic syndrome and 14 patients (19.7%) with steroid dependent nephrotic syndrome. Abnormal renal function was presented in 8 cases (11.26%), only 2 cases (2.8%) of them developed hypertension later on. Acute renal failure was reported in 3 cases (4.20%), 42 patients (59.20%) had urinary tract infection, one patient (1.40%) developed thrombosis, peritonitis was reported in 4 cases (5.6%) and respiratory tract infection was reported in 9 cases (12.70%). Family history of hypertension was reported in 4 cases (5.6%). Family history of renal problems were reported in 8 cases (11.3%) .

Conclusions: Hypertension in patients with nephrotic syndrome presented in males more than females and is more in patients with frequent relapses and in steroid dependent nephrotic syndrome and steroid resistant nephrotic syndrome. Urinary tract infection was the most common complication.

Keywords:

Introduction:

The nephrotic syndrome (NS) is a clinical entity characterized by massive loss of urinary protein (primarily albuminuria) leading to hypoproteinemia (and hypoalbuminemia) and its result edema.

Hyperlipidemia, hypercholesterolemia, and increased lipiduria are usually associated.

NS generally has a glomerular cause and is currently categorized into primary and secondary forms.^[1,2]

Useful definitions: Nephrotic syndrome: Edema, plasma albumin < 2.5 g /dl. Proteinuria > 40 mg / m 2/ hr. or protein/ creatinine ratio > 200 mg/ mmol^[1]

Remission: urinary protein excretion < 4 mg/ m2/hr or Albustix = o / trace for 3 consecutive days.^[1]

Steroid responsive: remission achieved with steroid therapy alone.^[1]

Late responder: remission occurring after 4 weeks prednisolone 60 mg/m2/daily without other drugs.^[1]

Relapse:

Urinary protein excretion > 40 mg/hr/m2 or albustix = ++ or more for 3 consecutive days plus edema, having previously been in remission^[1] .

Frequent relapses: two or more relapses within 6 months of initial response or 4 or more relapses within any 12 months period.^[1]

Steroid dependence: two consecutive relapses occurring during corticosteroid treatment or within 14 days of its cessation.^[1]

Steroid resistance: children who fail to respond to prednisone therapy within 8 wks.^[1]

Aim of study:

*To study the relative frequency of HT in children with nephrotic syndrome.

*To determine complication rates in NS.

Patients & Methods:

Subjects:

This prospective study was carried out in Nephrology Department at central pediatric teaching hospital and a total of (71) patients with nephrotic syndrome diagnosed and/ or treated and followed up in the pediatric nephrology consultation clinic through, clinical examination and investigation (GUE, CBP and others) that was carried out over 7 months period from 15th of Jan. 2008 to 15th of July 2008. Patients with congenital nephrotic syndrome were excluded from the study.

Information about the patients were collected and recorded, which include the following information:

1-Age, sex, time of diagnosis, clinical presentation, predisposing factor.

2-Relapse, family history of NS, family history of HT, drug history.

3-Investigations, treatment, complications.

Technique of blood pressure measurement:

Indirect technique: Auscultation method.

Instrument of measurement of blood pressure:

Mercury gravity manometer (Table A and B).

Statistical analysis:

Using chi-square to evaluate if there statistical significant relationship between age, sex, frequency of relapses, steroid responsive and chemotherapy treatment of patients with nephrotic syndrome and hypertension.

Results:

The total number of patients enrolled during the study period was 71. Males (46) outnumbered females (25) with male to female ratio 1.8:1

Age range between 1-18 years. A total of 50 patients (70%) (Male and female) were in the age group 1-5 years, followed by 17(23.9%) in the age group (6-10) and 4(5.6%) in age group > 10 years.

Table (1)

Hypertension was presented in 5 patients (7%) with initial attacks, 23 patients (32.4%) developed hypertension later. As shown in **figure (1)**.

Table (1): The age at time of diagnosis and sex distribution of patients with nephrotic syndrome

Age at time of diagnosis (years)	Sex					
	Female		Male		Total	
	No	%	No	%	No	%
1-5 years	14	19.7%	36	50.7%	50	70.4%
6-10 years	8	11.26%	9	12.7%	17	23.9%
>10 years	3	4.2%	1	1.4%	4	5.6%
Total	25	35.2%	46	64.8%	71	100.0%

-Not significant (P=0.084)

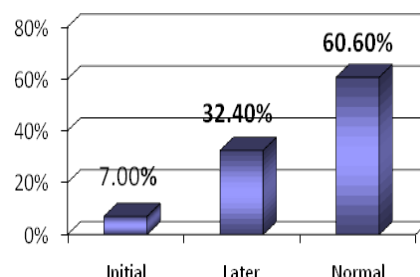


Figure (1): The blood pressure in patients with nephrotic syndrome.

HT was observed in 5 cases (7%) of steroid sensitive nephrotic syndrome, following by 9 cases (12.7%) with steroid resistant nephrotic syndrome and 14

cases (50.0%) in steroid dependent nephrotic syndrome patients. As shown in **table (2)**.

Table (2): Types of steroid response in patients with nephrotic syndrome according to blood pressure status.

The steroid response	Blood pressure status			
	Hypertension		Normal	
	No	%	No	%
Dependent	14	19.7	14	19.7
Resistant	9	12.7	1	1.4
Sensitive	5	7	28	39.4
Total	28	39.4	43	60.6

-Highly significant (P=0.0001).

According to age, sex distribution of the patients with nephrotic syndrome in relation to hypertension in which it presented in 18 males, 4 patients (5.6%) developed HT at initial attack and 14 patients (19.7%) later on, while in females 10 patients developed HT, 1 patient (1.4%) initially and 9 patients (12.7%) later on.

High blood pressure was reported in age group (1-5) years in 20 cases, initially 3 (4.2%) and 17 (23.9%) later while in age group (6-10) years it reported in 6 cases, 2 (2.8%) initially and 4 (5.6%) later. In age group >10

years it reported in 2 cases (2.8%) which presented later. As shown in **table (3)**.

Five patients with initial attacks were hypertensive, 4 patients (5.6%) with frequent relapses found to be hypertensive initially, and 16 patients (22.5%) later on. With infrequent relapses hypertension found in 4 patients (5.6%) who developed HT later on and in patients with no relapses HT presented with one patient with initial attack (1.4%) and 3 (4.2%) later on. As shown in **table (4)**.

Table (3): The age at time of diagnosis and sex distribution of patients with nephrotic syndrome according to high blood pressure.

		Blood pressure status						χ^2 ;d.f.;P
		High blood Pressure		Normal				
		Initial		Later				
		No	%	No	%	No	%	
Age at time of diagnosis (years)	1-5 years	3	4.2	17	23.9	30	42.2	1.857; 4; 0.762
	6-10 years	2	2.8	4	5.6	11	15.5	
	>10 years	-	-	2	2.8	2	2.8	
Sex	Female	1	1.4	9	12.7	15	21.1	0.664; 2; 0.717
	Male	4	5.6	14	19.7	28	39.4	

Table (4): The distribution of relapses in patients with nephrotic syndrome according to high blood pressure.

Number of relapses	High blood Pressure						χ^2 ;d.f.;P
	Initial		Later		Normal		
	No	%	No	%	No	%	
Frequent	4	5.6	16	22.5	22	30.9	5.109; 4; 0.276
Infrequent	-	-	4	5.6	16	22.5	
No relapse	1	1.4	3	4.2	5	7	

Hypertension was found in 5 patients (7%) with steroid sensitive nephrotic syndrome at late presentation, while 2 patients (2.8%) with steroid resistant nephrotic syndrome and 3 patients (4.2%) with steroid dependent nephrotic syndrome developed

HT at initial attacks and 7 (9.8%) of steroid resistant, 11 patients (15.5%) of steroid dependent developed HT later on respectively (p value 0.0001 highly significant).

Chemotherapy with alternative day steroid was prescribed for (13) patients: 3(30.0%) steroid resistant nephrotic syndrome, 8(28.6%) steroid dependent nephrotic syndrome and 2 (6.1%) steroid sensitive nephrotic syndrome, ten(14%) of them developed hypertension. Thirteen patients (22.4%) who were

treated with steroid alone developed HT later on (p value 0.001 significant). As shown in **table (5)**.

Histological characters of the patients who are hypertensive and with normal BP are shown in **table (6)**.

Table (5): The steroid and chemotherapy response distribution of patients with nephrotic syndrome according to high blood pressure.

The steroid response	High blood Pressure						χ^2 ;d.f.;P
	Initial		Later		Normal		
	No	%	No	%	No	%	
Dependent	3	4.2	11	15.5	14	19.7	21.00; 4; 0.0001*
Resistant	2	2.8	7	9.8	1	1.4	
Sensitive	-	-	5	7	28	39.4	
Treatment Chemotherapy & steroid	-	-	10	14	3	4.2	14.554; 2; 0.001*
Steroid	5	7	13	22.4	40	69.0	

Table 6: Renal biopsy of patients with nephrotic syndrome according high blood pressure.

Biopsy	High blood Pressure					
	Initial		Later		Normal	
	No	%	No	%	No	%
Minimal change nephrotic syndrome	-	-	5	7	-	-
Focal segmental glomerulosclerosis	2	2.8	3	4.2	2	2.8
Membranoproliferative glomerulonephritis	-	-	2	2.8	-	-

Acute renal failure was reported in 3cases (4.20%), 42 patients (59.20%) had urinary tract infection, one patient (1.40%) developed thrombosis, peritonitis was

reported in 4 cases (5.6%) and respiratory tract infection was reported in 9cases (12.70%) . As shown in **figure (2)**.

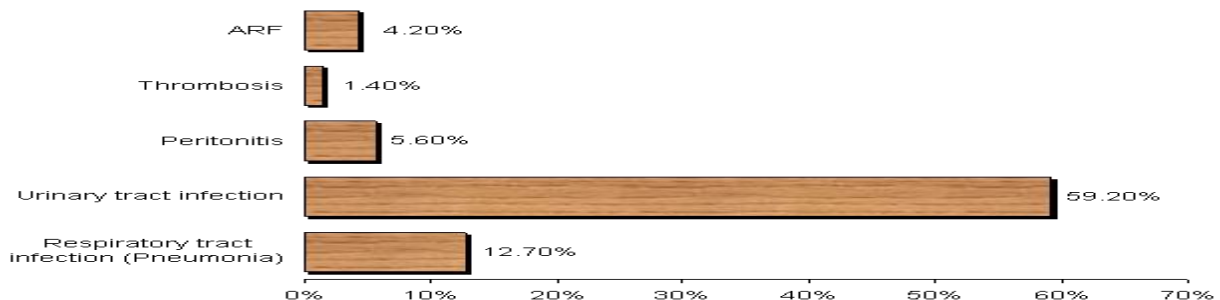


Figure (2): The complication of patients with nephrotic syndrome (some patients developed more than one complication).

Discussion:

Nephrotic syndrome remains a major cause of referral to pediatric nephrologists because of the chronicity of the disorder and the complexity of its evaluation.^[3]

In this study which included seventy one patients aged (1-18) years, male: female ratio was found to be 1.8:1. Consistent with epidemiologic findings in which NS is twice as prevalent in males as in New Jersey study.^[4]

Hypertension was found in patients with relapse and long time treatment with steroid. In this study 28 patients (39.4%) were hypertensive a figure higher than that found in Iranian and Jordanian study,^[5,6] which reported (15.6%) and (14.28%) hypertensive patients respectively, and lower than Ibadin MO, Abiodun PO study (41.4%) patients.^[7]

Steroid therapy was given to all patients with initial attack and relapses. Steroid sensitive NS was found in 33 cases (46.5%), SDNS and SRNS were found in 28 (39.4%) and 10 cases (14.1%) respectively. High prevalence of SSNS also found in Port Harcourt contrasts with earlier reports from other parts of Nigeria where poor response to steroid therapy was common.^[8,9]

Steroid and alkylating agents were used for 13 patients (18.3%) who had no response to steroid alone.

Ten (76.9%) of them developed hypertension.

This result is higher than Saudi Arabia study which recorded that cyclosporine causes HT in only (20%).^[10]

The frequency of hypertension was observed in 5 cases (7%) of SSNS, 9 cases (12.7%) with SRNS and

14 cases (19.7%) in SDNS patients (p value 0.0001 highly significant), these figures are higher than that of previous Iraqi study (2000) by AL-Mewashi H.H. Which reported (11.2%), (10.2%), (6.1%) of SSNS, SRNS, SDNS respectively.^[11]

Hypertension was found in 5 cases (7.0%) cases with initial attacks a figure lower than Amin study (16.0%),^[12] and in 23 cases (32.4%) as a complication which is higher than Iranian study (28%).^[5] Abnormal renal function was presented in 8 (11.26%) cases, two of them developed hypertension.

Some studies found that there is correlation between renal insufficiency and hypertension.^[13] In Anochie (Nigeria) study four patients from 28 developed HT and renal failure.^[14]

In this study, complications found in patients with nephrotic syndrome were: urinary tract infection was the most common complication which was recorded in 42 patients (59.20%). Acute renal failure was reported in 3 cases (4.20%), one patient (1.40%) developed thrombosis, peritonitis was reported in 4 cases (5.6%) and respiratory tract infection was reported in 9 cases (12.70%). In Ibadin MO, Abiodun PO study UTI was found in (44.6%) cases.^[7] Du DZ study showed that pulmonary arterial pressure was increased in the 17.5% of children with NS,^[15] with only one patient presented with deep venous thrombosis. The incidence is similar to previous reports.^[16,17,18] Renal failure was found in 14.2% cases in Anochie (Nigeria) study,^[14] which is higher than our study.

Family history of hypertension was reported in 4 cases (5.6%). Family history of renal problems were reported in 8 cases (11.3%).

followed up over long duration so encouragement and enforcement of patients for regular follow up in nephrology clinic and early recognition and treatment of long term complications.

*The clinician who cares for those children must strive to maintain difficult balance between therapeutic effectiveness while avoiding undesirable medical consequences.

Conclusions:

*The peak age incidence of NS is between 1-5 years with almost double frequency in males than females.

*Hypertension is found to be more in males than females especially in patients with initial presentations.

*Development of hypertension among frequent relapse patients and steroid dependent on maintenance steroid therapy was high that effective treatment of these patients is still far from optimal.

*Hypertension in SRNS is higher than that of SSNS.

*UTI is the most common complication.

Recommendation:

*BP measurement should be part of routine examination to any child attend nephrology consultation clinic or admitted to hospital.

*Children who developed hypertension during treatment or relapse indicate that NS should be

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