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Original Research Article

A STUDY TO ASSESS THE PREDICTORS OF RELAPSE WITH COMPLICATIONS IN CHILDREN WITH NEPHROTIC SYNDROME AT A TERTIARY CARE CENTRE

Jagadish Naidu Velamala[1], Ragam Shalini Yadav[1], Saritha Cheruku[2]

[1]*Assistant professor, Department of Pediatrics, Malla Reddy Medical College for Women, Suraram, Hyderabad, Telangana, India*
[2]*Assistant Professor, Department of Pediatrics, Patnam Mahender Reddy Medical College and Hospital, Chevella, Rangareddy, Telangana, India*

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Corresponding Author:
Dr. Jagadish Naidu Velamala,
Assistant professor, Department of Pediatrics, Malla Reddy Medical College for Women, Suraram, Hyderabad, Telangana, India
Email: jagdish.naidu95@gmail.com

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ABSTRACT

Background: Relapse is common even after treatment of nephrotic syndrome and it can go up-to 20, even after treated with steroids in first six months. It is associated with morbidity and there is heavy economic burden for patients as well as health care system. If we can predict relapse with complications, we can take necessary precautions to prevent it. The objective is to study predictors of relapse with complications in children with nephrotic syndrome at a tertiary care centre.

Materials and Methods: Single-centre, hospital-based, cross-sectional study carried out among 60 children 1-12 years with nephrotic syndrome. Detailed history, thorough clinical examination and necessary investigations were carried out. Weight, height, Dry weight, pulse, respiratory rate, capillary filling time, blood pressure was measured. Specific measurements of inferior vena cava (IVC) caliber diameter and Aorta diameter was measured using an Ultrasound.

Results: Most common complication was pneumonia in 20%. Mean age, Systolic and diastolic blood pressure, total proteins, albumin, weight, height, body surface area (BSA), inferior vena cava index, IVC diameter on expiration were significantly lower in relapse with complications group. But diameter of aorta was not significantly lower in relapse with complications group. The IVC/aorta ratio and the IVC/BSA ratio was significantly lower in relapse with complications group.

Conclusion: Children with low levels/values of age, Systolic and diastolic blood pressure, total proteins, albumin, weight, height, body surface area, inferior vena cava index, inferior vena cava diameter on expiration, IVC/aorta ratio and IVC/BSA ratio can be considered as high risk for development of relapse with complications.

Keywords: Inferior vena cava, fluid volume status, ultrasound.

INTRODUCTION

It has been estimated that the incidence of the nephrotic syndrome ranges from 1.15 to 16.9 for every one lakh children annually. It is the chronic kidney disease and the most common form of it. There is heavy proteinuria in the nephrotic syndrome which can go beyond 40 mg/m2/h. This leads to the depletion of albumin levels in the blood which in turn can lead to edema. At the same time, the serum total cholesterol also increases to more than 200 mg/dl.[1]

This heavy protein loss in the urine is because of changes in the glomerular basement membrane. Nephrotic syndrome in children is generally most of the time idiopathic. On histological examination, there are features suggestive of minimal change nephrotic syndrome. This occurs in majority (90%) of the cases. Relapse is common even after treatment of the patients. The number of relapses

can go up to 20 for each case of pediatric nephrotic syndrome, even after treated with steroids. Thus, the pediatric nephrotic syndrome is associated with a lot of morbidity. Hence, it is obvious that this condition is associated with lot of economic burden for the patients as well as burden for the existing health care system. Relapse of the case demands admission to the hospital. There is need to control the infections, manage the edema. Sometimes, kidney biopsy may be required.[2,3]

Some children with relapse of nephrotic syndrome can land into complications like pneumonia, infections, cataract, high blood pressure, acute kidney injury, shock, retardation of the growth etc.[4]

It is necessary to know factors that when present can give some idea (prediction) regarding occurrence of complications. But it may not be easy to predict the relapse in these cases. There is remission after appropriate treatment. However, relapse can occur in some cases. The incidence of relapse after treatment may be more than 50% in the first six months of treatment.[5]

If we can predict the relapse with complications, we can take necessary precautions to try to prevent it in children with nephrotic syndrome. Hence, present study was carried out to study the predictors of relapse with complications in children with nephrotic syndrome at a tertiary care centre.

MATERIALS AND METHODS

Present study was a single centre, hospital based, cross sectional study carried out over a period of two years at the Department of Pediatrics among 60 children of age 1-12 years with nephrotic syndrome. Institution Ethics Committee permission was obtained vide letter number IEC/GMC/2020/12/01, dated 2-12-2020. Child assent was taken from the parents/guardian of the children.

Children of age 1-12 years of age of either gender, diagnosed with typical nephrotic syndrome with relapse were included in the present study.

Early case of nephrotic syndrome was defined as those children who were diagnosed with typical nephrotic syndrome in the last 10 days. Relapse case was defined as those having the value of urine albumin as 3+ or more for three consecutive days. Remission was defined as those having the value of the urine albumin as less than four mg/m2/hr for three consecutive early morning specimen. Complicated nephrotic syndrome was defined as those who in addition to nephrotic syndrome had any one of the following: infections, shock, respiratory distress, renal insufficiency, thromboembolism.

This children in whom it was difficult to measure the calibre of inferior vena cava (IVC), those who never had natural consequences of disease, those on ventilator and those who had a combination of nephritic-nephrotic pathologies were excluded from the present study.

For each case, detailed history, thorough clinical examination and necessary investigations were carried out. The data was recorded in the pre-designed, pre-tested, semi-structured study questionnaire. Weight and height were taken. Dry weight of the patient also noted. Pulse, respiratory rate, capillary filling time (CFT), blood pressure (BP) was measured. Shock was defined clinically as tachycardia, prolonged CFT, cold/pale skin, weak pulses and low blood pressure. Specific measurements of IVC caliber diameter and Aorta diameter were measured using an Ultrasound by the Investigator under supervision by a Radiologist as per the standard guidelines and procedures.

The data was entered and analysed using the SPSS version 22. (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). The categorical data was expressed as proportions and the continuous data as mean with its standard deviation. For proportions, chi square test and for comparison of mean in two groups, independent samples to test were used. P value of less than 0.05 was considered as statistically significant.

RESULTS

Out of 78 cases eight were excluded as they were either not cooperative or lost to follow up. In remaining 70 cases, 10 were again excluded as they were not the typical cases of nephrotic syndrome. In remaining 60 cases, 30 were with complications and 30 were without complications.

Table 1: Secondary complications of nephrotic syndrome

Complications	Number	%
Pneumonia	12	20
High systolic blood pressure	9	15
Acute kidney injury	5	8
Urinary tract infection	4	7
No complications	30	50
Total	60	100

Table 2: Comparison of Clinico demographical parameters in two groups.

	Relapse without complications (N=30)	Relapse with complications (N=30)	P
Age (years)	8.58 ± 4.89	5.15 ± 3.47	0.003
Sex	M =15, F = 15	M =15, F = 15	1
Pulse per min	94.67 ± 14.91	113.70 ± 16.12	0.000
Systolic blood pressure (mmHg)	104.17 ± 8.04	98.63 ±12.07	0.003
Diastolic blood pressure (mmHg)	70.10 ± 7.07	60.67 ± 10.74	0.004
Total proteins (g/dl)	4.11 ±.74	3.88 ± .71	0.223
Albumin (g/dl)	2.37 ±0.81	2.12 ±0.78	0.065
Weight (kg)	25.86 ± 6.91	16.16 ± 4.89	0.010
Height (cm)	120.13 ± 25.20	103.22 ± 21.34	009
Body surface area (BSA) (m2)	0.908 ± .156	0.75 ± .25	0.009
Inferior vena cava (IVC) index (%)	7.94±1.61	5.25±2.06	0.040
Inferior vena cava diameter on expiration (mm)	10.76±2.43	7.13±2.60	0.000
Diameter of aorta (mm)	11.44±2.7	10.21±2.24	0.085
IVC/aorta	0.84±0.13	0.70±0.15	0.000
IVC/BSA	11.48±2.23	9.99±2.52	0.019

Most common complication with which the children presented in the present study was pneumonia in 20% of the cases followed by hypertension in 15% of the cases. Acute kidney injury was seen in 8% of the cases and 7% had urinary tract infection. [Table 1]

Mean age was significantly lower in complications group compared to no-complications group. Males and females were equal in two groups. Systolic and diastolic blood pressure was significantly lower in the relapse with complications group. Total proteins and albumin were also significantly lower in the relapse with complications group. Weight and height were significantly lower in the relapse with complications group. Body surface and inferior vena cava index were significantly lower in the relapse with complications group. Inferior vena cava diameter on expiration was significantly lower in the relapse with complications group. But the diameter of aorta was not significantly lower in the relapse with complications group. The IVC/aorta ratio and the IVC/BSA ratio was significantly lower in the relapse with complications group. [Table 2]

DISCUSSION

Most common complication with which the children presented in the present study was pneumonia in 20% of the cases followed by hypertension in 15% of the cases. Acute kidney injury was seen in 8% of the cases and 7% had urinary tract infection. Mean age was significantly lower in complications group compared to no-complications group. Males and females were equal in two groups. Systolic and diastolic blood pressure was significantly lower in the relapse with complications group. Total proteins and albumin were also significantly lower in the relapse with complications group. Weight and height were significantly lower in the relapse with complications group. Body surface and inferior vena cava index were significantly lower in the relapse with complications group. Inferior vena cava diameter on expiration was significantly lower in the relapse with complications group. But the diameter of aorta was not significantly lower in the relapse with complications group. The IVC/aorta ratio and the IVC/BSA ratio was significantly lower in the relapse with complications group.

Bharati J et al,[6] carried out an observational study among children of age less than 15 years to study the long-term complications of nephrotic syndrome. They defined the childhood nephrotic syndrome as diagnosis of nephrotic syndrome below the age of 10 years. They studied incidence of obesity, failure to thrive, hypertension, low bone mineral density and increased carotid intima media thickness as long-term complications of nephrotic syndrome among 101 cases. In this, 89.1% of the cases had long term complications. Obesity was seen in 22.7% of the cases. Failure to thrive was seen in 31.7% of the cases. 53.5% of the cases had low bone mineral density. Hypertension was found in 31.7% of the cases. Increased carotid intima media thickness was seen in 50.5% of the cases. The authors concluded that majority i.e. 90% had long term complications and the most common complication was low bone mineral density in 53.5% of the cases.

Karakaya D et al,[7] from Turkey carried out hospital-based study among 411 cases of idiopathic nephrotic syndrome in children. They found that the incidence of complications was 31.1%. They also observed that the mean age was 7.54 years and the males and females were almost equal. These findings are in accordance with the findings of the present study. 96.9% of the complications were related to the disease. 50.8% of the complications were related to the treatment. The significant risk factors for occurrence of the complications were increased levels of protein in urine, low rate of glomerular filtration, and being female. 7% of the cases had chronic kidney disease. End stage renal disease was seen in 2.9% of the cases. The authors concluded that those cases with pediatric idiopathic nephrotic syndrome should be carefully monitored. This will help to improve the outcome in the long term.

Skrzypczyk P et al,[8] included 118 adults in their study. These cases had idiopathic nephrotic syndrome in their childhood. In these, 61 responded. In these 61 people the age of onset of the nephrotic

syndrome ranged from 1.3 years to 14 years. Overall, they had about five relapse of disease below the age of 18 years. 60.7% had steroid sensitive nephrotic syndrome. 29.5% of the cases had steroid dependent nephrotic syndrome. 9.8% of the cases had steroid resistant nephrotic syndrome. 35.7% of the cases showed mesangial proliferation in biopsy. All cases by the age of their 18 years, had normal renal function. The relapse rate after the age of 18 was 16.4% of the cases. Those who had more relapses below the age of 18 years were at more risk of relapse of the disease after the age of 18 years. Most common long-term complications observed in these 61 cases were hypertension in 16.1% of the cases. The idiopathic nephrotic syndrome was found to affect the height in five cases. They concluded that a greater number of relapse for idiopathic nephrotic syndrome was a significant risk factor for relapse in the adult life.

Mishra R et al,[9] studied 100 pediatric cases of age one year to 12 years who were cases of steroid sensitive nephrotic syndrome. Those who had infection while initial attack of the disease was more likely to relapse. Another risk factors was lack of time gap between first episode and first relapse. If the treatment was not taken properly, it was a risk factor for relapse. High levels of cholesterol and low levels of albumin were also found to be important risk factors of relapse.

One study from China,[10] included results from nationwide survey in 37,134 children of age less than 18 years of age. They found that 20% of the cases had primary nephrotic syndrome. Males were three times more than females. But, in the present study, we found that the males and females were equal. This is because of purposive sampling used in the present study where we put equal number of males and females in each group. Simple nephrotic syndrome was seen in 85.5% of the cases. 14.5% of the cases had nephritic nephrotic syndrome. Relapse was seen in 28.2% of the cases. 5.9% had steroid dependent nephrotic syndrome. 20.1% of the cases had frequently relapse nephrotic syndrome. 87.5% of the cases had heavy proteinuria. They concluded that first episode cases were most common.

Behera MR et al,[11] carried out hospital-based study in 53 children of age 1-15 years. The relapse rate in their study was found out to be 47%. Among these relapse cases, males were more than females. But, in the present study, we found that the males and females were equal. This is because of purposive sampling used in the present study where we put equal number of males and females in each group. Both the groups viz. first episode group and the relapse group presented with similar clinical manifestations. The serum albumin was lower in the relapse group and this finding is in accordance with the finding of the present study. 59% of the cases had levels of serum albumin of less than 1.8 g/dl. 41% of the cases had shown remission within two weeks of treatment.

Limitations: Present study was single centre with small sample size and hence the external validity of the study is limited. However, the present study throws light on some important aspects of this condition for which more studies with sufficient sample size may be required.

CONCLUSION

Children with low levels/values of age, Systolic and diastolic blood pressure, total proteins, albumin, weight, height, body surface area, inferior vena cava index, inferior vena cava diameter on expiration, IVC/aorta ratio and IVC/BSA ratio can be considered as high risk for development of relapse with complications.

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