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ORIGINAL ARTICLE

Prevalence of Infection and Changing Pattern of Organisms Causing Infections in Childhood Nephrotic Syndrome

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Abstract

Background: *Infection remains an important complication of children with nephrotic syndrome. It results in significant morbidity and may also be responsible for a poor response to steroid therapy or induce relapse in child who has already attained remission.*

Objectives: *This study was conducted to find out pattern of infection and type of organisms causing infections in nephrotic syndrome.*

Methods: *This cross sectional study was conducted in the Paediatric Nephrology Department of Dhaka Shishu (Children) Hospital from January 2010 to November 2010. One hundred fifteen (115) cases of nephrotic syndrome, age between 1 to 13 years were enrolled according to the inclusion criteria. Along with routine investigations, urine, blood and throat swab culture and sensitivity and MT test were done. Risk factors of infection were also determined. Statistical analysis was done by SPSS version 12. Level of significance was taken as <0.05.*

Results: *Prevalence of infection in nephrotic syndrome was 54.78%. Infections were more common in childhood nephrotic syndrome below 6 years of age. Infections encountered in nephrotic syndrome were UTI 51(44.34%), septicemia 4(3.47%), pneumonia 5(4.34%), peritonitis 1(0.87%), cellulitis 1(0.87%) and tuberculosis 1(0.87%). Statistically significant risk factors associated with infection were generalized edema, steroid dependence, steroid resistance, persistent proteinuria and high spot urine protein creatinine ratio. In case of UTI E. coli was the commonest 27(52.9%) organism followed by Morganella and Pseudomonas 5(9.8%).*

Conclusion: *Prevalence of infection in nephrotic syndrome is very high and E. coli is the commonest organism found in this study. Generalized edema, persistent proteinuria, hypoalbuminemia, steroid dependence, steroid resistance are important risk factors for infection.*

Keywords: *Prevalence, infection, organisms, childhood nephrotic syndrome.*

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Introduction

About one third of every nephrotic syndrome admission was due to an infection. In a study the rate of infection was 38%.[1] A recent study by Moorani et al[2] points to URTI, cellulitis, diarrhoea UTI and peritonitis as the most frequent infections. In the various published results, the type of infection is variable.[3] In a study conducted by Senguttuvan et al[4] found UTI is the commonest infection followed by peritonitis, acute RTI and tuberculosis. Regarding bacteriology of UTI, 76.7% urine cultures are positive and 23.3% are culture negative. Regarding causative organisms, E.coli was the commonest organisms (36.6%) followed by Klebsiella (27.5%). This varies from the study by Gulati et al. where E. coli was responsible for 60% cases and non E. coli organisms accounted for 39% of the culture isolates in UTI.[5] In children with nephrotic syndrome serious infection may be acute and fulminate and manifest with vague or nonspecific features, which may delay an early diagnosis.[6] Because fever and physical findings may be minimal in the presence of corticosteroid therapy. A high index of suspicion, prompt evaluation and early initiation of antibiotic therapy are critical.[7] Occult infections may manifest as a steroid non response or relapse in a child who has already attained remission.

Therefore it is essential to know the current trend of prevalence of infection in children with nephrotic syndrome, the organisms prevalent in our set up to decide about appropriate antibiotics, duration of treatment, and to observe the response of treatment and how quick patients enter into remission. The knowledge of the etiological profile of infection in nephrotic children will help to raise the awareness level of treating physicians so that avoidable infectious process could be minimized. It is important to know the infectious agents and their sensitivity pattern among the nephrotic patients who are already immunocompromized and also need treatment with immunosuppressive agents. Different study conducted in both developed and developing countries showing different prevalence rate for different type of infections and changing organisms are also found. There is also a changing pattern of antibiotics sensitivity.

There is overcrowding, malnutrition, increased prevalence of infections in Bangladesh and patients with nephrotic syndrome are immunocompromised. So the study is designed to find out the type of infections and their changing pattern of sensitivity to antibiotics to reduce the morbidity and mortality.

Materials and Methods

This cross sectional study was conducted in the Pediatric Nephrology Department of Dhaka Shishu (Children) Hospital from January 2010 to November 2010. Prior to the commencement of this study the research was approved by the Institutional Ethical Review Committee. All Nephrotic Syndrome patients admitted in hospital during study period were included in the study. Critically ill patients having respiratory distress, children with ARF/CRF/Urogenital anomalies were excluded from the study. Risk factors of infection were also determined.

Thorough history taking and elaborate clinical examination was performed and recorded on an appropriate questionnaire. Routine investigations like urine microscopy, urine culture, spot urine protein creatinine ratio, lipid profile, complete blood count (CBC) with examination of the blood film, platelet count, ESR, serum total protein (STP), serum albumin, serum electrolytes, blood urea, serum creatinine and ultra sonography of KUB region were done in all patients. Renal biopsy was done in cases where there were indications like: persistent hematuria, persistant hypertension, hypocomplementemia, impaired renal functions, frequently relapsing nephrotic syndrome (FRNS) with steroid toxicity, FRNS with steroid dependence, steroid non responders.

HBsAg and anti HCV was performed in all patients by ELISA. These children were screened for other infections by one or more of the following investigations as needed: peritoneal fluid and cerebrospinal fluid examination (Gram stain, cytology, biochemistry and culture); chest X-ray.

Along with routine investigations, urine culture and sensitivity, blood culture and sensitivity, throat swab culture and sensitivity, MT test was done. Urine specimens were collected under the direct supervision of staff nurse or doctor after proper cleaning of the genital area with soap and water thoroughly. In case of boys the glance was washed by retracting the foreskin and in case of girls urine was collected after washing the vulva with their legs and labia apart. Clean catch, freshly voided, midstream urine was collected in a sterile container and were transferred to the laboratory and was subjected to microscopy as early as possible. Urine and blood culture was done on blood agar and McConkeys agar media. A positive urine culture was defined as midstream clean voided specimens with isolation of $>10^5$ CFU/ml of a single organism. When the colony count was $<10^4$ organisms/ml, or when there was mixed growth, culture was repeated.

All investigations were done in the microbiology, pathology and biochemistry department of Dhaka Shishu (Children) Hospital. Radiological investigations i.e., chest X-ray and ultrasonography (USG) of the kidney, ureter and bladder (KUB) region was done at the Department of Radiology, Dhaka Shishu (Children) Hospital.

Data entry and analysis was done by using SPSS version 12. In addition to descriptive statistics such as frequency tabulation, mean, standard deviation, statistical test such as 't' test was applied accordingly to determine statistically significant association. Level of significance was taken as <0.05.

Results

A total of 115 nephrotic syndrome children were included in this study and among them 63(54.78%) presented with infection (Fig.-1).

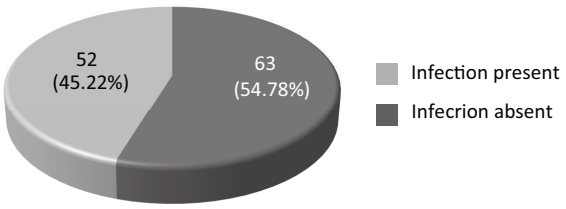

Fig.-1 *Prevalence of infection in nephrotic syndrome (N=115)*

Infection in nephrotic syndrome was common (63.49%) in children age between 2-6 years (Table I).

Table I
Age distribution of Nephrotic Syndrome patients (N=115)

Age in years	Number of patients (Percent)	With infection (n=63)
<2 yrs	4(3.47)	3(4.76)
2-6 yrs	61(53.04)	40(63.49)
>6 yrs	50(43.47)	20(31.75)

Most common infection in nephrotic syndrome is UTI. Out of 115 patients 51(44.34%) had UTI, followed by Pneumonia 5(4.34%), Septicemia 4(3.47%), Peritonitis 1(0.87%), Cellulitis1(0.87%) and Tuberculosis 1(0.87%) [Fig.-2].

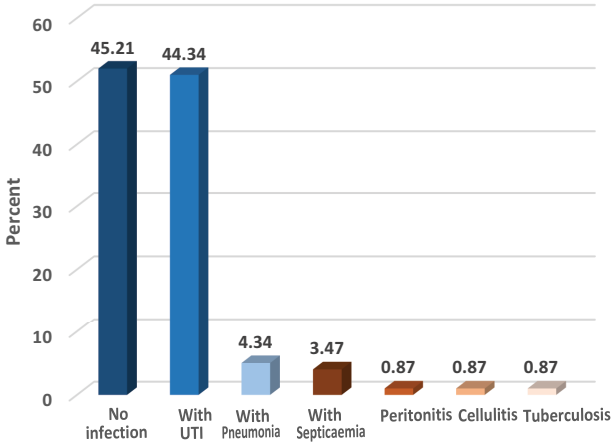

Fig.-2 *Pattern of infections in nephrotic syndrome*

Statistically significant risk factors associated with infection were generalized edema, steroid dependence, steroid resistance, persistent proteinuria and high spot urine protein creatinine ratio (Table-II).

Table-II
Risk factors of infection in nephrotic syndrome

Risk factors		Infection		χ^2	p value
		Present	Absent		
Age	<6 years	28	37	1.351	0.16
	>6 years	27	23		
Sex	Male	35	46	2.340	0.09
	Female	20	14		
Relapse	Present	46	50	0.002	0.58
	Absent	9	10		
Steroid dependence	Present	14	06	4.771	0.03
	Absent	41	54		
Steroid Resistance	Present	15	3	10.782	0.001
	Absent	40	57		
Facial puffiness	Present	54	58	0.259	0.53
	Absent	1	2		
Leg edema	Present	54	58	0.259	0.53
	Absent	1	20		
Swelling of the genitalia	Present	53	60	2.220	0.23
	Absent	2	0		
Generalized anasarca	Present	15	6	5.736	0.02
	Absent	40	54		
Oliguria	Present	54	56	1.622	0.21
	Absent	1	4		
Fever (Temp >100^0F)	Present	41	44	0.022	0.53
	Absent	14	16		
Pain abdomen	Present	51	57	0.259	0.45
	Absent	4	3		
Vomiting	Present	52	54	0.822	0.29
	Absent	3	6		
Skin infection	Present	52	59	1.226	0.28
	Absent	3	1		
Sore throat	Present	53	60	20220	0.23
	Absent	2	0		
Immunization	Immunized	41	40	0.855	0.23
	Not immunized	14	20		
Albumin in urine	<2.5+	1	8	5.275	0.02
	>2.5+	54	52		
RBC in urine	<25	41	52	2.725	0.08
	>25	14	08		
Protein creatinine ratio	<2	16	6	6.760	0.01
	>2	39	54		
Pus cell	>20/HPF	32	6	6.760	0.01
	<20/HPF	39	54		

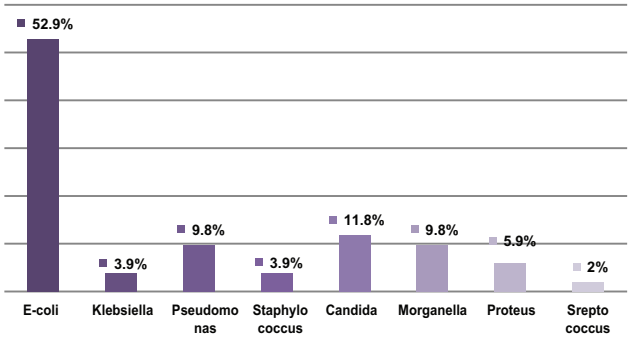

Fig.-3 *Organisms causing UTI in patients having nephrotic syndrome (n=51)*

Out of 51 UTI cases, 27 caused by E.coli (52.9%), followded by Pseudomonas 5(9.8%) & Morganella 5(9.8%).

Discussion

A total of 115 nephrotic syndrome children were included in this study. Infection was present in 63(54.78%) cases. Infection in nephrotic syndrome was common (63.49%) in children age between 2-6 years. Most common infection in nephrotic syndrome was UTI. Out of 115 patients 51(44.34%) had UTI, followed by Pneumonia 5(4.34%), Septicemia 4(3.47%), Peritonitis 1(0.87%), Cellulitis 1(0.87%) and Tuberculosis 1(0.87%). Statistically significant risk factors associated with infection were generalized edema, steroid dependent, steroid resistance, persistent proteinuria and high spot urine protein creatinine ratio. Out 51 UTI cases, 27 caused by E.coli (52.9%), followded by Pseudomonas 5(9.8%) & Morganella 5(9.8%). This finding is consistent with Shenguttuvan et al[4] report where they found 62.7 % infection in Children below 6 years of age. The mean age of 4.5 years was also observed by Chowdhury et al[8] in Bangladesh, whereas Gulati et al[5] found the mean age to be 6.2 years. In this study increased susceptibility to UTI in lower age group nephrotic children may be due to significant hypoalbuminemia, this factor may have a pathophysiological role in predisposing lower age group children to infection. Moreover, nephrotic syndrome in childhood is common between two to six years of ages, and they were found more immunodeficient during active disease and more prone to bacterial infection.[7]

Majority of our study population were from rural areas (73.19%). Our study subjects were mostly from poor and average social class (52.17%). It had a definite reason because the patients from different parts of the country were referred to Dhaka Shishu (Children) Hospital and treatment cost was minimum. Most of the mothers were illiterate or with primary education. So they had very poor knowledge regarding hygiene, sanitation and ifection control. In this study we could not find measles or varicella infection but tuberculosis cases were detected. It reflects the effect of successful immunization programme against those diseases.

The prevalence of UTI in this study population was 51(44.35) which was consistent with previous studies 40.26% by Gulati et al[5], 46% Shenguttuvan et al[4], 65.20% by Karim et al[9], 58.83% by Chowdhury et al[8], 42.22% by Sultana et al[10]. But other previous studies by Gorensec et al[11]; Srivastav et al[12]; Tsa et al[13] suggested much lower incidence of UTI in nephrotic syndrome children which may be due to inclusion of only hospitalized children with complications. In this series the prevalence of UTI is 44.35% which is much higher than the prevalence of 1 to 3% reported in the general population by Stull et al[14]. Maximum UTI were asymtomatic. Steroid non response or relapse was their presenting feature and UTI was diagnosed during screenig of urine for infection as part of the study protocol. Asymtomatic UTI in nephrotic syndrome has also been found in different previous reports.[5,8]

Pus cell count >20/HPF is found in 32(62.75%) cases. Different study reported various findings regarding pyuria and UTI in general population and in cases with suspected UTI.[8,14] In general population pyuria is a recognized finding for diagnosis of UTI. But in nephrotic children pyuria has no diagnostic value; it may present as a feature of chronic disease process or may be due to steroid.

In this study among 51 culture positive cases of UTI, E. coli was the commonest organism 27(52.9%). Similar results were observed by different authors. Shenguttuvan et al[4] observed 36.6%, Gulati et al[5] observed 39%, Chowdhury et al[8] observed 80%, Sultana et al[10] observed 78.94% and 90% observed by Khan et al[15] in UTI cases with nephrotic syndrome. Non E. coli, Gram negative organism accounted for Pseudomonas 5(9.8%), Proteus 3(5.9%) and Klebsiella 2(3.9%). Morganella was 5(9.8%), Candida 6(11.8), Staphylococcus 2(3.9%) and Streptococcus 1(2%). Prasad et al[16] found similar results - 14% Pseudomonas, 8% Klebsiella in 30

nephrotic syndrome children with UTI. Emilia et al[17] also found E coli is the commonest organism followed by Klebsiella. Barua et al[18] found UTI in 30.8% nephrotic children and causative organisms were E coli 50%, Klebsiella 25%, Coliforms 18.7% and Proteus 6.3%.

Conclusion

Prevalence of infection in nephrotic syndrome is very high and E coli is the commonest organism found in this study. Early intervention with relapse is important as generalized edema, persistent proteinuria, hypoalbuminemia, steroid dependence, steroid resistance are important risk factors for infection.

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