

Original Article

Pattern of Aerobic bacterial infections in Nephrotic children

Saima Easin¹, Naima Muazzam², S.M. Shamsuzzaman³, Moushumi Sarker³, Akhtaruzzaman Chowdhury³

¹Department of Microbiology, NICRH, Mohakhali, Dhaka. ²Department of Microbiology (former), Dhaka Medical College, Dhaka.

³Department of Microbiology, Dhaka medical College, Dhaka.

Abstract

100 nephrotic children were studied in the Microbiology Department of Dhaka Medical College, Dhaka, from January to December/ 2004. The mean age was 5.4 years (range 1-15 yrs.), 68 were male and the rest 32 were female. All children were diagnosed case of nephrotic syndrome having International Study of Kidney Diseases in Children (ISKDC) criteria with normal renal functions. The patients were monitored clinically presented with any infections as a complication of nephrotic syndrome and investigations were carried out accordingly. 59 patients were found to have various types of infections. Urinary tract infection (UTI) was the commonest and seen in 50 patients. Peritonitis and cellulitis were present in two patients each. The most common isolated organism was E.coli and Pseudomonas in urine. E.coli was mostly susceptible to Ciprofloxacin but resistant to Ceftriaxone. Pseudomonas was mostly resistant to ceftriaxone but susceptible to imipenem.

Key words: Nephrotic syndrome, Infection, Resistance.

Introduction:

Nephrotic Syndrome is a common renal disease, which is characterized by massive proteinuria, hypoalbuminaemia, hyperlipidaemia and generalized oedema.¹ According to International Study of Kidney Diseases in Children (ISKDC), nephrotic proteinuria is defined as urinary protein excretion exceeds 2.5 gm. in 24 hours (>1 gm./m²/24 hours) and serum albumin drops below 2.5 gm/dl.² In developing countries, infection is an important complication of nephrotic children resulting significant morbidity and may also be responsible for a poor response to steroid therapy or induce relapse in children who has already attained remission.³

The incidence of infections in nephrotic children is high. Physical findings may be minimal due to extensive use of corticosteroids with or without use of other

immunosuppressive agents in the treatment of Nephrotic Syndrome. Bacterial infections in nephrotic children comprise urinary tract infection (UTI), pneumonia, septicemia, pulmonary tuberculosis (PTB), skin infection, peritonitis etc. Recent reports suggest that UTI is the predominant infection in nephrotic children. So, urine should be cultured in following circumstances, (1) on admission, as a screening investigation before initiation of steroid therapy, (2) In all children with steroid non-response with 4 weeks course of steroids, (3) In patients in remission with symptoms suggestive of UTI such as fever, dysuria or hematuria; (4) In nephrotic children with relapse.⁴ Previously gram positive as well as gram negative organisms were responsible for various infections in nephrotic children. Subsequently with corticosteroid treatment and overuse of antibiotics, Gram negative organisms were found predominantly with their changing antimicrobial susceptibility pattern.⁵

Materials and methods:

Place and duration of the Study: This cross sectional study was carried out in the Department of Microbiology, Dhaka Medical College (DMC), Dhaka, Bangladesh, for a period of one year.

✉ **Correspondence:**

Dr. Saima Easin
Asstt. Professor
Department of Microbiology
NICRH, Mohakhali, Dhaka.
Tel: 01552-396711

Study population, Inclusion criteria: Total 100 clinically diagnosed nephrotic syndrome patients (based on generalized oedema, proteinuria, detected by heat coagulation test, oliguria or scanty micturition) were included. Samples were collected from patients admitted in the Pediatric department of Dhaka Medical College Hospital (DMCH), Dhaka, National Institute of Kidney diseases and urology (NIKDU), Dhaka and Pediatric Nephrology department of Bangobondhu Sheikh Mujib Medical University (BSMMU), Dhaka.

Methodology: About 20 ml of mid-stream urine was aseptically collected from all patients and transported to the laboratory as early as possible. By using standard loop (4mm) method, a fixed known volume (0.004ml) of urine was inoculated into Blood and MacConkey agar media and aerobically incubated at 37°C for 24 hours. If growth occurred, the number of colony were counted to calculate the number of viable bacteria in urine. A count of 1x10⁵ or more bacteria/ml of urine was taken as clinically significant. Two ml of blood was aseptically collected from eight suspected septicemicnephrotic patients and were inoculated into 20 ml of Trypticase Soya broth (TSB) and aerobically incubated at 37°C. Among 100 nephrotic cases, eight patients were tested for cellulitis/abscess and pus or cellular exudates were aseptically collected from infected sites by using sterile cotton-wool swab and inoculated into Blood and MacConkey agar media and aerobically incubated at 37°C for 24 hours. 2-3 ml of peritoneal fluid was collected aseptically from 4 asciticnephrotic cases and were inoculated into Blood and MacConkey agar media and aerobically incubated at 37°C for 24 hours. The organisms were isolated by using various chemical tests (fermentation reaction in KIA media, motility test in MIU media and citrate utilization test).⁶ The bacterial isolates were tested for antimicrobial susceptibility test by agar disc diffusion method against different antimicrobial agents like ampicillin (AMP), gentamycin (CN), cotrimoxazole (STX), cephalixin (CEF), ciprofloxacin (CIP), ceftriaxone (CRO), nalidixic acid (NA), nitrofurantoin (F), carbenicillin (CAR), ceftazidime (CAZ), imipenem (IMP) etc. The diameter of complete zone of inhibition around each disc was measured in mm.⁷

Results:

In this study of 100 nephrotic children, 77 cases were up to 6 years of age, of them 48 (81.4%) were culture positive (Table-I). The rest 23 cases were between six to fifteen years of age, of which 11(18.6%) cases were culture positive (p<0.001). The ratio of male and female was 2:1. Among 59 culture positive cases, male children were significantly more than female (p <0.001) (Table-II). Out of 59 culture positive patients, UTI was the commonest infection (84.7%). Among

the aetiological agents, 37 (74 %) patients were found to have *E. coli* in their urine samples. *Pseudomonas*, *Klebsiella*, *Proteus* were found in 7 (14 %), 4 (8 %) and 2 (4 %) patients respectively (Table-III). Most of the isolated organisms were susceptible to ciprofloxacin except *Pseudomonas*, which was 100 % resistant. 65% *E.coli* was susceptible to ciprofloxacin, 35% to nitrofurantoin, 30% to nalidixic acid and 25% of *E.coli* were susceptible to gentamycin. 100% *E.coli* were resistant to ceftazidime and carbenicillin whereas 30% and 20% *Pseudomonas* was sensitive to ceftazidime and carbenicillin respectively. 100% *Klebsiella* and 100% *Proteus* were resistant to ampicillin, carbenicillin, ceftazidime, cephalixine, cotrimoxazole but 100% were susceptible to ciprofloxacin. 100% *Pseudomonas* were resistant to ciprofloxacin and ceftriaxone whereas 80% of them were susceptible to only imipenem. Among 88 nephrotic patients who were diagnosed as initial cases, 50 (56.81%) were culture positive and 9 (75%) of the 12 cases who developed relapse were culture positive (p<0.01).

Table-I: Age distribution of the nephrotic syndrome cases (n=100)

Age (years)	Culture positive cases (n=59)	Culture negative cases (n=41)	Mean age
	No (%)	No (%)	
≤ 6	48 (81.4)	29 (70.47)	5.4
> 6-15	11 (18.6)	12 (29.53)	
Total (n=100)	59 (100)	41 (100)	

P value (Z test): P < 0.001

Table-II: Sex distribution of the nephrotic syndrome cases (n=100)

Sex	n=100	Culture positive cases (n=59)	Culture negative cases (n=41)
		No (%)	No (%)
Male	68	43 (72.9)	25 (61.0)
Female	32	16 (27.1)	16 (39.0)
Total	100	59 (100)	41 (100)

P value (Z test): P <0.001

Table-III: Organisms isolated from different samples of culture positive nephrotic cases (n=59).

Types of infection	Material used for culture	n	Organism isolated			
			<i>E.coli</i> n (%)	<i>Pseudomonas</i> n (%)	<i>Klebsiella</i> n (%)	<i>Proteus</i> n (%)
UTI	Urine	50	37 (74)	7 (14)	4 (8.0)	2 (4.0)
Cellulitis/skin infection	Pus/cellular exudates	5	1 (20)	2 (40)	0 (00)	2 (40)
Septicemia	Blood	2	1 (50)	1 (50)	0 (00)	0 (00)
Peritonitis	Peritoneal fluid	2	1 (50)	0 (00)	1 (50)	0 (00)
Total		59	40	10	5	4

Discussion:

Nephrotic syndrome is primarily a pediatric disorder, which is characterized by massive proteinuria, hypoalbuminaemia, hyperlipidaemia and generalized oedema. Male children are predominantly affected and most commonly appears between 2-6 years of age. In this study of 100 nephrotic cases, 77 cases were up to 6 years of age and 23 cases were between 6-15 years of age. In a study at IPRM&R, Dhaka, found maximum cases between the age 2-10 years of age.⁸ Among 59 culture positive cases, 48 (81.40 %) cases were up to six years and the rest 11 (18.6 %) were between > 6-15 years of age ($p < 0.001$). Childhood nephrotic syndrome is common between 2-6 years of age and become more immunodeficient during active disease and become more susceptible to bacterial infections.⁹ There may be a relation that nephrotic children with hypoalbuminaemia and lower level of serum Ig G may predispose to bacterial infection.¹⁰ In this study, the ratio of male and female was 2:1. Among 59 culture positive cases, male children were significantly more than female ($p < 0.001$). The ratio between male and female were 2.5:1 and 3:1 reported in different studies.^{11,4} In this study, UTI was the commonest infection with a prevalence of 50 %. It was found that UTI was the commonest infection among nephrotic children.^{12,8} Among the isolated organisms, 74 % were *E. coli* in their urine samples followed by *Pseudomonas*, *Klebsiella*, *Proteus*, were found in 14%, 8 % and 4 % patients respectively. Cellulitis was the second common (62.5%) which was similar with the study of Senguttuvan.¹³ In this study, 2 septicemic and 2 cases were diagnosed as peritonitis. W. Scott reported 13.4 % of nephrotic children presenting with the type of acute abdominal emergency.¹⁴ Fowler (1957) established that the majority of cases were caused by gram positive organisms particularly *Pneumococci* and *Haemolytic streptococci*. In this study, *E.coli* and *klebsiella* were found in one patient each.¹⁵ Previously gram-positive organisms were responsible for peritonitis. Subsequently with corticosteroid treatment and overuse of antibiotics, gram-negative organisms have been found predominately with their changing antimicrobial susceptibility pattern. In the present study of nephrotic syndrome, a majority of patients were initially attended by general practitioners or at other hospitals and had received symptomatic treatment and antibiotics resulting low bacterial culture positivity. As a result, occult infections were found to be responsible for non-response to steroid therapy, resulting hospitalization of the patients. Infected nephrotic syndrome cases had significantly delayed protein free urine despite adequate treatment. Wilfert had similar observations.¹⁶

The isolated gram-negative organisms of this study were tested against different antimicrobial discs according to the

samples and organisms. They were susceptible to ciprofloxacin in most of the cases except *Pseudomonas*, which was 100 % resistant. *E.coli* were mostly susceptible to ciprofloxacin, nitrofurantoin, nalidixic acid and gentamycin. Only 15 % *E.coli* were susceptible to ceftriaxone and cotrimoxazole. 100% *E.coli* were resistant to ceftazidime and carbenicillin whereas *Pseudomonas* was 30 % and 20 % sensitive to them respectively. 100 % *Klebsiella* and 100 % *Proteus* were resistant to ampicillin, carbenicillin, ceftazidime, cephalexine, cotrimoxazole but 100 % were susceptible to ciprofloxacin. 100 % *Pseudomonas* were resistant to ciprofloxacin and ceftriaxone. The antibiogram of this study was dissimilar to the previous studies in which third generation cephalosporin therapy covered most of the gram-negative organisms.^{17,18} UTI in nephrotic patients is increasing worldwide with the prevalence of antimicrobial resistance. In this study, as all the samples were collected from admitted patients and gram negative bacilli were the most common causes of nosocomial infection, possess multiple modes of antibiotic resistance and were highly efficient in horizontally transferring them between species. The emergence and spread of resistance can be reduced by appropriate & careful use of antimicrobial agents.¹⁹

Conclusion:

Infection is an important complication of nephrotic syndrome patients as observed in 59 patients out of total 100 patients. UTI was the commonest infection followed by cellulitis, peritonitis and septicemia. Infections were caused by Gram-negative bacteria, which were mostly resistant to ceftriaxone. Infections remain the chief cause of mortality and considerably morbidity. So prevention and early recognition of infections are crucial in nephrotic syndrome.

REFERENCES:

1. Behrman RE, Kligman Rm, Nelson WE, Vaughan VC, editors. Nelson Textbook of Pediatrics. 14th ed. Philadelphia; W.B. Saunders company, 2004: 1341-43.
2. Brodehil J, Nephrotic syndrome in children: Diagnosis and treatment. World Pediatr. Child care 1986; 1: 9-18.
3. Abrass C: Clinical spectrum and complications of nephrotic syndrome. J Clin. Invest Med 45:143. 1997.
4. Gulati S; Kher V; Gupta S; Kali S. Urinary tract infection in nephrotic syndrome. Pediatr infect Dis J 1996 Mar; 15 (3): 237-40.
5. Tapaneya-Olarn-C; .Tapaneya-Olarn-W. Primary peritonitis in childhood nephrotic syndrome: a changing trend in causative organisms. J-Med-Assoc-Thai. 1991 Nov; 74(11): 502-6.

6. Cheesbrough M. Medical Laboratory Manual for tropical countries. Vol-11. Cambridgeshire: ELBS, 2000:pp-182-8.
7. Bauer AW, Kirby WMM, Sherris. Antibiotic susceptibility testing by a standard single disc method. *Am J Clin. Pathol.* 1996; 45; 493-6.
8. Chowdhury M A, Rahman M E, Hossain M. Pattern of infections in childhood Nephrotic Syndrome, Dhaka shishu (children) Hospital Journal 1998; 14: 13-17.
9. Behrman RE, Kligman Rm, In: Nelson WB, Vaughan VC Nelson Textbook of Pediatrics. 14th ed. Philadelphia; W.B. Saunders company, 2004: 1341-43.
10. Andal A, Chellani H, Anand N K, Chandra M; Low serum immunoglobulin G --a predictor of frequent relapses in idiopathic nephrotic syndrome. *Indian pediatr.* 1990 (Oct) ; 27 (10): 1045-9.
11. Moorani KN, Khan KM, Ramzan A. Infections in children with nephrotic syndrome. *J Coll Physicians Surg Pak.* 2003 Jan; 13(6): 337-9.
12. FKeFu. EK-N. Renal disorder in children: A Nigerian study; *PediatrNephrol*, 1994; Jun; 8(13): 383-6.
13. Shenguttuvan P, Ravanan K, Pravu N, Tamilarasi V. Infections encountered in childhood nephrotics in a pediatrics renal unit. An untitled document of 2004.
14. W. Scott, Macdougall, Robert, J Izant, Robert M. Primary peritonitis in infancy and childhood. 1978; 40: 132-135.
15. Fowler R. Primary peritonitis. *Aust NZ srg* 1957; 26: 204-213.
16. Wilfert CM, Katz CL. Etiology of bacterial sepsis in nephrotic syndrome. *Pediatrics* 1968 ; 42: 840-43.
17. Tain YL, Lin G, Cher TW. Microbiological spectrum of septicemia and peritonitis in nephrotic children. *PediatrNephrol.* 1999 Nov; 13(9): 835-7.
18. Liponski I, Cochat P, Gagnadoux MF, Parchoux B, Niaudet P, David L, Broyer M. Bacterial complications of nephrotic syndrome in children. *Presse Med.* 1995 Jan; 13(1): 19-25.
19. Abdul Rahman Abdullah Kader, A. Kumar, Seivarayan Mahimai Dass; Anti-microbial resistance pattern of Gram-negative bacteria isolated from urine culture at a general hospital. *Saudi J Kidney Dis Transplant* 2004; 15(2);135-139.