

# Frequency of Peritonitis in children with Nephrotic Syndrome

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## ABSTRACT

**Objective:** This prospective descriptive study was aimed at determining the frequency of peritonitis in children with Nephrotic Syndrome.

**Methods:** It was carried out in Department of Pediatrics, Jinnah Hospital, Lahore from Jan 2005 to Jan 2006. All patients admitted with the diagnosis of Nephrotic syndrome either (new or known) excluding those with congenital nephrosis were included. Peritonitis was primarily a clinical diagnosis with CBC, Peritoneal tap and abdominal ultrasound as supportive investigations

**Results:** Out of 100 of nephrotic syndrome patients, 19 had peritonitis with male to female ratio of 2:1. Peritonitis was more common in patients with relapse (n=16; 84%) as compare to newly diagnosed cases (n=3; 15%). All presented with abdominal distension, pain (94%), tenderness (94%), fever (63%) and vomiting (52%). Ascitic fluid, morphology & cytology was positive in 17 patients (89%), culture & sensitivity was positive in only 4 patients (21%) with growth of Pneumococcus in 3 patients (15%) and E. coli in one patient (5%). 12 developed peritonitis within the first year of diagnosis of nephrotic, 5 patients after first year of establishing the diagnosis and two patients after two years of diagnosis of nephrotic syndrome.

**Conclusion:** 19% of nephrotic syndrome (mostly known cases with relapse within the first year of diagnosis) presented with peritonitis with male predominance. Most common presentation of peritonitis in nephrotics is abdominal distension and abdominal pain. Ascitic fluid is positive for peritonitis in 89 % with positive culture in only 21% (mainly Pneumococcus).

**Keywords:** Nephrotic syndrome, peritonitis.

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## INTRODUCTION

Nephrotic Syndrome is one of the most common diseases in children, which is characterized by proteinuria, hypoalbuminemia, hypercholesterolemia and edema. According to the underlying histological lesion the nephrotic syndrome is classified as minimal change, focal glomerulosclerosis (segmental / global), mesangial proliferative glomerulonephritis, diffuse mesangiocapillary glomerulonephritis, diffuse membranous glomerulonephritis and chronic glomerulonephritis. Minimal change disease is the commonest lesion in Nephrotic Syndrome.<sup>1</sup> Minimal change disease occurs predominantly between 2-8 years of age and it is responsive to steroid in 90% of cases. Focal segmental is the second most common lesion and it is usually steroid resistant<sup>1,1</sup>.

Peritonitis is an important complication in Nephrotic Syndrome<sup>2</sup>. Streptococcus pneumoniae (Pneumococcus) has been found to be primarily responsible organism in most cases of peritonitis. E.coli is the other bacterium found in these patients. Although Nephrotic Syndrome is well known as a predisposing factor to bacterial infections in children including peritonitis, urinary tract infections, skin infections, sepsis, respiratory tract infections and

osteo-myelitis, but data on the frequency of peritonitis is limited. Peritonitis is defined as the inflammation of peritoneal lining of the abdominal cavity. In the pre-antibiotic era fatal peritonitis and sepsis have led to 40-50% mortality but now with the use of antibiotics and steroids, this mortality has decreased to 1.5-4.6% only. The diagnosis of peritonitis is usually clinical<sup>3</sup>. Essentially, all patients present with some degree of abdominal pain. Anorexia and nausea are frequently present and may precede the development of abdominal pain by some time. Vomiting may occur because of the underlying visceral organ pathology (i.e., obstruction) or secondary to the peritoneal irritation. Most patients with intra-abdominal infections demonstrate leukocytosis (>11,000 cells/mm<sup>3</sup>) with a shift to the immature forms on the differential cell count. Blood chemistry findings are often within the reference range initially, but they may show evidence of dehydration with elevated BUN and altered electrolyte concentrations caused by protracted vomiting, diarrhea, renal dysfunction, and ascites. When assessing a peritoneal fluid sample for peritoneal infection, it generally demonstrates low pH that is more pronounced in mixed infections and severe bacterial contamination, with increased numbers of anaerobic bacteria in these circumstances and glucose as well as elevated protein and LDH levels.<sup>3</sup> In SBP, a WBC count of

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more than 250 cells/mm<sup>3</sup>, with more than 50% polymorphonuclear leukocytes (PMNs) is an indication to begin antibiotic therapy. Although up to 30% of culture findings remain negative in these patients, most of these patients are presumed to have bacterial peritonitis; they should be treated. There is increase susceptibility to infections in nephrotics<sup>4</sup>. In addition infections may be responsible for frequent relapses, requiring hospitalization. Multiple factors including defective phagocytosis, opsonization, decreased immunoglobulins levels, loss of properdin in urine and edema are responsible for bacterial infections in Nephrotic Syndrome.

A precise knowledge of organism causing infections especially peritonitis is important in many ways. Firstly, to treat infection and decrease morbidity, second to prevent relapses and third to reduce mortality. Therefore early diagnosis and treatment of peritonitis may be helpful in this regard.

## METHODS

**Study settings:** Jinnah Hospital is a government based 1250 bedded tertiary care hospital attached with Allama Iqbal Medical College. Department of Pediatrics is a 70 bedded unit with emergency, neonatal, intensive care, outdoor facilities and cadres undergraduates and post graduates in the given subject.

**Patient enrollment:** The sampling procedure adopted by the researcher in this study was purposive type of non-probability sampling. Over a period of one calendar year a sample of 100 cases within the age group of 1 – 12 years, fulfilling the inclusion and exclusion criteria was taken. **Inclusion criteria:** Patients diagnosed on the basis of definition of Nephrotic Syndrome considered as new cases and known cases of Nephrotic Syndrome presenting with relapse. **Exclusion criteria:** Children with congenital and secondary Nephrotic Syndrome.

New cases were diagnosed on the basis of definition of Nephrotic Syndrome (Children having proteinuria > 1gm/m<sup>2</sup>/24hrs, hypoalbuminemia < 2.5 gm/dl, hypercholesterolemia >250mg/ dl, edema). A complete history, physical examination and relevant laboratory investigation were carried out and recorded in proforma. 24hr urinary proteins, serum albumin and cholesterol were performed in all new patients to establish the diagnosis of nephrotic syndrome. In diagnosed cases relapse was defined as patients having proteinuria and edema at the time of presentation.

New and previously diagnosed cases with relapse were assessed for signs and symptoms of peritonitis. Peritonitis was defined as patient having abdominal swelling (ascites), tenderness and fever.

Ascitic tap was done after counseling and written consent of parents. Ascitic tap was done under aseptic measures and ascitic fluid was sent to hospital pathology lab for complete examination including cytology, biochemistry, culture and sensitivity. Meanwhile antibiotics were started empirically.

**Data collection & analysis:** The purpose of the study was explained at the start of evaluation and filling up of the designed proforma. Each respondent's verbal consent was obtained and confidentiality assured. Data analysis was done on quarterly basis, and data evaluation was simple and mathematical with percentages of study denominators calculated and tabulated.

## RESULTS

During the study period of one-year 100 patients admitted with nephrotic syndrome in Pediatrics unit of Jinnah Hospital, Lahore were included in the study. Out of 100 patients 19 were found to have peritonitis. Out of 19 cases, 13 were male and 6 were females and the male to female ratio was 2:1 (Table 1).

Among patients who developed peritonitis three were new cases of nephrotic syndrome and 16 were known nephrotics presented with relapse. Frequency of peritonitis was more common in patients with relapse (84%) as compare to newly diagnosed cases (15%) of nephrotic syndrome (Table 2). The data shows that in patients with peritonitis, most common presentation of peritonitis in nephrotics is abdominal distension (100%) and abdominal pain (94%) followed by abdominal tenderness (94%), fever (63%) and vomiting (52%), Table 3.

Ascitic fluid examination (morphology and cytology) positive for peritonitis (cloudy peritoneal fluid with > 100 WBCs/mm<sup>3</sup> and > 50% polys) was seen in 17 patients out of 19 (89%) patients with nephrotic syndrome. On culture and sensitivity of ascitic fluid positive reports were seen in only 21% of cases of nephrotic syndrome. Pneumococcus was the most common organism (15%) causing peritonitis in children with nephrotic syndrome and the second one was E. coli (5%), (Table 5.). Peritonitis is more common within the first year of diagnosis of nephrotic syndrome (12 patients out of 19), 5 patients after first year of establishing the diagnosis and two patients developed peritonitis after two years of diagnosis of nephrotic syndrome (Table 4).

Table-1: Age distribution of nephrotics with peritonitis (n=19)

Sex	Number	% age
Male	13	68
Female	6	32

Male to female ratio= 2:1

Table-2: Frequency of peritonitis among new and known nephrotics with relapse

Cases	Number	% age
New	3	15
Relapse	16	84

Table-3: Frequency of signs and symptoms of peritonitis

Signs & Symptoms	Number	% age
Abdominal distension	19	100
Abdominal tenderness	18	94
Abdominal pain	18	94
Fever	12	63
Vomiting	10	52

Table-4: Time between diagnosis of nephrotic syndrome and development of peritonitis

One year after diagnosis	Two years after diagnosis	More than two years after diagnosis
12	05	02

Table-5: Result of ascitic fluid culture and sensitivity

Organism	Number	% age
Pneumococcus	03	15
E. coli	01	05
Total	04	21

## DISCUSSION

Children with nephrotic syndrome are at higher risk for the development of infections, which in turn constitute the leading cause of death during the initial years of disturbed renal functions.

Many factors are responsible for higher susceptibility of infections in nephrotics, including low serum levels of immunoglobulins, inadequate opsonization, defective immunity, loss of properin factor in the urine, presence of ascites, vitamin D deficiency, malnutrition and immunosuppression therapy. The main site of serious infection is the peritoneum. In the present study of 13 months duration, out of 100 patients of nephrotic syndrome, 19 were found to have peritonitis, reflecting a frequency 19 % (Table 1). In a study conducted at Germany, frequency of peritonitis in nephrotic syndrome was found to be 16%.<sup>5</sup> In another study conducted at New Delhi, India, the frequency was found to be 15.8%.<sup>6</sup> According to another study conducted in Pakistan few years ago, the frequency of peritonitis in children with nephrotic syndrome was 32%.<sup>7</sup> The reports about the causes of peritonitis demonstrated more or less different results. To date, initial reports have established that majority of cases were caused by gram-positive organism particularly the Pneumococcus and hemolytic streptococci. But some of them described the altered pattern of infecting organisms with a relative increase in the

proportion of gram-negative organism and culture negative cases. From an initial prevalence of pneumococcal infections in earlier years, the frequency of gram-negative infections have increased since the late 1950's, an occurrence that is presumably related to the introduction of steroid therapy and broader use of antibiotics. In 1975, Rubin reported two cases of H. influenza type b peritonitis in two nephrotic children.<sup>8</sup> In the same year, Dougal found that gram-negative bacteria, usually E. coli accounted for the 69% of cultured organisms in cases of primary peritonitis during a 10-year period.<sup>9</sup> In 1982, Krensky found 24 episodes of peritonitis in 351 nephrotic children.<sup>10</sup> Streptococcus was the most common pathogen, but the E. coli was the other common organism in 25% of these cases, suggesting that the E. coli is a significant pathogen. Tapaneya described 55 episodes of peritonitis in 347 children with primary nephrotic syndrome during 1969 to 1989.<sup>11</sup> Gram positive and gram-negative bacilli were found in equal numbers with definite increasing trend of gram-negative bacilli over the last four years. Adhikari found 35 episodes of peritonitis in 191 children with nephrotic syndrome between 1981 and 1988.<sup>12</sup> Gram-negative organisms were cultured in 55% of positive blood cultures. In our study it was found that culture was positive in 4 patients out of 19 patients of peritonitis (21%). Pneumococcus was present in 03 (15%) and E. coli in 01 patient (05%) as shown in table 5. Anaerobic bacteria have generally been thought to play a minor role in primary nephrotics. In our study no case of anaerobic gram-negative infection was found (table 5). The predominant symptoms of peritonitis in this study were abdominal distension (100%), abdominal pain (94%), abdominal tenderness (94%) and fever (63%) as shown in table 3. Similar results were found in another study conducted in Texas in which abdominal pain was most common symptom present in 98% of children.<sup>13</sup> Peritonitis should always be considered in a patient with nephrotic syndrome who complains of abdominal pain. Differently from the Adhikari's study<sup>12</sup> we could not find any difference of signs and symptoms between culture positive and culture negative patients. Peritonitis was more common in patients with relapse as compared to the patients who were newly diagnosed (Table 1). Similar results were found in a study in 1995 conducted at Lucknow, India<sup>14</sup>. Krensky found significantly lower IgG levels in nephrotics with peritonitis than in patients with relapse without peritonitis<sup>10</sup>. Aype Balat indicated a higher risk of peritonitis within the first year of diagnosis that was 53.3%.<sup>15</sup> In our study 12 patients out of 19 developed peritonitis within the first year of diagnosis (63%), five after two years of diagnosis (26%), and two patients after two years of

diagnosis (10%) as shown in table-4. Deaths associated with severe infection is the most featured outcome of nephrotic syndrome in childhood. In some studies the mortality ranges from 0% to 20%.<sup>16</sup> There is no mortality because of peritonitis in our study. It was probably related to early diagnosis and initiation of treatment with broad-spectrum antibiotics in these patients. The prognosis of peritonitis in childhood nephrotic syndrome remains excellent when a high degree of suspicion is maintained and diagnosis is made and subsequent appropriate therapy is started.

## CONCLUSIONS

Frequency of peritonitis is 19% in children with nephrotic syndrome. It is more common in males as compared to female and is more common in patients with relapse as compared to newly diagnosed cases. It is also more common within the first year of diagnosis of nephrotic syndrome. Ascitic fluid culture is positive in only 21% of cases and *Pneumococcus* is the most common organism.

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