

# The Clinical Profile of Infections in Childhood Primary Nephrotic Syndrome\*\*

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## Abstract

**Objectives:** To study the clinical profile of infections in a primary nephritic syndrome.

**Patients and Methods:** We conducted a retrospective analysis of infections in 98 consecutive children (males 65, females 33) with primary nephrotic syndrome, who satisfied the International Study of Kidney Disease in Children criteria.

**Results:** Their mean age at onset of symptoms was  $55 \pm 3.4$  months (range: 6 months to 17 years). The mean duration of follow-up was  $38 \pm 3.4$  months (range: 12 to 60 months). A total of 379 episodes of infection were observed in 87 of the 98 children. There was no relationship between age, sex, and severity or frequency of infections.

The most common infections were upper respiratory tract infection (30.64%), gastroenteritis (11.08%), urinary tract infection (9.50%), and peritonitis (5.54%).

Other infections included multiple warts, polyoma virus nephropathy, and pneumococcal appendicitis, which were not previously reported.

**Conclusions:** Nephrotic children may get a variety of bacterial and viral infections.

**Keywords:** infection, nephrotic, peritonitis, sinusitis, appendicitis, warts.

(*J Med J 2011; Vol. 45 (4):303- 307*)

Received

October 12, 2009

Accepted

June 19, 2011

## Introduction

While the majority of nephrotic children respond to steroids and do well, some get serious bacterial infections that contribute to morbidity and mortality.<sup>1,2</sup>

Most of the reports on nephrotic infections were from the industrialized countries.<sup>2-5</sup> Children with the nephrotic syndrome are susceptible to a wide variety of infections because of defective cellular and humoral immunity.<sup>6,7</sup>

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\*\* **Acknowledgement:** The study was supported by a fund from the University of Jordan. We wish to thank Miss Wafaa Abu Rub and Miss Heba Habash for secretarial assistance and statistics

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The purpose of this study was to review the clinical profile of infections encountered in children with primary nephrotic syndrome.

### **Patients and Methods**

The medical records of 98 consecutive patients with primary nephrotic syndrome seen by the Pediatric Renal Service at a tertiary care center from January 2002 to January 2007 were studied retrospectively.

**Inclusion criteria:** children up to 17 years of age fulfilling the International Study of Kidney Diseases in Children (ISKDC)<sup>2</sup> for nephrotic syndrome : edema, proteinuria > 40 mg/m<sup>2</sup>/hour, and hypoalbuminemia.

**Exclusion criteria:** secondary and congenital nephrotic syndromes.

After reviewing the history, physical examination, laboratory data, and course of the disease, infectious episodes were registered.

Standard treatment with steroids was similar to the International Study of Kidney Disease in Children recommendation.<sup>8</sup> The majority of patients who were steroid dependent, frequent relapsers, or steroid resistant, received treatment with calcineurin inhibitors (cyclosporin, tacrolimus) in addition to a minimum dose of every other day steroids.

**Statistics:** Statistical parameters were determined using the Statistical Package for the Social Sciences (SPSS) version 16.

### **Results**

There were 98 children (65 males, 33 females) with primary nephrotic syndrome. The mean age at diagnosis was  $55 \pm 3.4$  months (range: 6 months to 17 years). The mean period of follow up was  $38 \pm 3.4$  months (range: 12 to 60 months). A total of 379 episodes of infections were observed in 87 of the 98 children. The majority of infections occurred in the ages 1-5 years, during or just prior to a relapse of the nephrotic state.

There were three deaths during the follow up period; two were related to suspected septic shock (organism not recovered), and the third was due to an unknown cause. All were on steroids and cyclosporine.

The most common infections were as shown in table (1).

Urinary tract infections (UTI) were found in 35 children who were symptomatic with a positive urine culture. The majority were due to *Escherichia coli*. *Staphylococcus aureus* coagulase positive was grown in three urine cultures.

There were 21 episodes of peritonitis in 15 patients. Eight were frequently relapsing nephrotics. Peritonitis episodes occurred three times in 2 patients, two times in 4 patients and once in 7.

The microbiology of bacteremia, with or without peritonitis, was due to gram positive organisms in 7 patients (*Streptococcus pneumoniae* in 4, anaerobic diphtheroids in 1, *Streptococcus viridans* in 1, and *Staphylococcus aureus* coagulase negative in 1) and gram negative organisms in 3 patients (*Escherichia coli* in 2, *Haemophilus influenzae* in 1).

One out of five patients with appendicitis had concomitant pneumococcal bacteremia.

There were sixteen episodes of sinusitis (4.2%). Three of them presented with headaches and recurrent syncope. Other infections included otitis media in 6 patients, preseptal cellulitis in 2, conjunctivitis in 4 and herpetic encephalitis in one.

Multiple warts occurred in 4 of the 98 patients.

In one out of the three patients with cellulitis, the skin color was violaceous, and the blood culture grew *Streptococcus pneumoniae*.

In the one patient with arthritis, the blood and purulent joint aspirate cultures were negative.

Other infections included varicella in 7 patients, candidemia in 2, and polyoma virus in 1(found on renal biopsy along with focal glomerulosclerosis) while on steroid monotherapy.

**Table (1): Most common infections in nephrotic children.**

<b>Infection</b>	<b>Number of patients</b>	<b>Episodes</b>	<b>Percent</b>
<b>URTI</b>	61	199	30.64%
<b>GE</b>	22	42	11.08%
<b>UTI</b>	35	36	9.50%
<b>Peritonitis</b>	15	21	5.54%

**URTI: Upper respiratory tract infection; GE: gastroenteritis; UTI: urinary tract infection**

## Discussion

Nephrotic children<sup>9</sup> may get infections even before the institution of steroid therapy.<sup>10</sup> Moorani et al, reported infections in 73% of 62 nephrotic children.<sup>11</sup> In our study, infections occurred in 87 of the 98 patients (89%).

The most frequently reported infections in nephrotics were URTI, UTI, GE, and peritonitis.<sup>10-12</sup> Likewise, the most frequent infections in our series were URTI, UTI, GE, and peritonitis, respectively. However, in our study, the incidence of URTI, 52.5%, was much higher than the 5.2% to 29.3% reported in the literature.<sup>10-12</sup> URTIs were frequently associated with a simultaneous relapse.

Moorani et al reported the frequency of GE to be 13.5%<sup>11</sup> compared to 11.08% in our study.

The reported incidence of UTI (12.5% to 22.8%)<sup>10-12</sup> was higher than that in our study (9.5%).

In the study of Gulati et al, 39% of the urine culture isolates were non-Escherichia coli organisms.<sup>13</sup>

The occurrence of staphylococcal aureus UTI was reported by Adeleke et al as the predominant microorganism in nephrotic children.<sup>14</sup> In our series, there were three episodes of staphylococcus aureus coagulase positive infections.

The incidence of peritonitis was reported to range from 9.1% to 15.8%<sup>10-12</sup> compared to 5.5% in

our study. The majority of peritonitis episodes were associated with streptococcal pneumoniae bacteremia, which was similar to others.<sup>4, 15</sup>

Amongst those with peritonitis, the episodes were recurrent in 47%, which was higher than the 26% reported by Krensky et al.<sup>4</sup> Thus, one episode of peritonitis in a nephrotic child may be a risk factor for recurrence.

Other infections included sinusitis (10.2%), appendicitis (5.1%), and multiple warts (4.1%).

The presence of sinusitis has not been emphasized in the literature.<sup>10-12</sup> However, headaches in a nephrotic child may herald an underlying sinusitis.

One patient with appendicitis had pneumococcal appendicitis which has not been mentioned in the literature before. It has, however, been reported in association with HIV infection,<sup>16</sup> and in non-nephrotic patients.<sup>17, 18</sup>

The incidence of skin infections was reported to be 5.2% to 27.0%,<sup>11, 12</sup> which was greater than our findings (1.85%).

In our study, the most frequent skin infections were multiple warts followed by cellulitis. Multiple warts were not previously reported in association with the nephrotic syndrome. The nephrotic state is a risk factor for pneumococcal cellulitis. The violaceous skin discoloration we observed in one patient is known to occur in such cases.<sup>19, 20</sup> Other pathogens reported to cause cellulitis in nephrotic children include Group B streptococci,<sup>21</sup> and Escherichia coli.<sup>22, 23</sup>

Septic arthritis has been reported once in a nephrotic child, with a positive blood culture for Group B salmonella.<sup>15</sup> Our patient had a negative blood culture and joint aspirate cultures.

The one patient with polyoma virus nephropathy had it while the child was in steroid monotherapy, which is rather unusual.<sup>24, 25</sup> Latent viral infections are known to be reactivated in the immuno-compromised host.<sup>26</sup>

### Conclusions

The most frequently encountered infections were URTI, UTI, gastroenteritis, peritonitis, sinusitis, and skin infections. Other infections included PVN which developed on steroid monotherapy and culture negative septic monoarthritis.

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## نوعيه الانتانات التي يتعرض لها مرضى النفروز الأولي عند الأطفال

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### الملخص

**الهدف:** الغاية من هذه الدراسة هي مراجعة نوعية الانتانات المصاحبة لمتلازمة الكلاء الأولية عند الاطفال.

**الطريقة:** تمت مراجعة السجلات الطبية لثمانية وتسعون طفلاً (ذكور 65 واثنا 33) من مرضى النفروز الذين استوفوا شروط الدراسة الدولية لأمراض الكلى عند الاطفال بمشفى الجامعة الاردنية في الفترة ما بين 2002 الى 2007.

**النتائج:** كان معدل العمر  $3.4 \pm 55$  شهر (تراوح من 6 اشهر الى 17 سنة)، ومعدل المتابعة  $3.4 \pm 38$  شهر (تراوح من 12 الى 60 شهر). اهم الانتانات كانت التهاب المسالك التنفسية العلوية (30.64%)، اثنا المعدة والامعاء (11.08%)، اثنا المسالك البولية (9.5%)، والتهاب الصفاق (5.54%).

و من الانتانات الاخرى التي لم تذكر في الادبيات المنشورة من قبل، التهاب الجيوب الانفية، الزائدة الدودية 5% (احدها مصحوباً بالمكورة الرئوية)، وتآليل جلدية متعددة. أما التهاب المفصل المتقيح فقد تم ذكره مرة واحدة من قبل. حصل التهاب فيروس بوليوما عند طفلة وهي قيد العلاج فقط بالستيرويدات. لم تكن هناك علاقة بين تكرار الانتانات والعمر والجنس.

**الاستنتاجات:** من اهم الانتانات التي يصاب بها مرضى متلازمة الكلاء الأولية التهابات المسالك التنفسية العلوية، السبيل البولي، المعدة والامعاء، والصفاق كذلك التهابات الجيوب النفية، الزائدة الدودية، والتآليل الجلدية والتي لم تذكر من قبل في الادبيات المنشورة.

**الكلمات الدالة:** متلازمة الكلاء، نفروز، الصفاق، الزائدة، الجيوب، تآليل.