



## Urinary Tract Infections in Children with Primary Nephrotic Syndrome and Acute Glomerulonephritis

*Infections urinaires chez l'enfant avec syndrome néphrotique primaire et glomérulonéphrite aiguë*

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### ABSTRACT

**BACKGROUND:** The occurrence of urinary tract infection (UTI) in children with Nephrotic syndrome (NS) has been widely reported by various workers, but not much has been documented about its occurrence among children with acute glomerulonephritis (AGN). Hence, the level of susceptibility to UTI by both diseases has not been compared.

**OBJECTIVE:** To determine and compare the prevalence of UTI in children newly diagnosed of AGN or NS.

**METHODS:** Urinary microscopy, culture and sensitivity of all children admitted with a diagnosis of NS and AGN between 1996–2004 were reviewed. Children with NS who had a relapse or were commenced on steroids, cytotoxic agents or antibiotics before admission were excluded from the study.

**RESULTS:** A total of 35 and 32 children diagnosed of AGN and NS respectively met the study criteria. Urinary tract infection occurred in three (9%) children with AGN and one (3%) of the children with NS. The organisms isolated among the AGN patients included *Coliforms*, *Klebsiella*, and *Staphylococcus aureus* while *Coliform* was isolated in the only NS patient with UTI.

**CONCLUSION:** There is a low prevalence of UTI in children newly diagnosed of AGN and NS. *WAJM* 2010; 29(4): 235–238.

**Keywords:** Urinary tract infection; Acute glomerulonephritis; Nephrotic syndrome; Children; *Klebsiella*.

### RÉSUMÉ

**CONTEXTE:** La survenue d'une infection des voies urinaires (IVU) chez les enfants présentant un syndrome néphrotique (NS) a été largement rapporté par les travailleurs diverses, mais on n'a pas beaucoup documenté sur son apparition chez les enfants atteints de glomérulonéphrite aiguë (AGN). Par conséquent, le niveau de sensibilité à UTI par les deux maladies n'a pas été comparé.

**OBJECTIF:** Déterminer et comparer la prévalence des infections urinaires chez les enfants nouvellement diagnostiqués d'AGN ou NS.

**METHODES:** la microscopie urinaire, de la culture et la sensibilité de tous les enfants hospitalisés avec un diagnostic de NS et AGN entre 1996-2004 ont été examinés. Les enfants NS qui avait une rechute ou ont été engagées sur les stéroïdes, les agents cytotoxiques ou d'antibiotiques avant l'admission ont été exclus de l'étude.

**RÉSULTATS:** Un total de 35 et 32 enfants atteints de l'AGN et NS respectivement rencontré les critères de l'étude. Infection des voies urinaires sont survenus dans trois (9%) des enfants avec des AGN et un (3%) des enfants avec NS. Les organismes isolés chez les patients inclus AGN coliformes, *Klebsiella* et *Staphylococcus aureus* a été isolé en coliformes dans le patient NS seulement avec UTI.

**CONCLUSION:** Il existe une faible prévalence de l'infection urinaire chez les enfants nouvellement diagnostiqués d'AGN et NS. *WAJM* 2010; 29 (4): 235–238.

**Mots-clés:** infection des voies urinaires; glomérulonéphrite aiguë, syndrome néphrotique, les enfants, *Klebsiella*.

## INTRODUCTION

Primary nephrotic syndrome (NS) and acute glomerulonephritis (AGN) remain the two commonest glomerulopathies seen in children in the tropics.<sup>1</sup> Both of them are associated with infections in different ways. Throat or skin infection may precede AGN, while children with NS are susceptible to infection due to the loss of IgG and properdin factors in the urine. Oedema, which is a common feature of both diseases, is also a good culture medium for bacteria.<sup>2</sup>

The occurrence of urinary tract infection (UTI) in NS has been widely reported.<sup>3-6</sup> It has also been implicated as a precipitating factor for relapse in NS. However, not much has been documented about the occurrence of UTI in patients with AGN, hence the level of susceptibility to UTI by both diseases has not been compared.

Furthermore, the occurrence of UTI in newly diagnosed NS patients in this geographic zone of Nigeria has not been reported for comparison with what obtains in other parts of Nigeria. This study therefore aimed to determine and compare the prevalence of UTI in NS and AGN patients.

## SUBJECTS, MATERIALS, AND METHODS

Urinary microscopy, culture, and sensitivity results of children admitted to the Children's Ward of the University of Ilorin Teaching Hospital, Ilorin, Nigeria with a diagnosis of NS and AGN between 1996 and 2004 were analysed. Nephrotic syndrome was diagnosed in the presence of anasarca, massive proteinuria >2gs/24hours, hypoproteinemia- serum protein <2g/dl and hypercholesterolemia >200mg/dl or 5.17 mmol/l, while AGN was diagnosed by the presence of haematuria, hypertension, proteinuria and azotaemia.

All the patients received the standard management for the acute stage of illness except the commencement of steroids in those with NS. Early morning mid-stream urine specimens were collected into a sterile universal bottle and sent to the laboratory where immediate processing took place or it was stored at 4°C in the refrigerator until processing was carried out within 12 hours of

collection. On microscopy, white blood cell (WBC) count of 10 and above per high power field (HPF) were considered significant pyuria. Incubation of the urine was carried out on sheep blood agar and McConkey or CLED (cysteine lactose electrolyte deficient) agar using the quantitative loop method. The plates were examined at between 18–24 hours. A yield of multiple organisms was considered as contaminant. Growth of 10<sup>5</sup>/milliliter (ml) of urine was considered significant bacteriuria. Sensitivity of organisms was done using the isosensitive tested agar plate and the appropriate antibiotic discs were placed at 4–5cm apart and incubated at 37°C for 18–24 hours. The diameter of the zone of inhibition was then measured and the values equal to or greater than 15 mm were considered sensitive. Laboratory diagnosis of UTI was made in the presence of significant bacteriuria and pyuria. However significant pyuria in the presence of bacteriuria of 10<sup>4</sup>–10<sup>5</sup> colony forming units (CFU) per ml were also considered significant in the diagnosis of UTI.

Children with NS who had a relapse or were commenced on steroid, cytotoxic agent or antibiotic before admission were excluded from the study. AGN patients who had been commenced on any antibiotic before admission were also excluded.

The mean and standard deviations of the urinary profiles were computed and comparison made among the 2 disease groups using a Student's t-test. P value <0.05 is considered significant.

## RESULTS

A total of 35 and 32 children diagnosed with AGN and NS respectively met the inclusion criteria. The age range of children with AGN was 1.6–15 years with a mean (SD) of 7(4) years. There were 27 males and eight females giving a male/female ratio of 3.4:1. The age range of children with NS was 3–16 years with a mean of 9.1(3.7) years. There were 23 males and nine females giving a male/female ratio of 2.6:1. Pyuria occurred in 9(26%) of children with AGN, and 6(19%) of patients with NS. Bacteria organisms were

**Table 1: Characteristics of Urinary Tract Infection in Children with Acute Glomerulonephritis and Nephrotic Syndrome**

Characteristic	AGN N = 35	NS N = 32	P-value
<b>Gender</b>			
Male	27	23	
Female	8	9	
Male : Female ratio	3.4: 1	2.6:1	
<b>Age (years)</b>	7(4)	9.1(3.7)	
<b>UTI present N(%)</b>	3(9)	1(3)	>0.05
<b>Organisms isolated in Children with UTI</b>	<i>Coliform Klebsiella</i>	<i>Coliform</i>	
	<i>Staphylococcus aureus</i>		
<b>Mean WBC/HPF in all Children</b>	6(14)	3(9)	>0.05
<b>Sensitivity of the organisms isolated</b>	Ceftriaxone	Ceftriaxone	
	Gentamicin	Gentamicin	
	Ofloxacin	Ofloxacin	
<b>Gender of children with UTI</b>			
Male	1	0	
Female	2	1	
<b>Ages of children with UTI (Year)</b>	5 – 11	10	
<b>WBC/HPF of the children with UTI</b>	10 – 50	50	
<b>CFU/ml of urine in children with UTI</b>	10 <sup>4</sup> – 10 <sup>5</sup>	10 <sup>5</sup>	

cultured in the urine of 3(9%) children with AGN and 1(3%) child with NS. Similarly, significant bacteriuria occurred in the same patients. The organisms isolated in the children with AGN include *Klebsiella sp.*, *Coliforms* and *Staphylococcus Aureus*. Two of the three children with UTI were females – 5 and 10 years of age, while the third was a male of 11 years. The urine WBC counts /HPF in the three AGN children with UTI were 13,50 and 10 respectively. The CFU/ml of urine were also  $10^4$ ,  $10^5$ , and  $10^5$  respectively. The *Coliform* and *Klebsiella* were sensitive to ceftriaxone, gentamicin and ofloxacin. The organism cultured in the only child with NS that also had UTI was *Coliform*. This child was 10 years old and a female. She also had 50 WBC/HPF with a CFU/ml of urine of  $10^5$ .

## DISCUSSION

Urinary tract infections (UTI) occur when there is invasion of the urinary tract by microorganisms. It is known to occur through haematogenous spread and ascending infection from the lower urinary tract.<sup>7</sup> Acute Glomerulonephritis on the other hand is acute inflammation of the glomeruli as a result of immunological injury caused by preceding streptococcal infection.<sup>8</sup> While microorganisms cause UTI, AGN is caused by immune complex deposition on the glomeruli. Urinary Tract Infection may affect any part of the urinary tract from the urethra to the kidney, AGN affect just the glomeruli. The occurrence of AGN also leads to the reduction of the C3 complement, which is not affected in UTI. There are also differences in the common complications found in both illnesses. While UTI may result in pyelonephritic scar, hypertension, vesico-ureteral reflux and renal failure, AGN is capable of leading to renal failure, hypertensive encephalopathy and metabolic imbalance.<sup>8</sup> All these go to corroborate the fact that both AGN and UTI are two different pathological processes. To further buttress this, there is paucity of data on the association between prevalence of UTI in children with AGN. Our finding revealed a 9% prevalence of UTI in children with AGN. This is low compared with a prevalence of 20.6% among children with AGN seen in Benin.<sup>9</sup> The role of the AGN in the

development of UTI is not clear. It is possible that the transient loss of protein in the urine of some AGN patients may have resulted in the loss of some complement factors that could have made them susceptible to infection. Other contributory factors include the presence of oedema fluid, which could act as a culture medium for microorganisms. If all the above reasons play a role in making AGN patients to be susceptible to infection, it is our opinion that nephrotic syndrome patients should be more disadvantaged, since they are more susceptible because of decreased immunoglobulin levels, the oedema fluid acting as a culture medium, protein deficiency, decreased bactericidal activity of the leucocytes, immunosuppressive therapy and decreased perfusion of the spleen due to hypovolemia and loss in the urine of a complement factor (properdin factor B) that opsonises certain bacteria.<sup>10</sup>

Just like AGN, NS and UTI are also completely different pathological processes. However, there is a meeting point in the fact that NS patients are susceptible to infections including UTI due to reasons already enumerated above. Furthermore, infections including UTI have been implicated as a trigger of relapse in some children with NS.<sup>11,12</sup> Our findings however, indicate that UTI is uncommon in new cases of NS as only a prevalence of 3% was recorded. This finding contrasts with that of other workers who found a higher prevalence of between 12.5–44.8%.<sup>3-6</sup> Some of these workers examined both children and adult.<sup>5</sup> All those studies except the one by Ibadin<sup>3</sup> lumped all their cases of NS together irrespective of whether they were new cases or relapses. In the Ibadin study, out of 18 relapsers, 10 (56%) had positive urine culture compared to 2(17%) out of 12 non-relapsers. There was no statistical significance indicating that the presence of UTI did not affect relapses.<sup>3</sup> In those studies where both new cases and relapses are lumped together, a higher prevalence of NS may occur as there would have been exposure to a large dose of steroids and cytotoxic drugs which would have compromised their immunity therefore making them susceptible to all forms of infection. New

cases obviously do not have this disadvantage. This may account for the low prevalence obtained in this study. The lack of statistical significance in the occurrence of UTI in children with AGN and NS implies that UTI is an uncommon complication in newly diagnosed children with AGN and NS.

The leading organisms causing UTI in the general population include the *Coliforms*, *Klebsiella spp.*, *Proteus mirabilis* and *Pseudomonas aeruginosa*.<sup>7</sup> However, our findings implicated *Coliform* in both AGN and NS. This is similar to what obtains in the general population and it also agrees with the findings of Ibadin in Benin among children with NS.<sup>3</sup> The only difference occurs among children with AGN who developed UTI due to *Staphylococcus aureus*. This finding cannot be conclusive because of the small sample size and the few number of patients with AGN who developed UTI. The antimicrobial sensitivity of the isolated organism to quinolone and the third generation antibiotics agrees with findings of other workers who are discovering increasing efficacy of the quinolones and third generation antibiotics in the treatment of UTI.<sup>13,14</sup> Our findings indicate that these drugs can also be useful in children with AGN and NS who develop UTI just like in the general population that developed UTI.

In conclusion, UTI is uncommon in newly diagnosed children with NS and AGN. However, if it occurs as could happen sporadically *Coliforms*, *Klebsiella* or *Staphylococcus aureus* could be the offending organisms. These organisms are all sensitive to the quinolones and third generation antibiotics

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