

Prevalence and antimicrobial sensitivity pattern of urinary tract infection among children with cerebral palsy, Moshi, Tanzania

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Background: Urinary tract infection (UTI) in children with cerebral palsy (CP) is a challenging yet common clinical condition. Children with CP bare the greatest risk of contracting UTI because of their difficulties in neuromotor control which lead to delay of bladder control, causing incomplete bladder emptying and urine retention.

Method: This was an analytical cross-sectional study that was conducted from September 2016 to March 2017 at Comprehensive Community Based Rehabilitation in Tanzania – Moshi and Kilimanjaro Christian Medical Centre Neurological Pediatrics Outpatient Clinic. All children who met the inclusion criteria were studied. Urine samples were collected at one point by catheterization, and urine dipstick and urine culture were done. Data were analyzed using SPSS version 20.

Results: A total of 99 children were enrolled in the study. The median age was 4 years (3–8 years); 53.5% were aged between 2 and 4 years. More than half were male. UTI was detected in 13.1% (n=13) of the children. Five causative agents of UTI were isolated, namely *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumonia*, *Staphylococcus aureus*, and *Enterococcus faecalis*. The two most common organisms, *E. coli* and *P. mirabilis*, both had low sensitivity to ampicillin and co-trimoxazole while they were sensitive to ciprofloxacin and ceftriaxone.

Conclusion: UTI is a common finding among children with CP. *E. coli* and *P. mirabilis* are the commonest causative agents and are sensitive to ciprofloxacin and ceftriaxone but have low sensitivity to ampicillin and co-trimoxazole.

Keywords: urinary tract infection, cerebral palsy, Moshi, Tanzania

Introduction

Urinary tract infection (UTI) is a challenging yet common and important clinical problem in children.^{1–3} A single encounter of UTI is enough to cause renal scarring, which may eventually lead to a child developing hypertension and even end-stage renal failure as long-term consequences.^{4–9}

The factors that increase the likelihood of acquiring UTI include delay to attain bladder and bowel control, difficulty in neuromotor control of posture, low cognition, limited ability to communicate the need to void, constipation, impaired mobility, and bladder dysfunction.^{10–12} All these are common findings among children with cerebral palsy (CP).¹³

The burden of UTIs among children with CP in the developed world ranges from 8.5% to 56.7% while in Africa, Nigeria in particular, the prevalence was found to be 38.5%.^{14–19} The most common causative pathogens include *Escherichia coli*, *Proteus*

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spp, *Enterococcus faecalis*, *Klebsiella spp*, and *Staphylococcus spp*.^{15,18,19} The recommended treatments for these pathogens are amoxiclav and co-trimoxazole.¹ There are however reports of resistance to these first-line agents.¹⁹

Children with CP often receive empirical antibiotics for the treatment of UTI without confirmation of the presence of UTI or testing of sensitivity pattern. They also have other frequent comorbidities like upper respiratory infections and aspiration pneumonia which increase their exposure to antibiotics.^{20,21} This puts them at the risk of accumulating antibiotic-resistant pathogens and increasing drug-resistant strains in the community which is a major concern in light of the limited choices we have. It has been reported that children who are exposed to antibiotics have higher odds of harboring resistant pathogens compared to those who are not.²²

Lack of evidence-based diagnosis and treatment also puts unnecessary costs on the families, who are often poor, to treat presumed UTIs with drugs that are not effective. We were unable to find any published studies about UTI in children with CP in Tanzania.

The aim of this study was to determine the burden of UTI, its causative organism, and the antimicrobial sensitivity pattern among children with CP in Moshi. The research will improve the knowledge of the burden of the disease and will also enable clinicians to select antibiotics that will maximize cure while decreasing complication and chances of antibiotic resistance.

Materials and methods

This was an analytical cross-sectional study conducted from September 2016 to March 2017. It was conducted at Comprehensive Community Based Rehabilitation in Tanzania (CCBRT)–Moshi and Kilimanjaro Christian Medical Centre Neurological Pediatrics Outpatient Clinic (KCMC NPOC) in Moshi. CCBRT Moshi (House of Hope) is a rehabilitation centre, located in Kaloleni, Moshi. Therapy provided is done through scheduled weeks of therapy, “week of intensive therapy (WIT)”, in which children with different disabilities have a week stay at the rehabilitation centre for both rehabilitative and medical interventions.

KCMC is a zonal referral hospital in northern Tanzania running a weekly pediatric neurology clinic (where this study was conducted), among other inpatient and outpatient services. The study population comprised all children who had a diagnosis of CP attending CCBRT Moshi and KCMC NPOC for any reasons during the study period.

The study included all children aged 2–18 years who were diagnosed with CP. Children whose caregivers did not consent, those with documented use of any antibiotic within 2 weeks prior to enrollment or who had menstrual periods or any vaginal discharge were excluded. Parents/caregivers provided written informed consent for the participation of the children in the study.

A questionnaire was used to collect demographic and clinical data. Clinical examination and gross motor dysfunction classification was done by the principal investigator. The information that was collected included age, sex, address, diagnosis, gross motor function, and a short history. The parents or caregivers were asked about history of fever, blood in urine, color of urine, bladder and bowel control, and previous history of UTI or abnormalities.

The gross motor function classification system (GMFCS) was used as described by other researchers.^{23,24} The GMFCS is a 5-level classification that has been categorized into four age groups, which are before second birthday, between second and fourth birthday, between fourth and sixth birthday, and between sixth and twelfth birthday. It focuses on a child's self-initiation of sitting and walking activities. GMFCS levels I and II are stated as mild, level III as moderate, and levels IV and V as severe.^{19,23}

Urine sample collection

The investigator examined the children and collected urine samples in two sterile bottles. The steps for urine sample collection were followed as described by Bajaj and Bothner.²⁵ Urine samples were collected by using Foley catheter (MEDEX Healthcare, Beijing, China) size 6, 8, and 10 French depending on the age of the child. Spot urine dipstick test (Neotest® urine multistix; Neomedic Ltd, Rickmansworth, UK) was performed in one urine sample to detect nitrites and leukocyte esterase. The second sample was taken for culture and sensitivity. All samples for culture were stored in a cool box at a temperature of 5°C–7°C and then transported to the laboratory (KCMC Clinical Laboratory) for culture within 3 hours of collection.

Laboratory methods

Culture processing was done by inoculation of urine into MacConkey agar and 5% blood agar medium plate by using a standard 1 µ loop, to allow growth of both Gram-negative and Gram-positive organisms. The plates were incubated at 37°C, and the number of colonies was counted at the 24th hour. Growth of a single uropathogen with at least 50,000

colony-forming units per microliter was considered as positive culture. Bacterial colonies on solid agar were then identified based on a characteristic morphology and gram stain appearance. Biochemical identification test, Kligler iron agar, sulfur indole motility, citrate agar, oxidase, and urea were used for organism identification.

Drug susceptibility testing

Antimicrobial sensitivity testing was performed on selected antibiotics recommended by the World Health Organization and are commonly used. They included ampicillin (10 µg), amoxicillin-clavulanic acid (20/10 µg), nitrofurantoin, co-trimoxazole (30 µg), gentamicin (10 µg), ciprofloxacin (5 µg), cefotaxime (30 µg), and ceftriaxone (30 µg). The testing was done by Kirby-Bauer diffusion method by using Muller Hinton agar which was then incubated for 18–24 hours at 37°C. Antimicrobial sensitivity was reported as resistant, intermediate, and sensitive according to Clinical Laboratory Standard Institute.²⁶

Ethical clearance

Ethical clearance was obtained from the Kilimanjaro Christian Medical University College Research Ethics Committee and certificate number 968 was granted, and those who did not participate received equal care.

Data analysis

Data were coded and entered into SPSS version 20 (IBM Corporation, Armonk, NY, USA). Descriptive statistics were summarized by frequency and proportions. Continuous data were summarized as median along with interquartile range (IQR) values. Test for association between dependent and independent categorical variables was carried by using chi-square test. *P*-value of ≤0.05 was considered significant.

Results

Demographic characteristics of the study participants

A total of 107 eligible children were recruited between September 2016 and March 2017. Participants from CCBRT Moshi and KCMCNPOC were 100 and 7, respectively. Ninety-nine children were included in the final analysis. Eight children were excluded because they could not tolerate catheterization (Figure 1).

A majority of the children (53.5%) were aged between 2 and 4 years. The median (IQR) age at enrollment was 4 years (range =3–8 years). Male gender constituted a higher proportion (58.6%) (Table 1).

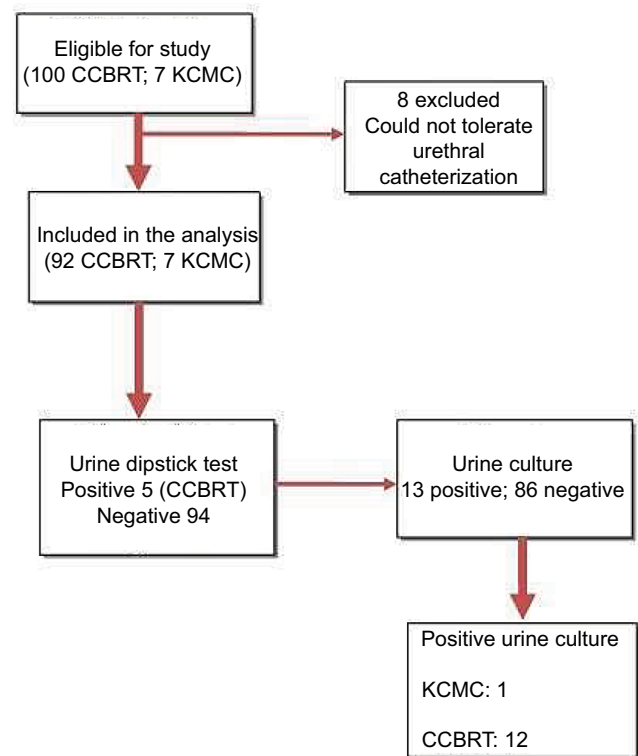


Figure 1 Study flow diagram.

Abbreviations: CCBRT, Comprehensive Community Based Rehabilitation in Tanzania; KCMC, Kilimanjaro Christian Medical Centre.

Table 1 Demographic characteristics of the study participants (N=99)

Characteristics	n (%)
Median age (IQR), years	4 (3–8)
Age, years	
2–4	53 (53.5)
5–7	21 (21.2)
8–10	16 (16.2)
≥11	9 (9.1)
Sex	
Male	58 (58.6)
Female	41 (41.4)
Residence	
Urban	50 (50.5)
Rural	37 (37.4)
Other	12 (12.1)

Abbreviation: IQR, interquartile range.

Clinical characteristics of the study participants

Those with a spastic quadriplegic type of CP constituted 64.6% of the children followed by hemiplegic CP (17.2%), athetoid CP (7.1%), mixed type CP (6.1%), diplegic CP (4%), and dystonic type of CP (1%). None had ataxic type of CP.

About 34% (n=34) of the study children had mild motor dysfunction, including 26.3% (n=26) with grade II and 8.1%

(n=8) with grade I. Moderate motor dysfunction was seen in 19.2% (n=19). Severe motor dysfunction was seen in 46.5% (n=46) of children; of these 25.3% (n=25) had grade IV and 21.2% (n=21) had grade V.

Symptoms and signs of UTI

Most (95%) of the interviewed caregivers or parents could not provide information regarding some of the UTI symptoms. The symptoms included frequency of urination, urgency, abdominal pain, and pain or straining during micturition. They reported that it was hard to ascertain because of their child's mental condition.

Information readily obtained from the caregivers included previous history of use of antibiotics, incontinence, constipation, fever, and smell and color of urine. About 18.1% had a history of using antibiotics at least 2 weeks before attending the rehabilitation center due to various reasons. Three of them were admitted due to respiratory infection and treated with intravenous drugs, probably antibiotics. None of them reported that they had malaria. The other 15 children were treated as outpatients. The antibiotics prescribed included amoxicillin, metronidazole, cephalexin, co-trimoxazole, and erythromycin. There was only one positive urine culture among those with a history of using antibiotics >2 weeks prior to enrollment.

About 14.1% had a previous history of UTI within 2 years prior to enrollment; the diagnosis was clinical, and they were treated with antibiotics. Of these, only one had a positive urine culture.

Regarding bladder control, among our study participants, 75.8% had urine incontinence, 18.2% were continent, and 6% either had day or night incontinence. Among those with incontinence, eight had positive urine cultures.

Other clinical information gathered in relation to UTI included constipation (less than three bowel motions in a week) which was reported among 30.3% of the participants. Over two thirds (71.7%) had cloudy and smelly urine. Among those with constipation and cloudy and smelly urine, there were four and 11 positive urine cultures, respectively. On examination, five children had temperatures above 37.5°C.

One female child tested positive for leukocyte esterase on urine dipstick with no nitrites. However, the urine culture and sensitivity analysis showed no growth. Three had aspiration pneumonia and were treated with ampiclox syrup plus metronidazole. Carbuncle was seen in one child, and she was given ampiclox syrup. All had recovered well upon follow-up. The clinical characteristics of the study participants are summarized in Table 2.

Table 2 Clinical characteristics of the study participants (N=99)

Characteristics	N (%)
Weight (kg)	
<10	34 (34.3)
11–20	50 (50.5)
>20	15 (15.2)
Types of cerebral palsy	
Spastic cerebral palsy	
Diplegia	4 (4.0)
Hemiplegia	17 (17.2)
Quadriplegia	64 (64.6)
Athetoid	7 (7.1)
Dystonia	1 (1.0)
Mixed type	6 (6.1)
Gross motor function	
Mild	34 (34.3)
Moderate	19 (19.2)
Severe	46 (46.5)
Urine is smelly and cloudy	
Yes	71 (71.7)
No	28 (28.3)
Pattern of continence	
Continent	18 (18.2)
Nocturnal only	2 (2.0)
Diurnal only	4 (4.0)
Incontinent	75 (75.8)
Constipation	
Yes	30 (30.3)
No	69 (69.7)
Previous history of urinary tract infection	
Yes	14 (14.1)
No	85 (85.9)
Fever	
Yes	5 (5.1)
No	94 (94.9)
Previous history of antibiotic use	
2 weeks + prior rehabilitation*	
Yes	18 (18.1)
No	81 (81.9)

Note: *Amoxicillin, metronidazole, cephalexin, co-trimoxazole, and erythromycin.

Prevalence of UTI

Urine culture was used as the confirmatory test in this study. The prevalence of UTI among children with CP attending CCBRT Moshi and KCMC NPOC was 13.1%. A few (5.1%) samples were leukocyte esterase positive and nitrite negative. None of the samples had either a positive nitrite or positive of both leukocyte esterase and nitrites.

There was no demographic or clinical characteristic which was associated with UTI among the study children (chi-square p -value >0.05) (Table 3).

Etiological agents

Five pathogens were isolated from 13 positive urine cultures. *E. coli* was the most common isolated pathogen

Table 3 Association between some characteristics of participants with cerebral palsy and presence of urinary tract infection (UTI)

Characteristics	Total	UTI, n (%)	χ^2	P-value
Age range, years				
2–4	53	9 (17.0)	2.738	0.434
5–7	21	3 (14.3)		
8–10	16	1 (6.2)		
>11	9	0 (0.0)		
Sex				
Male	58	8 (13.8)	0.054	0.817
Female	41	5 (12.2)		
Temperature				
Fever	5	2 (40.0)	3.333	0.068
No fever	94	11 (11.7)		
Gross motor function				
Mild	34	5 (14.7)	1.281	0.527
Moderate	19	1 (5.3)		
Severe	46	7 (15.2)		
Urine smell and color				
Yes	28	2 (7.1)	1.227	0.268
No	71	11 (15.5)		
Continence				
Continent	18	3 (16.7)	3.474	0.324
Nocturnal only	2	1 (50.0)		
Diurnal only	4	1 (25.0)		
Incontinent	75	8 (10.7)		
Constipation				
Yes	30	4 (13.3)	0.002	0.969
No	69	9 (13.0)		
Previous history of UTI				
Yes	14	1 (7.1)	0.513	0.474
No	85	12 (14.1)		
Medications taken for UTI				
Yes	18	1 (5.6)	1.107	0.293
No	81	13 (13.1%)		

found in seven (53.8%) children. Others included *Proteus mirabilis*, identified from three (23.1%) children, *Klebsiella pneumoniae* from one (7.7%) child, and two Gram-positive organisms, *Staphylococcus aureus* and *E. faecalis*, from two children.

Table 4 Antimicrobial drug sensitivity patterns of the isolated organisms (n=13)

Antimicrobial drug	Isolated organism n (%)*				
	<i>Escherichia coli</i>	<i>Proteus mirabilis</i>	<i>Klebsiella pneumoniae</i>	<i>Staphylococcus aureus</i>	<i>Enterococcus faecalis</i>
Cefotaxime	5 (71)	1 (33.3)	1 (100)	1 (100)	1 (100)
Ciprofloxacin	7 (100)	3 (100)	1 (100)	1 (100)	1 (100)
Gentamicin	6 (85)	3 (100)	1 (100)	1 (100)	1 (100)
Nitrofurantoin	6 (85)	1 (33.3)	0 (0.0)	1 (100)	1 (100)
Amoxicillin-clavulanic acid	6 (85)	2 (66.6)	1 (100)	1 (100)	1 (100)
Ceftriaxone	7 (100)	3 (100)	1 (100)	1 (100)	1 (100)
Ampicillin	2 (28.6)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100)
Co-trimoxazole	2 (28.6)	1 (33.3)	0 (0.0)	1 (100)	1 (100)

Note: *n (%) represents number (%) of sensitivity for each isolated organism.

Antimicrobial drug sensitivity pattern

E. coli isolated from the urine of seven children was least susceptible to co-trimoxazole (28.5%) and ampicillin (28.5%). *P. mirabilis* was also least susceptible to the same antibiotics. *E. coli* was 100% sensitive to ciprofloxacin and ceftriaxone but was less sensitive to amoxicillin-clavulanic acid, nitrofurantoin, gentamicin, and cefotaxime (71%–85%). *P. mirabilis* showed a similar trend. There was no mixed growth or contaminants (Table 4).

Discussion

The prevalence of UTI among children with CP in Tanzania was 13.1%. This was similar to studies performed in Turkey.^{14,18} It was lower compared to the majority of studies conducted elsewhere.^{15–17,19} The causative organisms of UTI and their sensitivity patterns were similar to previous studies.^{15,18,19} The similarities in findings observed in the current study and the few conducted in Turkey can be attributed to them sharing similar study designs and inclusion of young children with CP regardless of their clinical symptoms, just like the current study.

The majority of the studies done previously documented a higher proportion of UTI compared to the current study. They included older children (mean age 8 years) with fewer urinary tract symptoms and they also collected urine samples by clean catch method.^{15,17}

Silva et al¹⁶ found that 56.7% of the children had UTI, which is a huge disparity with the current study. This can be explained by the small sample size (N=37), and the characteristics of the participants studied by Silva et al. A majority of the participants were female with moderate to severe motor dysfunction using wheelchairs and they had fewer urinary tract symptoms, although the mode of urine collection was not stated.

In the African setting, only one study has been published on UTI in CP. Anígilájé and Bitto¹⁹ in Nigeria reported a higher prevalence (38.5%) compared to that of the current

study because of the difference in mode of urine sample collection and where it was collected. The observed prevalence might have been due to contamination from the genitalia or perineum and not organisms from the bladder, as urine sample collection was done at home and only routine personal hygiene was required. The time lapse between the time of urine sample collection and the testing of the urine was not accounted for. To minimize false positives, it is recommended that urine analysis should be done on a fresh urine sample at room temperature in less than an hour after its collection.^{1,27} In the current study, urine samples were collected by sterile transurethral catheterization. This minimized the chances of contamination.

Also, the observed prevalence in the current study could be influenced by the use of antibiotics at least 2 weeks before attending the rehabilitation center, due to various reasons that were reported by 18 of the respondents. The most used antibiotic was amoxicillin; this could have cleared off any organisms that could be isolated as it was observed in a previous study.²⁸

In the current study, no factors were associated with UTI. This is different from the study by Anígilájé and Bitto¹⁹ who found that motor disability and constipation had association with UTI. Despite the absence of association, motor function, incontinence, and constipation are of clinical significance.

Incontinence is common among children with CP who have moderate to severe motor impairment. In the present study, two thirds of the children (75.8%) were incontinent, majority being male. This is similar to studies performed elsewhere.^{16,17,28} The higher proportion of incontinence observed in this study can be explained by the presence of a higher percentage of children aged between 2 and 4 years (53.5%) who are not bladder trained. Children with CP attain spontaneous bladder control at around 47 months of age.¹⁵

Constipation has been demonstrated to have impact on UTI.³⁰ In children with motor disability, a full rectum compresses the bladder and causes bladder dysfunction which leads to incomplete bladder emptying and increase in residual urine volume. Constipation occurs in 27%–50% of children with CP.^{16,17,19,29,30} In the current study, 30.3% had constipation. This proportion might not be a true representation due to unawareness of constipation as a problem leading to possible underreporting, as has been observed by Halachmi and Farhat.³¹

A majority of children in our study had cloudy and turbid urine. There was no association between UTI and smelly or turbid urine, which is a similar finding to Struthers et al.³² The observed high proportion of those with smelly and turbid

urine is attributed to more than half of the participants having moderate to severe motor function and depending entirely on someone else to help them drink, feed, and sometimes even taking them to the toilet. They might be getting less fluid than required.³³

In the etiology of UTI in children with CP, Gram-negative organisms predominated. *E. coli* and *P. mirabilis* were the most common causative agents. The other was *K. pneumoniae*. The Gram-positive agents isolated were *S. aureus* and *E. faecalis*. These findings are similar to those of previous studies.^{15,18,19}

The current study adds on the finding that *E. coli* in UTI is highly resistant to first-line antibiotics, co-trimoxazole and ampicillin, and is sensitive to ciprofloxacin and ceftriaxone, as has been found by other studies.^{19,22,28} We rarely use quinolones in children, and ceftriaxone is used in hospitals when there is severe infection. Exposure to the first-line antibiotics is however frequent as they are commonly given in primary health facilities and can even be procured over the counter. The observed resistance to first-line antibiotics may be explained by inappropriate use of these antibiotics, that is either patients use low doses or they do not adhere to the prescriptions, if any are provided. This observation is alarming, necessitating a call for local epidemiological surveillance of the antibiotic resistance patterns in our setting.

Generalization of the findings may not be plausible because of the minimal representation of older children. Also, there could be underreporting of antibiotic use. This was a strict exclusion criterion, and blood drug levels were not measured.

Conclusion

The prevalence of UTI among children with CP attending CCBRT Moshi and KCMC NPOC was 13.1%. *E. coli* and *P. mirabilis* were found to be the common causative agent of UTI among children with CP in this study. Both *E. coli* and *P. mirabilis* have low sensitivity to the first-line antibiotics used; ampicillin and co-trimoxazole. Their sensitivity pattern to other antibiotics is of a varying degree.

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Disclosure

The authors report no conflicts of interest in this work.

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