Frequency and Antimicrobial Susceptibility Pattern of Urinary Tract Infections in Children Having Cerebral Palsy

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Abstract

Objective: This study aimed to ascertain the frequency of UTIs, identify causative organisms, and assess their antimicrobial susceptibility among CP children at Children's Hospital, Lahore.

Material and Methods: This study was conducted over six months from February to August 2022, this was a cross-sectional study. The study was conducted at the Children's Hospital, Lahore (CHL). 125 CP children (aged 2-12 years, both genders) were evaluated for urinary tract issues. Isolated organisms underwent susceptibility testing against common antibiotics.

Results: CP children (mean age: 6.3±3.1 years) exhibited varying CP subtypes: spastic diplegia (35.2%), spastic hemiplegia (26.4%), spastic quadriplegia (22.4%), and dyskinetic CP (16.0%). UTIs were diagnosed in 34.4% of cases, predominantly caused by E. coli (53.5%), streptococcus fecalis (20.9%), Proteus Mirablis (14.0%), and Klebsiella (11.6%). Notably, E. coli, Proteus, and Klebsiella displayed 100% sensitivity to ciprofloxacin, ceftriaxone, cotrimoxazole, and gentamicin. However, susceptibility of streptococcus fecalis varied, being 100% sensitive to both ceftriaxone and ciprofloxacin, while exhibiting 55.6% sensitivity to cotrimoxazole and 66.7% to gentamicin.

Conclusion: A significant proportion of CP children exhibited UTIs primarily caused by E. coli and streptococcus fecalis, both fully susceptible to ceftriaxone and ciprofloxacin. These findings advocate for routine UTI screenings in CP children, emphasizing the preference for ceftriaxone and ciprofloxacin in managing positive cases.

Keywords: Cerebral palsy, urinary tract infection, antimicrobial susceptibility.

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Introduction

Cerebral palsy (CP) is a group of disorder related to movement and posture, leading to limitation of activity due to the non-progressive injury to immature developing brain of fetus or infant.[1] CP can result from any injury or damage to the brain during the prenatal, perinatal or postnatal period of life.[2] Its prevalence is around 2 to 3 children per 1,000 live births and is considered to be the most common cause of childhood disabilities.[1,3,4] Cerebral palsy can not only lead to reduced life expectancy, but it is also a very commonly cause of morbidity in children, which may include menial disabilities, recurrent respiratory infections or aspiration pneumonias, epilepsy, vision or hearing defects and infections of urinary tract.[5,6]

Urinary tract infection (UTI) is common among children having cerebral palsy with prevalence of around 8.5 to 56.7%.7 The factors leading to increased chances of UTI among CP patients include delayed attainment of bowel and bladder control, neuromotor dysfunctions, low mental capabilities including difficulty in communicating the desire to void, bowel and bladder dysfunc-

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tions.[7] The repeated urinary tract infections can lead to vesicoureteral reflex and upper urinary tract damage. Therefore, it is pivotal to diagnose urinary tract infections in pediatric population to prevent any long-term morbidity or mortality related to undiagnosed urinary tract infections.[8] A previous Nigerian study suggests a high prevalence (38.5%) of UTI among CP patients, especially among ones having severe immobility. The major organism causing UTI were reported to be E. coli (45%), Streptococcus fecal is (20%) while Proteus and Klebsiella were 10% each. All the isolated organisms were 100% resistant to amoxiclave, cotrimoxazole, nitrofurantoin, and nalidixic acid, while sensitivity to quinolones and ceftriaxone was 100%.[9] In a study conducted by Ryaktiimbo, a frequency of UTI in CP children was 13.1%. The major organism causing UTI were reported to be E. coli (58.3%) and P. mirablis (23.1%), both had low sensitivity to ampicillin (28.5%) and cotrimoxazole (28.5%) while they were sensitive to ciprofloxacin and ceftriaxone (both 100%).[7]

Although many studies in other countries showed a correlation between both frequency and antimicrobial susceptibility pattern of UTI with CP child, but there has been only one previous such study conducted in Pakistan at Hayatabad Medical complex, Peshawar suggesting increased frequency of UTI (32.7%) in children having CP but it did not report antimicrobial susceptibility pattern[(10)]. Now a day, one of the major problems faced by Pakistani physicians is lack of any locally published data on antimicrobial susceptibility pattern, which results in injudicious use of antibiotics. Therefore, this research was conducted to determine the frequency as well antimicrobial susceptibility pattern of UTI among cerebral palsy patients at the Children's Hospital, Lahore to guide establishment of evidence based clinical management of UTI among CP children.

Material and Methods

It was an observational cross-sectional study was conducted at Children's Hospital, Lahore (CHL)., over 6 months from February 2022 to August 2022. After the taking approval from CPSP/REU/PED-2020-075-5868 2nd Feb. 2022. The sample size of 125 cases was calculated with 6% margin of error and 95% confidence level while taking expected frequency of UTI among children with CP as 13.1%.[7] Patients were selected by non-probability technique of consecutive sampling. The children having age 2 to 12 years, both genders presenting with Cerebral palsy with different functional impairment according to European Classification were included in the study. The children who had used any antibiotic within 2 weeks of presentation to hospital or having menstruation, vaginal or penile discharge at presentation or ones having diabetes mellitus (BSR ≥ 200mg/dl), chronic heart disease (medical record) or hypertension (BP ≥ 140/90mmHg) were excluded from the study. The UTI was labelled if there was detection of ≥ 100,000 colony forming units per mL of pathogen organism cultured from specimen obtained. The antibiotic susceptibility pattern was determined as reaction of the most commonly isolated organisms i.e. E. coli, Proteus Mirablis, Streptococcus fecalis and Klebsiella to the antibiotics by CLSI criteria (Ceftriaxone: MIC=64µg/mL, Zone diameter ≤ 13mm resistant and ≥ 18 mm sensitive, Gentamicin: MIC=2µg/mL, Zone diameter ≤ 12mm resistant and ≥ 15 mm sensitive, Cotrimoxazole: MIC=2µg/mL, Zone diameter ≤ 10mm resistant and ≥ 16 mm sensitive, Amikacin: MIC=32µg/mL, Zone diameter ≤ 14mm resistant and ≥ 17 mm sensitive, Ciprofloxacin: M1C= 15µg/mL, Zone diameter ≤ 16mm resistant and ≥ 20 mm sensitive and Ampicillin: MIC=16µg/mL, Zone diameter ≤ 13mm resistant and ≥ 17 mm sensitive)

After ethical committee of the College of Physicians and Surgeon of Pakistan approved the study synopsis, 125 patients visiting the CHL were selected, who fulfilled the inclusion and exclusion criteria. After obtaining informed consent in written, a detailed history was taken (name, age, gender and weight, functional impairment of cerebral palsy and duration of symptoms). A urine sample was taken via aseptic technique in a sterile container. All samples were sent to the laboratory for complete urine analysis and antibiotic susceptibility. Reports were assessed and if bacterium and pus cells detected on urine sample, then urinary tract infection was labelled as per the operational definition. In patients with positive urinary tract infection, organisms and antibiotic susceptibility was checked by using minimal inhibitory concentration method as described in operational definition. All the data was noted and recorded on the pre-designed proforma. All the urine analyses were done from the same hospital laboratory and important confounding factors were controlled by exclusion. The data was then entered into and analyzed through SPSS version 22.0. The numerical variables i.e., weight, age and duration of symptoms were presented as mean ±SD. The categorical variables i.e., the type of CP, gender, presence of UTI, organism and antimicrobial

susceptibility pattern were presented as frequency and percentage. To address effect modifiers, data was stratified for age, weight, gender, duration of symptoms and type of CP. Post-stratification, Fisher's exact test/ chi-square was applied to compare the presence of UTI, organisms and antimicrobial susceptibility pattern in stratified groups taking P-value of ≤0.05 as significant.

Results

The mean age of the participants was 6.3±3.1 years where 2 year was minimum age and maximum age was 12 years. Majority (n=72, 57.6%) of the children were aged ≤ 5 years with 31 (24.8%) children aged between 6-10 years and 22 (17.6%) children aged above 10 years. There were 82 (65.6%) boys and 43 (34.4%) girls and male to female ratio was 1.9:1. The commonest type of CP among participant was spastic diplegia (n=44, 35.2%) followed by spastic hemiplegia in 33 (26.4%) **(Table 1).** The UTI was diagnosed in 43 (34.4%) children with cerebral palsy. There was no statistically significant difference in the frequency of UTI across various sub-groups of children based on age (p=0.956), gender (p=0.934), weight (p=0.976) and type of CP (p=0.998) as shown in Table 1. E. coli was the most frequent causa-tive organism and was isolated in 23 (53.5%) cases of UTI followed by streptococcus fecalis in 9 (20.9%) cases, Proteus Mirablis in 6 (14.0%) cases and Klebsiella in 5 (11.6%) cases as shown in **(Table 2)**. None of the organism showed sensitivity to amikacin and ampicillin. E. coli, Klebsiella and Proteus were 100% sensitive to ciprofloxacin, ceftriaxone, cotrimoxazole and genta-micin.

Table 1: *Characteristics of participants and comparison of urinary tract infection across various subgroups of children with cerebral palsy.*

Characteristics	n	UTI n (%)	P-value
Age			
• ≤5 years	72	24 (33.3%)	0.956
• 6-10 years	31	11 (35.5%)	
• >10 years	22	8 (36.4%)	
Gender			
• Boy	82	28 (34.1%)	0.934
• Girl	43	15 (34.9%)	
Type			
• Spastic Hemiplegia	33	11 (33.3%)	0.998
• Spastic Diplegia	44	15 (34.1%)	
• Spastic Quadriplegia	28	10 (35.7%)	
• Athetoid/Dyskinetic	20	7 (35.0%)	

Table 2: *Frequency of Various Organisms Isolated in Children with Urinary Tract Infection and Cerebral Palsy.*

Causative Organism	Frequency (n)	Percent (%)
E. coli	23	53.5 %
Proteus Mirablis	6	14.0 %
Streptococcus Fecalis	9	20.9 %
Klebsiella	5	11.6 %
Total	43	100.0 %

Table 3: *Susceptibility Pattern of Various Isolates to Common Antibiotics*

Antibiotic	E. Coli	Proteus M.	Strepto-coccus F.	Klebsiella
Ciprofloxacin	23(100.0%)	6(100.0%)	9 (100.0%)	5(100.0%)
Ceftriaxone	23(100.0%)	6(100.0%)	9 (100.0%)	5(100.0%)
Cotrimoxazole	23(100.0%)	6(100.0%)	5 (55.6%)	5(100.0%)
Gentamicin	23(100.0%)	6(100.0%)	6 (66.7%)	5(100.0%)
Amikacin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ampicillin	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

However, susceptibility of streptococcus fecalis varied, being 100% sensitive to both ceftriaxone and ciprofloxacin, while exhibiting 55.6% sensitivity to cotrimoxazole and 66.7% to gentamicin as shown in **(Table 3).**

Discussion

In children with cerebral palsy, there is disturbed immune function which is multifactorial in origin and leads to increased risk of infection that has been identified as a significant contributor of early death.[3,4,11] A few recent studies suggested that a considerable proportion of CP children had undiagnosed urinary tract infection which required appropriate management depending upon causative organism and its antimicrobial susceptibility.[7,9,10] Recurrent febrile UTIs have been associated with upper urinary tract deterioration in children having CP and therefore necessitate proper urological evaluation.[8,9] However, the available evidence on the frequency of UTI, underlying organism and its antimicrobial susceptibility was limited and varied among studies which called for the present study.

In our study, the mean age was 6.3±3.1 years. Mahmood et al. (2019) reported similar mean age of 6.8±2.3 years at the time of diagnosis of cerebral palsy in children presenting at National Institute of Rehabilitation Medicine (NIRM) Islamabad.[12] Roheen et al. (2019) observed similar mean age of 6.6±9.9 years among such CP children.[13] Khandaker et al. (2018) reported mean age of

7.7±4.6 years in Bangladesh[14] while Shrestha et al. (2017) observed it to be 8.3±2.9 years in Nepalese children with cerebral palsy.15 Al-Hammad et al. (2015) reported similar mean age of 6.7±2.7 years in Saudi such children.[16] We observed that there was male (1.9:1) predominance among CP child. In a similar local study, Iqbal et al. (2019) observed similar male to female ratio (1.9:1) among CP children presenting at Jinnah Hospital Gujranwala.[17] Whereas, Khandaker et al. (2018) observed it to be 1.8:1 in Bangladesh.14 And Shrestha et al. (2017) found it to be 1.6:1 in Nepal.[15] Our finding is also similar to that Awan et al. (2019) who also reported male to female ratio of 1.9:1 among CP children in KSA.[18] We observed that majority of the patients had spastic diplegia (n=44, 35.2%) followed by spastic hemiplegia in 33(26.4%) cases and spastic quadriplegia in 28 (22.4%) cases.[20] (16.0%) children had athetoid/dyskinetic cerebral palsy. Ghazal et al. (2019) reported similar frequency of spastic diplegia (35.8%), spastic hemiplegia (27.4%), spastic quadriplegia (18.8%) and athetoid/dyskinetic CP (23.0%) among children presenting at the CHL.[19] Yalçinkaya et al. (2014) observed similar frequency of spastic diplegia, spastic hemiplegia, spastic quadriplegia and athetoid CP and reported it to be 31.5%, 31.4%, 25.3% and 11.8% respectively in Turkish such children.[20] In a similar Iranian study, Inaloo et al. (2016) documented comparable frequency of spastic diplegia (35.0%), spastic hemiplegia (25.0%), spastic quadriplegia (23.0%) and athetoid/dyskinetic CP(17.0%) among such children.[21] Similar frequency of spastic diplegia, spastic hemiplegia, spastic quadriplegia and athetoid CP has been observed by Al-Hammad et al. (2015) who reported it to be 40.3%, 31.8%, 13.8% and 14.1% respectively in KSA.[16] Whereas in a study conducted at Children's Hospital Lahore, involving 100 patients with cerebral palsy (CP), the mean age was 4.090±1.672 years compared to 6.3±3.1 years in our study. Though in that study around 2/3rd patients were male like our study but the most common type of CP was spastic quadriplegic (79%) variety.[22] In the present study, UTI was diagnosed in 34.4% children with cerebral palsy. E. coli was isolated in 53.5% cases followed by streptococcus fecalis (20.9%), Proteus Mirablis (14.0%) and Klebsiella (11.6%). E. coli, Klebsiella and proteus were 100% sensitive to ciprofloxacin, ceftriaxone, cotrimoxazole and gentamicin. The susceptibility of streptococcus fecalis varied, being 100% sensitive to both ceftriaxone and ciprofloxacin, while exhibiting 55.6% sensitivity to cotrimoxazole and 66.7% to gentamicin.

Our observation is comparable with a similar local study conducted at Sir Ganga Ram Hospital, Lahore where Anwar et al. (2020) observed UTI among 34.0% of children having cerebral palsy. However, the author didn't investigate causative organism or its antimicrobial susceptibility.[23] A comparable frequency of 33.8% for UTI has been reported by Kanta et al. (2021) in Bangladeshi children with cerebral palsy. Yet again, the author didn't investigate causative organism or its antimicrobial susceptibility.[24]

Similar frequency of urinary tract infection among CP children has been observed by Anigilaje et al. (2013) who reported it to be 38.5% in Nigeria. The author also observed comparable frequency of E. coli (45.0%), streptococcus fecalis (20.0%), Proteus Mirablis (10.0%) and Klebsiella (10.0%) among such children. They also reported that these isolates were 100% sensitive to ceftriaxone and ciprofloxacin.[9]

In a recent Indian study, Chate et al. (2021) observed urinary tract infection in 32.3% of children with cerebral palsy. The author reported comparable frequency of E. coli (53.8%), streptococcus fecalis (23.1%), Proteus Mirablis (15.4%) and Klebsiella (7.7%) among such children. They too observed that these microbes were 100% sensitive to ciprofloxacin and ceftriaxone. Streptococcus fecalis in their series was 50.0% sensitive to cotrimoxazole and 75.0% sensitive to gentamicin.[25]

The present study is first of its kind in local population giving insight into type and susceptibility pattern of organisms causing UTI in CP children. This adds to the limited previously published evidence on the topic. The strengths of our study is large sample size of 125 cases along with strict exclusion criteria. Our data was also stratified to address various effect modifiers. In the current study, we observed that a substantial proportion of CP children had urinary tract infection with E. coli and streptococcus fecalis as the frequent causative organism. We also observed that these microbes were 100% susceptible to ceftriaxone and ciprofloxacin which are cheap and routinely available antibiotics at government as well as private setups. In the light of this evidence, we advocate that in future practice CP children should be screened for UTI and these antibiotics should be preferred in the management of positive cases. This is of prime importance as children having repeated UTI have risk of developing renal damage and long term complications and need to be investigated properly to manage underlying cause.[26] The cross-sectional study design was one of the limitation of our study

as we didn't follow these children to determine the response to treatment and long term outcome which could have further helped us in the management planning of such cases. Such a study is of vital importance and is strongly favoured in future clinical research.

Conclusion

A significant proportion of CP children exhibited UTIs primarily caused by E. coli and streptococcus fecalis, both fully susceptible to ceftriaxone and ciprofloxacin. These findings advocate for routine UTI screenings in CP children, emphasizing the preference for ceftriaxone and ciprofloxacin in managing positive cases.

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Authors Contribution

WR: Conceptualization of Project
MS: Data Collection
ZRA: Literature Search

MS: Statistical Analysis

ZRA: Drafting, Revision
ZRA, WR: Writing of Manuscript