

## PREVALENCE, MICROBIOLOGICAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY PATTERN OF URINARY TRACT INFECTION IN CHILDREN BETWEEN 2 TO 14 YEARS OF AGE- A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL

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### Abstract

**Background:** UTI is a major health problem. The urinary tract is a common site of infection in young children. Urinary tract infections (UTIs) are cause acute morbidity and may result in long-term medical problems, including hypertension and reduced renal function. **Materials and Methods:** After obtaining informed consent and applying the inclusion and exclusion criteria, 122 children with clinically diagnosed UTI were included in the study. The study was a cross-sectional study conducted in the IPD and OPD of Department of Paediatrics, MGM Muthoot Medical Centre, Pathanamthitta, Kerala. Urine cultures were obtained after urine routine examination. A positive result was defined as growth of a single urinary tract pathogen >10<sup>5</sup> CFU/ml. Data was collected meeting the objectives of the study and was analysed using appropriate statistical methods. **Result:** The prevalence of culture positive UTI in children between 2 to 14 years is 32.78 %. There was a higher prevalence of UTI was found in our study. Highest prevalence of UTI was seen in 2 to 5 years and female gender. There was also a statistically significant association of UTI and symptoms like fever (male and female) and loose stools in male. The age group of children having UTI is less than 5 years in most of the cases. Prevalence of culture positive UTI was high (32.78%). Prevalence was higher in age group between 2 to 5 years and in females. **Conclusion:** In this study it is quite alarming to note that almost all of the isolates in the urine culture were found resistant to many commonly used antibiotics. Antibiotic resistance is becoming a big problem for the public health which cause complications and leads to chronic conditions and add considerably to health care cost. Therefore, it is an important issue to be addressed by the policy makers to formulate a strict antibiotics prescription policy in our country.

## INTRODUCTION

Urinary Tract Infection (UTI) is caused by the presence and growth of microorganism anywhere in the urinary tract and is perhaps the single commonest bacterial infection of mankind.<sup>[1]</sup> Infection of the urinary tract is identified by growth of a significant number of organisms of a single species in the urine, in the presence of symptoms. Urinary Tract Infections (UTI) are a common bacterial infection in children. A clinically suspected case of a new infection of the urinary tract appearing after the

healing of a preceding one, demonstrated either by a change of the bacterial species or of the serogroup of the infecting bacterial strain between two consecutive infections. Two or more negative cultures between two infections caused by identical strains may also indicate reinfection.

Recrudescence of a preceding infection which had never healed referred as relapse. Midstream urine sample showing a colony count of more than 10<sup>5</sup>/ml of a single organism is called significant bacteriuria. Any bacterial growth in suprapubic aspirate of urine specimen is considered significant.<sup>[2,3]</sup>

Acute complications of UTI which include bacteraemia, sepsis and in severe cases multiple organ system dysfunction, shock etc, whereas renal complications like APN (acute pyelonephritis) are uncommon in otherwise healthy children. But renal abscess or complete occlusion may occur in a pre-existing, partial ureteropelvic junction obstruction. Acute kidney injury may occur because of dehydration or an administration of a NSAID or antibiotics, which may diminish renal function by causing papillary necrosis or interstitial nephritis. Urosepsis may occur, particularly with Gram negative infections.<sup>[4]</sup>

The most consequential long-term complication of APN is renal scarring. In most children, renal scarring may not be clinically significant, but it may cause hypertension and proteinuria and a progressive decline in renal function in those with bilateral significant scarring. Delayed initiation of antibiotic treatment is associated with increased risk of scarring.<sup>[5]</sup>

## MATERIALS AND METHODS

It was a Hospital based Prospective cross-sectional study. This study was conducted on paediatric patients between age of 2 to 14 years admitted in paediatric ward as well as shown in paediatric OPD with diagnosed case of UTI (clinical features suggestive of UTI and pyuria) in MGM Muthoot Medical Centre, Pathanamthitta, Kerala during the study period of 12 months, who fulfilled the inclusion criteria. The study was carried out from December 2020 to November 2021.

### Inclusion Criteria

Children age group  $\geq 2$  years &  $\leq 14$  years with urine routine examination showing pus cells  $> 5$ /HPF.

### Exclusion Criteria

Definite Source of Fever (by investigation)

Any obvious or suspected focus of infection (by clinical examination), Current antibiotic therapy, Immunodeficiency (ANC - 500), Caretaker absent or unable to communicate, Parents who are not willing to give consent.

Sample size and sampling-Assuming the prevalence of UTI among children (p) as 28.27% from previous study<sup>6</sup>, confidence level as 95% and desired precision (d) as 8% of (p), the sample size was calculated as 122 using the following formula:

$$n = (Z\alpha)^2 \times p \times q / \delta^2$$

Where, n = Sample size

$Z\alpha = 1.96$  at 5% level of significance

p = Prevalence of desired variable of interest = 28.27%

q = 100-p

$\delta$  = desired precision

### Methodology

After obtaining clearance of the ethical committee, 122 paediatric patients between age of 2 to 14 years admitted in paediatric ward as well as shown in

paediatric opd with diagnosed case of UTI in MGM Muthoot Medical Centre, Pathanamthitta, Kerala who fulfilled the inclusion criteria were included as the study subjects. After obtaining written informed consent, the parents were interviewed using a questionnaire. Once filled, it was collected and entered into Microsoft Excel.

The questionnaire used had sections on socio-demographic variables, past history, history of UTI, and symptoms of UTI. Urine cultures are obtained from the patient having pus cells  $> 5$  / HPF in urine routine examination. Clean catch midstream sample collected are sent to the microbiology laboratory in sterile container. Sample is refrigerated, if not plated, within 2 hours of receipt. Standard quantitative culture was performed by laboratory technologists. A loop calibrated to deliver approximately 0.001 mL of urine is used to plate blood and MacConkey agar plates. All plates are incubated at 35°C and examined daily for growth for 48 hours. A positive result is defined as growth of a single urinary tract pathogen  $> 10^5$  CFU/ml. The plate showing growths are further incubated into Mueller Hinton agar plate for checking antibiotic disc sensitivity pattern.

### Statistical Analysis

The clinical data collected from paediatric admissions and during OPD visits was documented in a standard proforma. The laboratory data at admissions was documented in a standard proforma. These data collected was entered in MS excel and analysed using SPSS (Statistical package for social sciences), version 16.0. All the qualitative data was expressed as frequency and percentage. Chi square test was applied to find the association between categorical variables. Comparison of the two groups was done using unpaired t-test with 95% level of significance and at 80% power. A p-value  $< 0.05$  is considered as significant. The study was approved by the Institute Ethics Committee of MGM Muthoot Medical Centre, Pathanamthitta, Kerala.

## RESULTS

Age distribution in the study- 2 to 5 years (54.2%), 5 to 12 years (40.2%) & 12 to 14 years (5.70%) respectively. The numbers of participants in the study were 34 (27.90%) were boys & 88 (72.10%) girls respectively. [Table 1]

As per [Table 2] the prevalence of culture positive UTI was 32.80% and culture negative UTI prevalence was 67.20%.

[Table 3] shows the isolates in culture, most common being gram negative organism (Ecoli and Klebsiella) 90%. Highest resistance is for Ampicillin and amoxicillin. Highest sensitivity was for nitrofurantoin, cefoperazone-sulbactam, Meropenem. Klebsiella is not susceptible to amoxicillin and ampicillin. High sensitivity to nitrofurantoin, cefoperazone sulbactam, meropenem and imipenem. Gram positive enterococcus is highly

resistant to Erythromycin and tetracycline, but susceptible to most of other antibiotics. [Table 3] shows the isolates in culture, most common being gram negative organism (Ecoli and Klebsiella) 90%. Highest resistance is for Ampicillin and amoxicillin. Highest sensitivity was for nitrofurantoin, cefoperazone -sulbactam, Meropenem. Klebsiella is not susceptible to amoxicillin and ampicillin. High sensitivity to nitrofurantoin, cefoperazone sulbactam, meropenem and imipenem. Gram positive enterococcus is highly resistant to Erythromycin and tetracycline, but susceptible to most of other antibiotics. [Table 4] The descriptive statistics of duration of increased frequency of urination according to age group is

shown. There is no significant relationship as increased frequency of urination and UTI according to age group (p value= .502). [Table 5] Descriptive statistics of number of UTI in the past according to age group is shown. Children in the younger age group developed recurrent UTI. There is no statistical significance with number of UTI in past and UTI according in the various age group in this study (p value =.335). [Table 6] The descriptive statistics of organism according to age group is shown in. Most common organism isolated in all age group is E coli. There is no statistically significance with organism isolated and UTI in the various age groups in this study (p value-.464). [Table 7]

**Table 1: Age and Gender of study participants**

Age group	Percentage
2-5 years	54.10%
5.1-12 years	40.20%
12.1- 14 years	5.70%

**Table 2: Prevalence of culture positive UTI in children 2 to 14 years**

Prevalence	Cases	Percentage
Culture positive UTI	40	32.80%
Culture negative UTI	82	67.20%
Total	122	100

**Table 3: Organism isolated**

Organism	Cases	Percentage
E COLI	32	80 %
KLEBSIELLA	4	10 %
ENTEROCOCCUS	4	10 %

**Table 4: Descriptive statistics of fever according to age group**

Age Group	Fever		Total	Chi Square (p value)
	Yes	No		
2-5 years	47	19	66	0.020
5.1-12 years	23	26	49	
12.1-14 years	3	4	7	
Total	73	49	122	

**Table 5: Descriptive statistics of increased frequency of urination according to age group**

AGE GROUP	Increased frequency of urination?		Total	Chi Square (p value)
	Yes	No		
1-5 years	23	43	66	0.502
5.1-12 years	18	31	49	
12.1-14 years	1	6	7	
Total	42	80	122	

**Table 6: Descriptive statistics of number of UTI in the past according to age group**

Age group	NUMBER OF UTI IN PAST						Chi Square
	1	2	3	5	6	10	
2-5 years	8	3	3	1	0	0	0.335
5.1-12 years	6	2	0	0	1	1	
12.1-14 years	0	0	0	0	0	0	

**Table 7: Descriptive statistics of organism according to age group**

Age group	Culture report				Total	Chi Square (p value)
	No Growth	E coli	Enterococcus	Klebsiella		
2-5 years	44	19	2	1	66	0.464
5.1-12 years	31	13	2	3	49	
12.1-14 years	7	0	0	0	7	
Total	82	32	4	4	122	

## DISCUSSION

The present study assesses the prevalence of UTI in children and also the possible risk factors that contribute to the development of UTI in Children. We also tried to find the association between the risk factors and UTI, prevalence of UTI based on risk factors and the most common organisms isolated from the urine cultures of these children. There by controlling the increase in antimicrobial resistance since it is a major issue confronting organized health care today. Although multiple factors play a role in this problem, the selective pressures of inappropriate and widespread use of antibiotics are considered major contributors.

All cultures were collected from children through clear catch midstream urine samples. The children diagnosed clinically and with pus cells > 5 were considered in this study. Due to economic aspects all symptomatic children cannot be evaluated with Urine C & S. Mahmoud Rashad et al conducted similar study initially using a screening test and positives were send for C & S.<sup>[7]</sup>

We did not do a repeat culture after antibiotic therapy, since similar studies conducted in other parts of world showed it as not significant in further management of UTI and added onto the financial burden. The study done by Melissa L et al showed repeat culture even in case of VUR or fever beyond 48 hours has no cost benefit.<sup>[8]</sup>

This is comparable with studies conducted by Palak Gupta et al., Taneja N et al which reported higher proportion of culture positive UTI (35%, 28.3 % and 34.2% respectively) 9,6. Kathy N. Shaw et al and Nader Shaikh, MD et al have reported a lower prevalence rate as opposed to our study since our study consider only high-risk children.<sup>[9-11]</sup>

Age group between 2 to 14 years has been studied, age below 2 years was not considered due to difficulty in collecting sample and contamination. Diagnostic accuracy of both clinical judgment and the DUTY (Diagnosis of Urinary Tract infection in young children) algorithm is less in nappy pad sample than clear catch sample and UTI symptoms are not reliable in children younger than 2 years of age as they are non-specific. Similar age group was studied by Taneja N et al, the group was divided into 1 to 5 years and 5 to 12 years 6.<sup>[12]</sup> In our study the most common organism isolated were gram negative E coli (80%), Klebsiella (20 %) and gram-positive Enterococcus which is similar to the study done by Palak gupta et al, Taneja N et al. 9,6.E coli remained most isolated organism irrespective of age group and gender. Our study is similar to the study done by Rachel S Edlin, MD et al in case of organism isolated in culture, the prevalence of organism causing UTI in male is E coli > Enterococcus > Klebsiella.<sup>[13]</sup>

The culture and sensitivity were done separately for gram-positive and gram-negative organism. E. coli as the predominant cause of UTI, showed the highest

percentage of resistance to ampicillin and amoxycillin (65.62%) followed by first generation cephalosporin Cephalexin(59.38%), second generation cephalosporin cefuroxime(56.25 %), Third generation cephalosporins- cefixime(46.87 %),ceftriaxone, cefotaxime (43.75% each), fourth generation cephalosporin-Cefepime (43.75%), Similar study done by Palak Gupta et al revealed sensitive pattern of E coli and Klebsiella to be sensitive tonitrofurantoin, amikacin, cefoperazone-sulbactam and meropenem.<sup>[9]</sup> Study by Taneja N et al study showed sensitivity to cefotaxime, ceftriaxone, nalidixic acid and nitrofurantoin and amoxycillin resistant E coli and klebsiella.<sup>[6]</sup>

The objective of this study is to identify the local antibiogram and risk factors for UTI in children there by starting antibiotics in early stages before developing complications. The study done by Nadershaikh, Kyriaki A. Karavanakiet al, Nadershaikh et al showed that by delaying treatment even 72 hours lead to renal scarring, so in order to start anempirical antibiotic this local antibiogram can be used.<sup>[13-16]</sup>

Our study has little strength like fewer studies have been done in Kerala which studies UTI in children. Our study determines the prevalence of culture positive UTI in children in Central Travancore, thereby helping to know the magnitude of the condition in this area. Our study determines the association between UTI and various risk factors, thereby facilitating early diagnosis and treatment of UTI in the children. Our study identified local sensitivity patterns empirical antibiotics can be started until culture results are available. In most cases, oral antibiotics are as effective as intravenous agents in initial phase. This study therefore, emphasizes the need to raise awareness of UTI in children and to expand the services for prevention, early diagnosis and management of UTI in children. Our study has few limitations. First, we cannot completely exclude recruitment bias. The data regarding the outcome may be influenced by other factors. We were not able to study all the habits of children which may have led to UTI, but it is interesting to note that improving personal hygiene and habits can help to avoid UTI. This study is carried out in a semi – urban tertiary care centre. Hence the prevalence of UTI in children belonging to rural areas and those attending secondary and primary health care facilities could not be assessed, which could influence the outcome.

## CONCLUSION

In this study it is quite alarming to note that almost all of the isolates in the urine culture were found resistant to many commonly used antibiotics. Antibiotic resistance is becoming a big problem for the public health which cause complications and leads to chronic conditions and add considerably to health care cost. Therefore, it is an important issue to

be addressed by the policy makers to formulate a strict antibiotics prescription policy in our country.

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