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Sensitivity and Resistant Pattern of Commonly Used Drugs in UTI in Younger Children: A Study in a Tertiary Care Level Hospital, Dhaka, Bangladesh

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Abstract: Urinary tract infections (UTIs) are one of the most common types of infections in children. Resistance to drug used in UTI is universal crisis in the present world. UTIs are usually caused by bacteria living on or in our bodies, and require treatment with antibiotics. A prospectively observational study was conducted in Kurmitola General Hospital (KGH) from January 2018 to December 2018. A total of 519 culture positive UTI children were considered for analysis. Colony counts for these samples were identified, and the profile of antibiotic resistance was identified. Here, samples with a colony count of ≥105 CFU/mL bacteria were considered positive. Among the children 416 children took antibiotics without prescription and among them 205 (49.2%) was culture positive. The most common pathogen was E-coli (74.31%) which prevailed that taking antibiotics without prescription is highly associated with the drug resistant UTI recurrent abdominal pain. Researcher took 19 antibiotics for susceptibility testing to identify the most resistant and safe drug for the UTI patients. According to the present study sensitive antibiotics were Cephradine 0%, Cefotaxim 0%, Imepenam 100%, Cotrimoxale 46%, amoxicillin and clavulanic acid 0%, Cefixime 36%, Cefuroxime 19%, Ceftriaxone 22%, Azithromycin 25%, Nitrofurantoin 66%, Ceftazidime 19%, Ciprofloxacin 47%, Nalidixic acid 36%, Levofloxacin 71% Colistin 79%, Gentamycin 80%, Netilmycin 80%, Amikacin 80% and Meropenam 40%. On the other hand, resistance was Cephradine 100%, Cefotaxim 100%, Imepenam 0%, Cotrimoxale 54%, Amoxicillin and clavulanic acid 100%, Cefixime 64%, Cefuroxime 81%, Ceftriaxone 78%, Azithromycin 75%, Nitrofurantoin 34%, Ceftazidime 81%, Ciprofloxacin 53%, Nalidixic acid 64%, Levofloxacin 29%, Colistin 21%, Gentamycin 20%, Netilmycin 20%, Amikacin 20% and Meropenam 60%. So, the most sensitive drug was Imepenam 100% and the most resistant drugs were Cephradine and Cefotaxim 100% resistance against urinary pathogens. Association between antibiotic use, drug resistance and use of with and without prescription in UTI patients was highly significant. We suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organism and their antibiotic resistance in a specific area rather than on universal or even national guidelines.

Keywords: UTI, Antibiotic Resistance, Urinary Pathogens, Resistance

1. Introduction

The prevalence of UTI varies with the ages of the children. It occurs in children of all ages. UTI are the most common in children under one year at age. The prevalence of a febrile symptomatic UTI in children over one year is 8% and in febrile infant is 7%. Male female ratio in 1st year of life is 2.8:5.9 and beyond 1-2 year male female ratio is 1:10 that is female more predominant. UTI in male is more common in 1st year of life and in uncircumcised male. UTI causes end stage renal failure in 2% cases. [25-26] Furthermore many children receive antibiotics for fever, or abdominal pain or otitis media etc. without specific prescription resulting in a partially treated UTI. UTI (urinary tract infections) causes scaring the dysplasia

reflux nephropathy. Antibiotic resistance is a global crisis in the present world and urinary tract infections (UTIs) are one of the most common types of infections. Like many human infections, UTIs are usually caused by bacteria E-Coli (80-90%) living on or in our bodies [27-29]. and require treatment with antibiotics. But there is a proper procedure of taking antibiotics in the field of medical science and technology. However, the parents of Bangladeshi children are not yet conscious to take antibiotics for their children. Consequently, it distresses the child, concerns the parents, and may cause permanent kidney damage. Occurrences of a first-time symptomatic UTI are highest in boys and girls during the first year of life and markedly decrease after that. Febrile infants younger than 2 months constitute an important subset of children who may present with fever without a localizing source. The workup of fever in these infants should always include evaluation for UTI. UTI (*Urinary tract infections)* is the most common serious bacterial infection in infants and children both in community and hospital setting. UTI is an important cause of morbidly and mortality in children. [1-3] UTI is an infection of the lower urinary tract, the upper urinary tract, or both. [4] Boys are more susceptible during the first year of life; thereafter the incidence is substantially higher in girls. [5-6] Rapid diagnosis and prompt antimicrobial treatment are required to minimize the related complications, such as urosepsis, urolithiasis and renal abscess as well as the prevention of renal scarring and permanent renal-parenchymal damage. To achieve these aims an empirical antibiotic prescription is often endorsed even before the culture results are available. On the other hand antibiotic resistance of urinary track pathogens has been known to increase worldwide, specially to commonly used antimicrobials [7-9]. The increase antibiotic resistance trends are likely to have important clinical implication for the empirical used of antibiotics. For this resistance knowledge of etiology pathogens of UTIs and there antimicrobial resistance patterns in specific geographical location may help clinicians in choosing the appropriate antimicrobial [10-11]. Reporting of antimicrobial susceptibility testing of the urinary tract is usually achieved 48hrs following sampling, and therefore, in the majority of UTI cases, the treatment decision is empirical, being influenced by available data reflecting antibiotic resistance. For the initiation of antimicrobial therapy in UTI knowledge of the antimicrobial resistance patterns of common uropathogens in each region is essential to provide appropriate therapy. Hence, there exists a great need for antimicrobial resistance surveillance at the local, national, and international levels. The effect of resistant microorganism is obvious in hospitals and other healthcare facilities, when infections caused by drag resistant microorganism. This result in a prolonged infectivity with the related mortality and mortality especially among immune compromised patients [12]. Anyway, it is an alarming message to the medical community now is that UTIs are becoming ever harder to treat with common antibiotics. Therefore, the aim of the present study was to assess the association of drug resistance with frequent use of antibiotics without prescription in case of UTI and to identify the most resistant and safe drug. The researcher also wants to determine the organisms responsible for UTI in school & preschool going children and to assess the common presentation of UTI.

2. Objectives

General Objective:

To determine the organisms responsible for UTI in school & preschool going children.

Specific Objective:

To assess the association between antibiotic use, drug resistance and use of with and without prescription in UTI patients.

To identify sensitivity and resistant pattern of commonly used drugs in UTI in children.

3. Materials & Methods

This was a prospective observational study carried out in Kurmitola General Hospital at Inpatient and Outpatient Department, Dhaka. The Ethical Committee approved this study as non-harmful and noninvasive. A total of 519 patients in inpatient and outpatients department who were presented with or without fever and high frequency of Micturition Park were enrolled in this study during January 2018 to December 2018. The unit patients were mainly from northern area of Dhaka city around Kurmitola General Hospital (Matihata, Mirpur, Bonani, DOHS, Badda, Natun Bazar and Mahakhali). Our study participants were pre-school and school going children. The parents of the patients were interviewed through questionnaire on regarding taking antibiotics. The study participants were divided into two groups on the basis of taking antibiotics with the prescription provided by the registered physicians and without prescriptions by self and other means. Then the culture test of the urine of the patients of both the groups were done through the following culture media: Urine specimen were cultured for isolation of microbial agent of UTI or blood and MacConkey and blood agar media and incubated over night at 37°C. Then the samples were plodded out on nutrient agar and Muller Hinton agar media for colony count. Samples that showed pure growth of isolate in a count of ≥105 colony forming units per ml of urine after overnight incubation were considered to indicator significant bacteriuria. Then Antibiotic susceptibility was done on Muller Hinton agar using disk diffusion method [30]. The results were analyzed by computer software SPSS (Statistical Package for Social Science) version 20. Unpaired t test was used to analyze the data between the groups. For analytical tests 95% confidence limit ($p<0.05$) was taken as level of significance.

4. Result

Total of 519 confirmed UTIs patients were enrolled to this study from in-out patient department of Kurmitola General Hospital: A Tertiary Care Hospital in Dhaka, Bangladesh. The researcher collected varieties of UTI patients'

complaints. Among them 416 (80.15%) took antibiotics without prescription and 103 (19.84) patients took antibiotics with prescription. All the patients urine 'was investigated in the lab and RE was found 325 (62.6%) which was <5 and 194 (37.4%) was>5. Among 416 patients who were taken antibiotics without prescription, culture positive was 205 (59.5%) and culture negative was 211 (50.8%). Out of 103 patients who were taken antibiotics with prescription, culture positive (+) was 13 (12.6%) and culture negative (-) was 90 (87.4%). According to the present study the most sensitive antibiotics were Cephradine 0%, Cefotaxim 0%, Imepenam 100%, Cotrim 46%, Amoxicillin and clavulanic acid 0%, Cefixime 36%, Cefuroxime 19%, Ceftriaxone 22%, Azithromycin 25%, Nitrofurantoin 66%, Ceftazidime 19%, Ciprofloxacin 47%, Nalidixic acid 36%, Levofloxacin 71%, Colistin 79%, Gentamycin 80%, Netilmycin 80%, Amikacin 80% and Meropenam 40%. On the other hand, resistance was Cephradine 100%, Cefotaxim 100%, Imepenam 0%, Cotrim 54%, Amoxicillin and clavulanic acid 100%, Cefixime 64%, Cefuroxime 81%, Ceftriaxone 78%, Azithromycin 75%, Nitrofurantoin 34%, Ceftazidime 81%, Ciprofloxacin 53%, Nalidixic acid 64%, Levofloxacin 29%, Colistin 21%, Gentamycin 20%, Netilmycin 20%, Amikacin 20% and Meropenam 60%. So, the most sensitive drug was Imepenam 100% and the most resistant drug were Cephradine and Cefotaxim 100% resistance against urinary pathogens. Association between antibiotic taken without prescription and antibiotic taken with prescription was highly significant.

Table 1. *Socio- demography of the patients. (n=519).*

Age (years)	n	%
<1	27	5.2
1-2	52	10
2-3	71	13.6
3-4	79	15.2
4-5	87	16
5-6	105	20
6-7	29	5.5
7-8	17	3.2
8-9	17	3.2
9-10	09	1.7
10-11	126	24.2
Male	167	32
Female	352	68
Pre-school going	229	44
School going	290	56

Table 2. *Monthly income of the parents of the participants. (n=519).*

Father's income (monthly)	n	n%
<5000	25	4.8
5000-10000	77	14.8
10000-15000	142	27.3
15000-20000	158	30.4
20000-25000	53	10.2
25000-30000	45	8.6
>30000	19	3.6

Table 3. *The patients presented complaints for abdominal pain. (n=519).*

Variable	n%
Fever	219 (42)
Constipation	311 (59)
Increased frequency of micturition	175 (34)
Taking antibiotics without prescription	416 (80)
Anatomical abnormity dribling	40 (8)
difficulty in micturition	80 (15)
Street food taking	319 (61)

Table 4. *Urine culture result of the study participants. (n=519).*

Total Patient With abdominal pain	N (519)	N% (100)
Taken antibiotics without prescription	416	80.15
Culture positive (+)	205	49.27
Culture positive (-)	211	50.73
Taken antibiotics with prescription	103	19.15
Culture positive (+)	13	12.62
Culture positive (-)	90	87.38

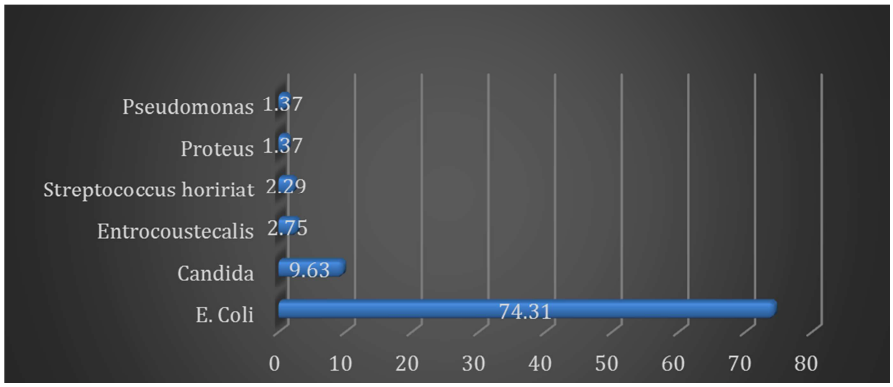

Figure 1. *Distribution of bacterial organisms of the participants. (n=519).*

Table 5. *Antimicrobial Resistance (%) of Isolated Uropathogenic Bacteria (n=519).*

Name of drugs	No of culture per pt	Sensitive	% of Sensitive	Resistant	% of resistant
Cephradine	17	0	0	17	100
Cefotaxim	19	0	0	19	100
Imepenam	19	19	100	0	0
Cotrim	114	54	46	60	54

Name of drugs	No of culture per pt	Sensitive	% of Sensitive	Resistant	% of resistant
Amoxicillin and clavulanic acid	17	0	0	17	100
Cefixime	193	69	36	123	64
Cefuroxime	184	34	19	150	81
Ceftriaxone	195	43	22	152	78
Azithromycin	175	44	25	131	75
Nitrofurantoin	193	127	66	65	34
Ceftazidime	192	36	19	156	81
Ciprofloxacin	186	78	47	89	53
Nalidixic acid	193	69	36	124	64
Levofloxacin	193	87	71	36	29
Colistin	123	86	79	36	30
Gentamycin	87	71	80	16	20
Netilmycin	87	70	80	17	20
Amikacin	87	70	80	17	20
Meropenam	87	35	40	52	60

Table 6. *Association between antibiotic taken without prescription and antibiotic taken with prescription. (n=519).*

	Taken antibiotics without prescription	Taken antibiotics with prescription	P-Value
Culture positive (+)	205	13	0.00001^{SN}
Culture positive (-)	211	90	

SN=Significant.

5. Discussion

Uropathogens are gaining resistance at an increased rate to commonly used antimicrobial agents. The sensitivity pattern is changing day by day and it varies from hospital to hospital. Constant survey of antimicrobial resistance is very important for empirical treatment of UTI. [13-14]This study showed drug resistant UTI presented as recurrent abdominal pain in younger children is highly associated with frequently use of antibiotics without prescription through a survey with a number of 519 pre-school and school going children. The study was carried on at in-out patients department of Kurmitola General Hospital: A Tertiary Care Hospital in Dhaka, Bangladesh during the period from January 2018 to December 2018. All the children were the patients of UTI recurrent abdominal pain. Among them 68% were female and 32% were male. Pre-school going children were 229 (44%) and school going were 290 (56%). Again the children were divided into two groups on the basis of taking antibiotics with prescription and without prescription. The number of children took antibiotics without prescription was 416 (80%) [31] and the number of students never took antibiotics without prescription was 103 (19.2%). Then the urine of the children who took antibiotics without prescription was investigated [22-24]. The R/E was below 5 (62.6%) of the children and (37.4%) was above 5. Then the culture was also investigated of 416 children. Among them positive culture was 205 (49.2) and negative culture was 211 (50.8%). The most common pathogens was found E Coli 74.31% which was mainly responsible for UTI infections in the present study. The same result was found in the study of Francesco MA and Ravizzola et al and Mendo A and Antunes J et al and Costa M, Pereira PM et al. [19-21]. Then a few number of drugs' (antibiotics) sensitivity and resistance were evaluated on the no of culture of per patient, culture positive (+) 13 (12.6%) and culture negative (-) 90 (87.4). Only two drugs were identified as 100% resistant and they were Cephradine, Amoxicillin and clavulanic acid and Cefotaxim. However, in the previous studies coli and Klebsiella spp. have also been isolated as the most common pathogens responsible for UTI among children. Anyway, E coli was the most frequent organism isolated in this study. This is similar to results of investigations in other countries. [15-16]. In this study, higher resistance rates to all antibiotics tested with the exception of amikacin, colistin, imepenum and Meropenum may be explained by high and uncontrolled usage of these antimicrobial agents, especially third-generation cephalosporins during the past few years in our country and these antibiotics were widely prescribed not only for UTI but also for other infections. E coil is steel the most common (70%) cause of UTI and the klebsiella being the second (13.6%). In a study conducted in India in 2007 has shown the distribution of urinary pathogen as follows. E, colli 63%, Klebsiella-spp 15.9% and Pseudomonas aeruginosa 5.30%. In the present study result of antibiotic susceptibility test reveal that the urinary isolates were 100% resistance three drugs and they were Cephradine, Cefotaxim and Amoxicillin and clavulanic acid. Previous study showed that the susceptibility of E-coli to impenum ranged from 98-100%.17-18. In the present study, most of the isolates were found Cephradine (100%) followed by Cefotaxim (100%), Imepenam (0%), Cotrim (54%), Amoxicillin and clavulanic acid (100%), Cefixime (64%), Cefuroxime (81%), Ceftriaxone (78%), Azithromycin (75%), Nitrofurantoin (34%), Ceftazidime (81%), Ciprofloxacin (53%), Nalidixicacid (64%), Levofloxacin (29%), Colistin (30%), Gentamycin (20%), Netilmycin (20%), Amikacin (20%) and Meropenam (60%). All the isolates showed strong resistance to Cephradine, Cefotaxim and Amoxicillin and clavulanic acid. Therefore, it was successfully revealed to the researcher that the drug resistant UTI presented as recurrent abdominal pain in Bangladeshi Children is highly associated with

frequently use of antibiotics without prescription.

Limitation of This Study

This study was done only in Dhaka city with limited sample size and also short period of time. So, the study result may not reflect the scenarios of the whole country.

6. Conclusion

This study provides valuable information regarding current distribution of urinary pathogens and their antimicrobial resistance pattern and successfully showed drug resistant UTI presented as recurrent abdominal pain in Bangladeshi Children is highly associated with frequently use of antibiotics without prescription. So, we suggest that empirical antibiotic selection should be based on knowledge of the local prevalence of bacterial organism and antibiotic resistance and none should have antibiotics without prescription.

Conflict of Interest

None Declared.

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Approval

From respective department.

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