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Prevalence and Drug Susceptibility of Isolates of Urinary Tract Infections Among Febrile Under-Fives in Nsambya Hospital, Uganda

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Abstract

Background: Urinary tract infections remain a silent cause of morbidity and complications among under-fives due to its non-specific presentation and incapacity of most health facilities in developing countries to diagnose it. Earlier studies present different prevalence of urinary tract infections among children. This study aimed to document prevalence and drug susceptibility patterns of isolates of bacterial urinary tract infections among under-fives in Nsambya hospital, Uganda. *Methodology:* We conducted a descriptive cross-sectional survey among 302 under-fives who presented in paediatric ambulatory care department of Nsambya hospital with fever (axillary temperature of >37.5°C or by history); and with no history of antibiotic therapy within three days preceding hospital visit. Midstream urine samples collected using bag and bottle collection (depending on age of child) were subjected to culture. We further subjected culture-positive urine samples to systematic bacteriologic and biochemical tests in order to identify the organisms in the colonies before performing drug susceptibility tests. *Results:* We found urinary tract infection prevalent in 26.8% of the under-fives. Bacterial isolates responsible for the infections were Proteus (39.5%), Escherichia coli (32.1%), Staphylococcus aureus (14.8%), Klebsiella spp. (6.2%), Staphylococcus haemolyticus (2.5%), Staphylococcus intermedius (2.5%), Citrobacter (1.2%) and Morganella (1.2%) in that order. The pathogens exhibited high-level of resistance to commonly used antibiotics like Cotrimoxazole, Amoxicillin, Nalidixic Acid, Nitrofurantoin, Gentamicin, Erythromycin, Chloramphenicol, Ampicillin, Ciproflaxin, Tetracycline and Azithromicin while the isolates showed no resistance to pharmaco-enhanced Amoxicillin and oral Cefatoxime. *Conclusion:* Prevalence of UTI among febrile under-fives in Nsambya hospital is higher than reports from majority of earlier studies. Similarly, the commonest bacterial isolates associated with UTI among under-fives in Nsambya hospital deviates from most studies in developing countries that majorly report Escherichia coli as the leading cause of UTI in this age category. The observed resistance patterns associated with common antibiotics in our study are in line with the current changing patterns of microbial-antibiotic resistance threatening not only the developing world but the entire glob.

Keywords

Prevalence, Drug Susceptibility, Urinary Tract Infection/UTI, Febrile Under-Fives, Nsambya Hospital

1. Introduction

Urinary tract infections (UTI) are a common cause of morbidity and complications among children globally. Studies have documented varying prevalence of urinary tract infections among the under-fives. A study conducted in in-patient pediatric ward ofMuhimbili hospital in Tanzania among febrile under-fives places prevalence of UTI at 16.8% [1]. The same study reports Escherichia coli, Klebsiellaspp, Staphylococcus epidermidis, Staphylococcus aureus and Pseudomonas aeruginosa in that order as causes of UTIs

among the under-fives.A similar study among febrile under-fives in a Nigerian hospital estimates prevalence at 11% [2]: greater than the 9% estimate among children with primary diagnosis of malaria in Nigeria [3]. Surprisingly, the latter study documents staphylococcus aureus as the leading cause of UTI among the under-fives. In Uganda, a study conducted in the acute care unit of the national referral hospital in 2008, among children aged 2 months to 12 years with fever showed a prevalence of 14.6% [4]. Despite the differential prevalence, these (earlier) studies highlight high prevalence of UTI among children presenting to hospitals with fever. This is further corroborated by the fact that high occurrence of UTI isdocumented among children with primary diagnosis of malaria [3]. The low priority accorded to UTI in the clinical hierarchy of importance in many African countries brews complications andat times mortality due to delay in diagnosis and treatment. For example, UTIs do not feature among the top 10 causes of morbidity and mortality among in-patients in Ugandan health facilities [5]. This rosy picture of rarity of UTIs could be consequent to difficulty in diagnosing (UTI among under-fives) due to non-specific presentation, poor diagnostic capacity of the health facilities as well as lack of appropriate policy for screening all febrile under-fives for UTI. The study in South Eastern Nigeria [2] details that 10.13%, 14.12%, 40.00%, 20.00%, 6.25% and 50.00% of all clinically diagnosed cases of malaria, upper respiratory tract infections (including otitis media and tonsillitis), sepsis/cellulitis/furunculosis, bronchopneumonia, gastroenteritis and enteric fever respectively were UTI – moreover, only 16.67% of UTI cases were diagnosed so.The common clinical features of UTIs among young children include fever, irritability, vomiting and failure to feed [6]. Renal scarring is one of the commonest complications of UTI among children. Shaikh, Ewing and Hoberman in a meta-analysis to assess complications of UTIs in children report post-infection renal scarring among 15% of children [7]. In the long run, renal scarring is associated with increased rates of hypertension and proteinuria, decreased renal function and increased end-stage kidney disease. Wiswell reports occurrence of meningitis among 3-5% of infants in the first month of life [8].

Policy decision on clinical management of bacterial UTIs, especially among children requires knowledge of its prevalence, the etiology and drug susceptibility profile of the offending bacteria. Notwithstanding that this study focuses on UTI, it is worth noting that there is an on-going global outcry about growing bacterial resistance to the spectra of current antibiotics. This calls for vigilance of all actors in the health care to as much as possible, base on up-to-date evidence in making clinical algorithms for treating infections requiring antibiotic therapy. We conducted this study as a response to the existing dilemma on prevalence, common etiology and bacterial susceptibility to treatment of UTIs among children. Specifically, we looked at prevalence, bacterial isolates of UTIs; and antibiotic susceptibility profile of the isolates.

2. Methodology

2.1. Study Setting

We conducted this study in the pediatric outpatients' department of St. Francis hospital, Nsambya in Kampala. Commonly known as Nsambya hospital, it is a private not for profit health facility located in the Southern part of Kampala, about 3 kilometers from the city centre. It is a 361-bed hospital owned by the Catholic arch diocese of Kampala.

2.2. Study Design

This was a descriptive cross-sectional study between December 2013 and April 2014.

2.3. Sample Size and Sampling Strategy

The sample size for this study was 302, arrived at using the Bouderer's formula at 95% level of confidence, +/-5% desired precision, 20.3% prevalence of urinary tract infection [1] and 96.0% anticipated sensitivity and after factoring in anticipated non-response. The children were enrolled into the study consecutively until the desired sample size was reached.

2.4. Urine Collection and Testing

We employed aseptic techniques for collecting mid-stream urine using the bag-collection for younger children (less than 2 years) and bottle-collection for older ones trained in toileting. We employed quantitative method earlier described by Cheesbrough [9] to culture urine for microorganisms using cystein-lactose electrolyte deficient culture medium. Using calibratedsterile standard nichrome wire loop we inoculated 1/200µl of the sample onto the culture medium after drying (the culture medium) at 37°C for 15-30 minutes. We then aerobically incubated the culture plates between 35-37°C for 24 hours before counting the colonies. Colony countsof more than 10^5 organisms/ml were suggestive of UTI while we regarded growths less than 10^5 from the midstream urine as contaminants. We then carried out systematic bacteriologic and biochemical tests to identify the organisms in the colonies. Drug susceptibility testing was carried out for some bacterial isolates and results reported as sensitive, intermediate or resistant. Due to low number drug susceptibility tests conducted, we did not perform independent-data-analysis for each of the isolates.

2.5. Data Analysis

The data were manually cleaned, entered into micro-soft excel before export to Statistical Package for Social Sciences (SPSS version 16.0) for analysis. The data were analyzed using descriptive statistics. We presented our findings in tables and narratives.

2.6. Quality Control

We adhered to all the standard protocols for urine collection and analysis for all the methods described above.

We trained qualified nurses to collect samples under strict supervision ofthe first author. We screened our study participants for antibiotic use and did not consider those with history of antibiotic intake 3 days preceding hospital visit. Data were checked for completeness and consistence on daily basis. The data were cleaned before double entry into excel sheets. The data analyses were conducted by two persons independently to ensure reliability.

2.7. Ethical Consideration

The research protocols were approved by the temporary ethics and review board of Mother Kevin School of Post Graduate Studies of Uganda Martyrs University before further seeking permission from the management of Nsambya hospital. We sought permission of mothers or care takers of the children before enrolling them into this study. We opted away from supra-pubic aspiration due to its invasive nature.

Study subjects who had UTIwere provided appropriate antibiotics based on the results of the drug susceptibility tests. Where there were suspected co-morbidities, we referred the subjects to appropriate experts for the required care.

3. Results

3.1. Characteristics of Study Participants

We recruited 302 children under the age of five years who presented with axillary temperature of > 37.5°C or fever by history and with no antibiotic therapy within three days preceding hospital visit. The majority of the respondents, 56.6% (171) were male. Table 1 cross-tabulates the age and sex distribution of the respondents.

Table 1. *Age and sex distribution of the study participants.*

Sex	Age category (months)				
	< 1	**1-5**	**6-11**	**≥12**	**Total (%)**
Female	2(0.7)	11 (3.6)	34 (11.3)	84 (27.8)	131(43.4)
Male	6 (2.0)	22 (7.3)	19 (6.3)	124 (41.1)	171(56.6)
Average (%)	8(2.6)	33(10.9)	53(17.6)	208(68.9)	302 (100.0)

3.2. Prevalence of UTI

We assessed the participants using urine culture. Out of the 302 children, 81 were culture positive and this represents prevalence of 26.8% (95% CI: 21.8 % to 31.8 %).

3.3. Bacterial Isolates Among Children with UTI

We re-evaluated all the culture positive samples so as to identify the differential etiology of UTI among under-fives. Proteus, Escherichia coli andStaphylococcus aureus were the commonest causes of UTI among children under five years of age.Table 2 details the finding of the bacteriological profile of UTIs.

Table 2. *Bacteriological profile of UTIs among under-fives in Nsambya hospital.*

Type of bacteria	Frequency	Percentage
Escherichia coli	26	32.1
Staphylococcus haemolyticus	2	2.5
Staphylococcus intermedius	2	2.5
Staphylococcus aurues	12	14.8
Proteus	32	39.5
Klebsiella	5	6.2
Citrobacter	1	1.2
Morganella	1	1.2
Total	81	100.0

3.4. Drug Susceptibility of Bacteria

Drug (antibiotic) susceptibility profile of the various isolates was evaluated using commonly used antibiotics. The antibiotics include; oral cotrimoxazole (Cotri), oral amoxicillin (Amoxyl), oral nalidixic acid (Nalid), oral coamoxiclav (Coamoxy), injectable ceftiraxone (Ceftri), oral cefuroxime (Cefuro), oral nitrofuradantine (Nitro), oral cephalexin (Cepha), injectable gentamicin (Genta), oral cefatoxime (Cefot), injectable amikacin (Amika), injectableoxacillin (Oxac), injectable methicillin (Methi), oral erythromycin (Erithro), oral chloramphenicol (Chloraphen), oral ampicillin, oral ciproflaxin (Cipro), oral tetracycline (Tetra), injectable clindamicin, injectable imipenem, oral metronidazole (Metro), injectable streptomycin, oral azithromicinand oral cefixime. Due to resource limitations, we were able to perform drug susceptibility tests on a few of the specimens. For the resultant small sample size, we did not breakdown our analysis per the bacterial isolates as such; our findings on drug susceptibility are suggestive but not conclusive. The results suggest high-level of resistance to the most commonly used antibiotics like cotrimoxazole, amoxicillin, nalidixic acid, nitrofurantoin, gentamicin, erythromycin, chloramphenicol, ampicillin,ciproflaxin, tetracycline and azithromicin. Similarly, non-commonly used antibiotics like amikacin, oxacillin and methicillin were suggestive of high resistance. Pharmaco-enhanced amoxicillin and oral cefatoxime suggested no resistance. Generally, there was low-level of resistance suggested by the few tests associated with cephalosporin's (table 3).

Table 3. *Results of drug susceptibility tests of isolates of UTI in under-fives.*

Drug	Sensitivity Analysis:freq(%)			
	Not done	**Sensitive**	**Intermediate**	**Resistant**
Cotrim	249 (82.5%)	2 (0.7%)	-	51 (16.9%)
Amoxyl	294 (97.4%)	-	-	8 (2.7%)
Nalid	225 (74.5%)	6 (2.0%)	7 (2.3%)	64 (21.2%)
Coamoxy	271 (89.7%)	31 (10.3%)	-	-
Ceftri	266 (88.1%)	34 (11.3%)	-	2 (0.7%)
Cefuro	293 (97.0%)	7 (2.3%)	-	2 (0.7%)
Nitro	236 (78.2%)	16 (5.3%)	7 (2.3%)	43 (14.2%)
Cepha	279 (92.4%)	21 (7.0%)	-	2 (0.7%)
Genta	225 (74.5%)	54 (17.9%)	-	23 (7.6%)
Cefot	297 (98.3%)	5 (1.7%)	-	-
Amika	273 (90.4%)	16 (5.3%)	-	13 (4.3%)
Oxac	239 (97.0%)	1 (0.3%)	-	8 (2.7%)
Methi	297 (98.3%)	1 (0.3%)	-	4 (1.3%)
Erthro	285 (94.4%)	-	-	17 (5.6%)
Choramphen	262 (86.8%)	17 (5.6%)	1 (0.3%)	22 (7.3%)
Ampicillin	294 (97.4%)	1 (0.3%)	-	7 (2.3%)
Cipro	241 (79.8%)	34 (11.3%)	4 (1.3%)	23 (7.6%)
Tetra	260 (86.1%)	6 (2.0%)	4 (1.3%)	32 (10.6%)
Clindamycin	294 (97.4%)	6 (2.0%)	-	2 (0.7%)
Imipenem	283 (93.7%)	17 (5.6%)	-	2 (0.7%)
Metro	296 (98.0%)	-	-	6 (2.0%)
Streptomycin	295 (97.7%)	6 (2.0%)	-	1 (0.3%)
Azithromycin	295 (97.7%)	-	-	7 (2.3%)
Cefixime	301 (99.7%)	-	-	1 (0.3%)

4. Discussion

Earlier studies report varying prevalence of UTI among under-fives. This study found 26.8% (95% CI: 21.8% to 31.8%) of febrile childrenwith urinary tract infection. We did not rule out other possible causes of fever as such; some of these children could have had asymptomatic bacteriuria since fever in our study units could have been consequent to other etiologies though we also did not rule out co-morbidities. Previous evidence that persons with asymptomatic UTI have progressed to symptomatic UTI, postpartum UTI and pyelonephritis in studies among pregnant women [10] [11] reflects its (asymptomatic bacteriuria) significance in public health. Earlier studies in Lalitpur and Nigeria [2], [12] report lower prevalence of UTI amongst children (at 18.49% and 11% respectively) than we have. The employment of supra-pubic aspiration alongside midstream urine in the Nigerian study could have accounted for this high difference in prevalence though smaller prevalence (than 11%) have been reported elsewhere by the World Health Organization. A study that assessed prevalence of UTI and drug susceptibility patterns among children aged 0-120 months reports prevalence as high as 65.3% [13]. Un-diagnosed UTI in under-fives among 10.13%, 14.12%, 40%, 20% 6.25% and 50% of clinically diagnosed malaria, upper respiratory tract infections, sepsis/cellulitis/furunculosis, bronchopneumonia and gastroenteritis respectively is documented elsewhere in Nigeria [2] and this depicts difficulty in clinical diagnosis of UTI in the younger ages. Another study among under-fives with primary diagnosis of malaria reports 9% co-morbidity with UTI [3]. The high prevalence of UTI and its poor diagnosis among under-fives illustrate urgency for screening programs to aid its early diagnosis and treatment; and further prevent UTI-related deaths and complications. A while ago, south Africa did suggest identification of UTI in the Integrated Management of Childhood Illnesses (IMCI) protocol based on leucocytes and nitrites as bio-markers using dipstick. Oman adapted IMCI (in primary health care) protocol to include screening of all febrile or symptomatic under-fives for UTI using laboratory tests and referral of those with results suggestive of UTI for paediatric consultation [14]. Symptomatic diagnosis of UTI with fever as a marker had moderate sensitivity (80%) and low specificity (40%) [15]. The World Health Organization recommends inclusion of UTI in IMCI protocols in countries without malaria and with high measles coverage provided; UTI is common among febrile children, health workers are aware of UTI among children, urine is collected and tested in first-level health facilities, health workers have capacity to treat UTI well, health facilities have functional water source, UTI is a significant contributor to morbidity, dipstick urinalysis can be made available, presumptive identification of UTI is not burdensome to the referral system and presumptive treatment of UTI does not contribute to rise in drug resistance, antibiotic side effects as well as high drug cost [14]. Most studies in the developing countries report Escherichia coli as the commonest bacterial isolate of UTI among children [1], [16], [17], [18], [19], [20]. Surprisingly, our study unearthed proteus as the leading cause of UTI among febrile under-fives in Nsambya hospital though this was closely followed by Escherichia coli. Staphylococcus

aureus showed a relatively high proportion at 14.8% while the rest of the isolates presented with very low proportions – falling below 10% and they include: klebsiella, staphylococcus haemolyticus, staphylococcus intermedius, citrobacter and morganella in that order. Understanding the frequency of isolates in causation of UTI helps in designing treatment protocols especially in making decisions to treat UTI clinically. The unique frequency of proteus documented herein points to inapplicability of global treatment alogarithms (based on studies in most of the developing countries) in our context. Appropriate treatment protocols based on drug susceptibility tests related to the commonest causes of UTI in our setting like proteus, Escherichia coli and staphylococcus aureus would suffice. Our findings on drug susceptibility suggest high-levels of resistance against commonly used antibiotics. Despite the smaller number of samples subjected to drug susceptibility tests, medicines like cotrimoxazole, amoxicillin, nalidixic acid, nitrofurantoin, oxacillin, methicillin, erythromycin, ampicillin, tetracycline and azithromycin almost confirmunacceptably high resistance while only two medicines (cefatoxime and amoxyclav) showed no evidence of resistance. Whereas the small sample may not permit comparison of our findings with earlier studies, it is obvious that the health system rethinks the treatment for un-complicated UTI among children in Uganda. The clinical guidelines of Uganda place single dose cotrimoxazole or ciproflaxin as first line treatments for un-complicated UTI (cystitis) while 10-14 days oral amoxicillin or cotrimoxazole for treatment of mild pyelonephritis [21]. The same guideline recommends intravenous ampicillin in combination with gentamicin for treatment of severe forms of pyelonephritis. These lines of treatment are based on the premise that Escherichia coli is the commonest cause of UTI in Uganda. Our finding underpins the need for a wider coverage survey to review the prevailing situation in terms of etiology of UTI: especially among the under fives. Even though the pattern of the bacterial spectrum remains un-changed (with Escherichia coli most prevalent), the pattern of resistance observed with the small sample suggests a bigger study in order to gain insight on treatment of UTI in Uganda. An earlier study in Uganda [22] recommends use of urine microscopy in screening for UTI among febrile under-fives. This study reveals that much as microscopy may be useful in 'ruling out' and 'ruling in' of UTI among febrile under-fives [22], urine culture and sensitivity remains equally important in choice of antibiotics for treatment of UTI among cases diagnosed with the same.

5. Conclusion

The prevalence of UTI among febrile under-fives in Nsambya hospital is higher than most of the earlier reports. Similarly, the commonest bacterial isolate associated with UTI among under-fives in Nsambya hospital deviates from most studies in developing countries that majorly report Escherichia coli as the leading cause of UTI in this age category. The observed resistance patterns associated with common antibiotics in our study are in line with the current changing patterns of microbial-antibiotic resistance threatening not only the developing world but the entire glob. Local scientists need to make deliberate effort to redesign a study with a nationwide coverage to better understand the distribution and frequency of bacterial isolates of UTI; and establish isolate-specific drug resistance profile based on the most common etiologies in order to re-structure the treatment alogarithms (for UTI) in Uganda. In the mean time, it would be appropriate to consider treatment of UTI based on results of culture and sensitivity though this may not be feasible due to resource constraints' and incapacity of primary and secondary health care facilities.

List of Abbreviations

IMCI: Integrated Management of Childhood Illnesses
UTI: Urinary Tract Infection

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