Original Article


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ABSTRACT

Objective: To evaluate the practicality of applying the new international guidelines for urinary tract infection (UTI) management in children hospitalized with their first UTI in a tertiary care hospital in Kuwait

Design: Retrospective study

Setting: Pediatric wards at the Mubarak Al Kabeer Hospital; period of study: from June 2011 - May 2012

Subjects: Children up to 12 years of age with pyuria and at least 50,000 colonies per ml of a single uropathologic organism in an appropriately collected urine sample

Intervention: None

Main Outcome Measures: Incidence of vesico-ureteric ultrasound (RUS)

Results: One hundred and forty nine children were included. 53% were male. Recurrent UTI was present in 15% of cases. The most commonly isolated bacteria were: E.coli (69%), Klebsiella pneumoniae (11.4%) and Pseudomonas aeruginosa (5.4%). VUR was found in 7.5% of children with first UTI and normal RUS and in 50% of children with abnormal RUS. In children with recurrent UTI, 23% had VUR. Renal scarring was found in five children.

Conclusions: The finding of low VUR rate in children with first UTI and normal RUS makes changing the current practice for the diagnosis and management of UTI to recent guidelines safe and valuable.

KEY WORDS: antibiotic resistance, children, DMSA, ESBL, MCUG, vesicoureteral reflux

INTRODUCTION

Since the introduction of effective conjugate vaccines against Haemophilus influenza type b, and Streptococcus pneumoniae, the rate of bacteremia and meningitis as causes of fever in children have significantly dropped. As a result, urinary tract infection (UTI) has emerged as the most common cause of fever without a focus in children. UTI affects approximately 7 - 8% of girls and 2% of boys during the first eight years of life[1,2].

Previously published UTI guidelines namely the Royal College of Physicians (RCP) guidelines in 1991[3] and the American Academy of Pediatrics (AAP) guidelines in 1999[4] have emphasized the role of extensive imaging using renal ultrasound (RUS), micturating cystourethrogram (MCUG) and nuclear scan with dimercaptosuccinic acid (DMSA) with the first UTI episode in children less than two years of age. This extensive imaging was aimed at detecting vesicoureteral reflux (VUR) and renal scarring. Also, children with VUR of any grade were given antibiotic prophylaxis. These guidelines have been updated in the last two years. AAP now recommends no more imaging in children with first UTI if RUS was normal[5]. The United Kingdom (UK) National Institute for Health and Clinical Excellence (NICE) makes the same recommendation but also recommends MCUG in all infants less than six months presenting with atypical UTI[6]. Both recommend imaging in case of recurrent UTI.

At the Department of Pediatrics, Mubarak Al-Kabeer Hospital (MKH), UTI is managed according to the AAP guidelines of 1999. All admitted infants

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with first UTI attack undergo RUS and MCUG. All children with suspected UTI are started empirically on intravenous cefotaxime until the urine culture results are available for proper antibiotic choice. On discharge from the hospital, children are started on antibiotic prophylaxis until their MCUG and continue on prophylaxis if there is vesico-ureteric reflux (VUR).

We conducted this study to evaluate the value of the currently applied guidelines in detecting VUR and renal scars in children with first UTI and if changing to the new guidelines will be safe and valuable. In addition, with the global increase in antibiotic resistance we want to identify if the currently empiric antibiotic used is suitable for the isolated bacteria.

SUBJECTS AND METHODS

We retrospectively reviewed the medical records of patients admitted to the pediatric wards at the Mubarak-Al-Kabeer hospital (MAKH) with the diagnosis of UTI from 1\textsuperscript{st} June 2011 to 31\textsuperscript{st} May 2012. We identified the admitted children by ICD code of 599.0. Children included were those who had both pyuria (white blood cells > 5 cells per high-power field) and a urine culture of 50,000 colonies per ml of a single uropathogenic organism in an appropriately-collected specimen of urine. We gathered the demographic data along with the clinical features of UTI for each patient. This included age, gender, symptoms, previous history of UTI, past medical history, urine culture results, organisms’ and their antibiotic susceptibilities, days of antibiotic use, days of hospital stay and findings on imaging studies.

The study protocol was reviewed and ethically approved by the “Joint Ethics Committee of the Ministry of Health in Kuwait and the Faculty of Medicine in Kuwait University”. The collected data were entered and analyzed using Statistical Package for Social Sciences SPSS (17.0). Frequencies and proportions were used to describe demographic, clinical and microbiological data. Chi-square analysis was done to study the association between the duration of hospitalization and age, fever duration and microorganism. A p-value of < 0.05 was considered as the cut-off value for statistical significance.

RESULTS

During the study period, 160 children were admitted with UTI. Only 149 fulfilled the study criteria and were subjected to further analysis, out of which 79 (53%) were boys. Out of the excluded patients, seven had mixed pathogens, two did not have pyuria and two had < 50,000 cfu/ml of bacteria. This was the first episode of UTI in 127 (85.2%) children. Eighty six (58%) children had UTI during the first six months of age. Fig. 1 shows the age and gender distribution of the children. Male children aged 0 - 6 months accounted for 31%, 69 (87%) out of which were not circumcised (p < 0.001). The top three presenting symptoms were: fever 129 (93.3%), vomiting 40 (26.8%), and poor feeding 29 (19.5%).

The isolated bacteria are shown in Fig. 2. Three bacterial agents constituted 88% of all bacteria isolated. These bacteria were: \textit{E.coli} 103 (69.1%), \textit{Klebsiella pneumoniae} 18 (12.1%) and \textit{Pseudomonas aeruginosa} 8 (5.4%). All children in the study were started empirically on cefotaxime and were switched to a narrower spectrum antibiotic according to the available susceptibilities. The antibiotic resistance

![Table 1: Antibiotic resistance in percentage for the most common organisms and among the three common organisms](image-url)
pattern for the previously listed bacteria is shown in Table 1. Duration of hospitalization was >7 days in 82 children (55%). Prolonged hospitalization was associated with age <3 months (p = 0.02) and duration of fever of more than 36 hours (p = 0.001) but no association was found with prolonged hospitalization and the isolated organism.

Renal ultrasound (RUS) was done for 136 (91%) children. MCUG was done for 59 (40%) of which 46 had the first attack of UTI and 13 had recurrent infection. DMSA scan was done for 50 (34%) patients out of which 40 had the first attack of UTI and 10 had recurrent infection. Only 6/46 (13%) children with first attack of UTI had VUR. In addition, only 3/40 (7.5%) children with first UTI episode and normal RUS were found to have VUR (Fig. 3). In those with abnormal RUS, VUR was found in 3/6 (50%) children (Fig. 3). In children with recurrent UTI, 3/13 (23%) had VUR (Fig. 4). There were three children who had normal RUS and still had VUR. Two of them had grade I VUR and the third had grade IV VUR.

Renal scarring was found in 5/50 (10%) children in our cohort, 3/40 (7.5%) with first UTI and 2/10 (20%) children with recurrent UTI. There were three children who had renal scarring with their first UTI, only one had normal RUS.

**DISCUSSION**

The overall rate of VUR in children with UTI (either first or recurrent attack) who had MCUG, in this study was 15% compared to the reported international rates of 25 - 40%[7,8]. This variation can be explained by the difference in the studied population in terms of genetic and racial backgrounds as VUR is thought to be genetically linked[8]. In this study, we found that only 7.5% of children admitted with first UTI had VUR. This is less than previously reported (22%) in two hospitals in Kuwait in 2003[9]. We think this might be related to

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**Fig. 3:** Imaging results in children presenting with first UTI attack.

US = ultra sound, MUCG = micturating cystourethrogram, DMSA = dimercaptosuccinic acid

**Fig. 4:** Imaging results in children with recurrent UTI

US = ultra sound, MUCG = micturating cystourethrogram, DMSA = dimercaptosuccinic acid
the characteristics of patients included in the study as their cohort had 72% female patients while our cohort had 47% females. In another study in Kuwait conducted at Al-Jahra Hospital, VUR rate was 43%,[10] but only 30% of their sample were children with first UTI episode.

The recent AAP and NICE guidelines recommend that children with first UTI and normal RUS, should not undergo MCUG and should not receive antibiotic prophylaxis.[8,9] We believe that this recommendation is applicable in Kuwait. In our study, children with first UTI and abnormal RUS were six times more likely to have VUR compared to children with normal RUS. None of patients with normal RUS had an abnormal DMSA which is the most important marker indicating long term complications.

The main uropathogens in our cohort were dominated by Gram negative bacteria namely; E.coli, Klebsiella, and Pseudomonas. These results differ from reports from Italy and Turkey where the gram positive Enterococcus spp. was one of the dominating organisms.[11,12] Pseudomonas spp. was responsible for 5.4% of the UTI's in our hospital, which will reflect on the empiric antibiotic used for managing UTI. It is worth noting that these organisms were not further analyzed in relation to gender, UTI recurrence, previous administration of antibiotics or an underlying renal abnormality.

Increased bacterial resistance to antibiotics is a global problem. We do not have the susceptibility pattern rates for the previous years to compare our data with. One of the most important findings in this study is the resistance to cefotaxime which is the empiric antibiotic used for UTI cases at MKH with a resistance rate of 28% for E.coli and 6% for Klebsiela. A similar rate of resistance was reported by Mohammad-Jafari from Iran,[13] while higher rates of resistance for both organisms of 51% and 42% respectively were reported from Turkey.[14] Recently, resistance of Gram negative bacteria to third generation cephalosporin is on the rise due to production of extended spectrum β-lactamases (ESBL). In a retrospective study in Italy from 2007 to 2011, the authors noted an increase in UTI in pediatrics due to ESBL-producing organisms over the years of the study from 11.63 / 1000 patient-days to 27.48 / 1000 patient-days (p = 0.05).[15] Tratselas et al found that clinical and microbiological outcomes, as well as formation of renal scars did not differ between groups of children with ESBL-producing UTI and non-ESBL.[16] Despite the findings of the latter study, AAP recommends knowing the local pattern of susceptibility of coliforms to antimicrobials before the initiation of empiric therapy[9]. In our study, two antibiotics with the least resistance against the three isolated uropathogens in our hospital were meropenem (0% resistance) and amikacin (0.8% resistance).

One limitation of this study, is that only 91% had RUS. The retrospective nature of this study and extraction of data from medical records might have resulted in loss of some data because of its unavailability. The other limitation is that we do not have the previous year’s antibiotic susceptibility data to compare with the current status. We would be interested in results of studies conducted after the application of the new guidelines. We also think that continuous monitoring of the resistance pattern of the uropathogens is essential to guide future appropriate antibiotic use.

CONCLUSIONS

Our results clearly demonstrate that children with normal RUS will unlikely have VUR. Hence; the new practice guidelines for imaging should be adopted when managing children with UTI as these guidelines are safe and decrease exposure to unnecessary radiation and antibiotics. We have also documented the increased resistance of uropathogens to cephalosporins which makes cefotaxime an unsuitable choice for empiric therapy for UTI. Empiric antibiotic therapy for children admitted with UTI should be re-evaluated. Empiric use of aminoglycosides until the sensitivity pattern is available might be a reasonable choice.

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REFERENCES


