Etiology and Antimicrobial Sensitivity of Common Uropathogens in Hilla Infants.

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Abstract

In this study, 100 febrile infants suffering from Urinary tract infection (rectal temperature > 38°C) who presented to the Pediatric Clinic or Emergency Department of Babylon Maternity and Children Hospital from February\2008 to June\2008 underwent a history and physical examination. In this study, *Escherichia coli* formed the major causative agent (49%) followed by *Pseudomonas aeruginosa* (25%), *Klebsiella pneumoniae* (18%) and *Proteus species* (8%).

E. coli isolates showed sensitivity to Amikacin, Chloromphenicol, Nitrofurantoin, Ofloxacin, Norfloxacin, while *Pseudomonas aeruginosa* shows sensitivity with Norfloxacin, Ofloxacin, Piperacillin, Tobramycin, *Proteus species* shows sensitivity with Amikacin, Amoxicillin , Cefodizime, Cefoxitin, Cephalexin, Gentamycin, , Norfloxacin, Piperacillin, Tobramycin and *Klebsiella pneumoniae* isolates shows sensitivity with Amikacin, Norfloxacin, Piperacillin, Tobramycin.

Our investigation showed that from the 100 febrile infants with UTI, 57 had pyuria > 5 WBCs/hpf, 90 had pyuria >10 WBCs/mL, 77 had CRP >24 mg/L, 82 had ESR >35 mm/hour, and 44 had WBC >15 000/mL.

الخلاصه

شملت هذه الدراسه ١٠٠ طفل تبلغ اعمارهم دون السنتين ، ادخلوا الى ردهات الاطفال او الطواريء في مستشفى بابل للنسائيه والاطفال للفتره من كانون الاول/٢٠٠٨ حتى حزيران/٢٠٠٨. تم استحصال التاريخ المرضي من الوالدين والفحص الطبي السريري من الطبيب المعالج. اظهرت هذه الدراسه بان لبكتريا الـ *Escherichia coli* الدور الاكبر في اصابة الاطفال الحميين الذين يعانون من التهاب في الجهاز البولي حيث بلغت نسبه الاصابه (٤٩%) بينما كانت نسب بقي المسببات البكتريه كالتالي : *Pseudomonas aeruginosa* (%٢٥) ، *Klebsiella pneumoniae* (%١٨) و *Proteus species* (%٨).

اظهرت سلالات الـ *Escherichia coli* حساسيه تجاه المضادات الحياتيه التاليه : Amikacin Chloromphenicol, Norfloxacin, Nitrofurantoin, Ofloxacin, Norfloxacin ، بينما بكتريا *Pseudomonas aeruginosa* كانت حساسه تجاه Ofloxacin, Piperacillin, Tobramycin، بكتريا *Proteus species* كانت حساسه للمضادات Amikacin, Amoxicillin , Cefodizime, Cefoxitin Cephalexin, Gentamycin, , Norfloxacin, Piperacillin, Tobramycin و *Klebsiella pneumoniae* كانت حساسه تجاه Amikacin, Norfloxacin, Piperacillin, Tobramycin.

اظهرت الدراسه انه من بين ١٠٠ طفل مصاب، ٥٧ منهم كانوا يعانون من البيله القيحيه بتعداد كريات الدم البيض اعلى من ٥ (pyuria > 5 WBCs/hpf)، ٩٠ طفلا اظهروا نسبة كريات الدم البيض اعلى من ١٠بطريقة الهيموسايتوميتير (pyuria >10 WBCs/mL)، ٧٧ طفلا كان تركيز CRP اعلى من ٢٤ ملغم/لتر ، ٨٢ طفلا كان معدل ترسيب كريات الدم الحمر اعلى من ٣٥ ملم/ساعه ، ٤٤ طفلا كان تعداد كريات الدم البيض لديهم اعلى من ١٥٠٠٠/مل.

Introduction

Urinary tract infection (UTI) is a frequent serious bacterial infection in young infants [1]. UTI is often associated with vesicoureteral reflux or urinary tract obstruction [2], conditions associated with a higher risk of recurrent UTI [3].

Moreover, UTI is believed to be the leading cause of renal scarring [4, 5], one of the most common causes of end-stage renal disease in children, the presumptive diagnosis of UTI in children is often based on the results of microscopic urinalysis (UA), and most infections remain undiagnosed if tests are not performed routinely to detect them. [6, 7].

The sensitivity, specificity, and positive predictive value of the standard UA are so low that only a third to half of patients with positive urine culture results can be identified correctly. Dukes [8. 9] described a more accurate microscopic analysis of uncentrifuged urine performed with a hemocytometer and reporting cells per cubic millimeter, herein referred to as hemocytometer white blood cell (WBC) counts. Stamm [10] defined pyuria as the presence of ≥10 WBCs/µL in uncentrifuged urine and found it to be very sensitive, identifying 96% of symptomatic adult patients with bacteriuria of ≥1000 colony-forming unit (CFU)/mL.

The present study was undertaken to evaluate a group of febrile infants younger than 2 years of age to assess the usefulness of the WBC count, C-reactive protein (CRP) concentration, erythrocyte sedimentation rate (ESR), and UA for identifying infants at risk for UTI; and antibiotics sensetivity of eacch pathogen , in addition to compare standard WBC counts and hemocytometer WBC counts in identifying very young infants with positive urine culture results.

Materials and methods

Prospectively studied 100 febrile infants (rectal temperature > 38°C) younger than two years of age who presented to the Pediatric Clinic or Emergency Department of Babylon Maternity and Children Hospital from February\2008 to June\2008. All infants were being hospitalized. Every infant underwent a history and physical examination, and a full evaluation for sepsis was performed, including peripheral WBC count and differential; ESR; CRP; blood culture (Blood samples were collected in screw capped tubes containing 20 ml Brain Heart Infusion broth without anticoagulant), Gram stain, and a UA and urine culture. Blood and urine specimens were cultured using standard media (Nutrient agar, MacConkey agar, Blood agar, Kleglar agar, Urea base agar, Peptone media, MR-VP broth and EMB agar) and techniques. Blood samples were cultured on aerobic and anaerobic media.

All urine specimens were obtained by clean containers with parent's assistance. Eligibility was limited to urine specimens of 3 mL obtained. All urinalyses were performed in a certified clinical laboratory. Specimens were analyzed with both standard UA and hemocytometer WBC counts simultaneously [11]. For the standard UA, specimens were centrifuged at 2000 rpm for 10 minutes and were examined microscopically for pyuria reported as the number of leukocytes per high-power field. For hemocytometer WBC counts, the uncentrifuged urine specimens were examined microscopically on a Neubauer chamber (Neubauer hemocytometer) by the same technician. C-reactive protein test done using latex kit from HUMATEX CRP (Germany) for qualitative and semi-quantitative determination [12]. In this study used 34 different antibiotics to detect the sensitivity of UTI causative agents, using disk diffusion agar using Muller Hinton agar.

Quantitative urine cultures were performed in the Microbiology Laboratory. A loop calibrated to deliver 0.01 mg was used to inoculate plates containing blood agar, nutrient agar, and MacConkey agar. All plates were incubated at 37°C and examined at 24 to 48 hours for colony count and bacterial identification. For standard UA, pyuria was defined as at least 5 WBCs/hfp. For hemocytometer WBC counts, pyuria was defined as at least 10 WBCs/mL, cultures with growth of mixed organisms or nonpathogenic Gram-positive cocci were considered contaminated [13].

Results and Discussion

This study investigated the percentage and antibiotic susceptibility patterns of bacterial pathogens isolated from patients with uncomplicated community-acquired UTI. The results showed that 100% of UTIs were caused by bacterial pathogen.

In this study, *Escherichia coli* formed the major causative agent (49%) followed by *Pseudomonas aeruginosa* (25%), *Klebsiella pneumonia* (18%) and *Proteus species* (8%) (Table 1). This is consistent with the findings of previous studies in which *E. coli Pseudomonas aeruginosa Klebsiella pneumonia* and others were the predominant pathogen isolated from patients with UTIs [14]. Uropathogenic *E. coli* is the most common pathogen in cute UTI in previous studies [15].

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Table1: Percentage of Etiological agents causes UTI in infants.

Etiological agents causes UTI	No.	%
Escherichia coli	49	49
Pseudomonas aeruginosa	25	25
Klebsiella pneumoniae	18	18
Proteus species	8	8
Total	100	100

This study shows the distribution and antibiotic susceptibility pattern of microbial species isolated from patients with UTIs (**Tables 3a, 3b and 3c**). These organisms cause a variety of infections including UTIs [16]. Antibiotic resistance is a major clinical problem in treating infections caused by these microorganisms. The resistance to the antimicrobials has increased over the years. Resistance rates vary from country to country [17]. Overall, isolates from Latin American countries show the lowest susceptibility rates to all antimicrobial agents followed by Asian-Pacific isolates and European strains. Strains from Canada exhibit the best global susceptibility testing results. In our study, it accounted for approximately all causative agents were belong to Enterobacteriaceae. This is consistent with the findings of previous studies in which *E. coli* was the predominant pathogen isolated from patients with community acquired UTIs [18]. However, *Klebsiella pneumoniae* are rarely encountered in cases of UTI

[19]. In the present study 18% of *Klebsiella* isolates were found to be present among all uropathogens studied. These isolates shows sensitivity with Amikacin, Norfloxacin, Piperacillin, Tobramycin which is consistent with the previous data of other community- based studies [15].

E. coli isolates showed sensitivity with Amikacin, Chloromphenicol, Nitrofurantoin, Ofloxacin, Norfloxacin and *Pseudomonas aeruginosa* shows sensitivity with Norfloxacin, Ofloxacin, Piperacillin, Tobramycin, while *Proteus species* shows sensitivity with Amikacin, Amoxicillin , Cefodizime, Cefoxitin, Cephalexin, Gentamycin, , Norfloxacin, Piperacillin, Tobramycin, it is nearly compatable with Indian, Taiwan, Spain, and Senegal isolates [20, 21].

In this study *E. coli*, *Pseudomonas aeruginosa*, Proteus *species* and *Klebsiella* isolates are resistant against many antibiotics. Whereas, this drug exhibited low resistance rate in the major part of the world, despite of it's being used for many years [22]. This is probably due to the fact that this antibiotic has been widely used in treating community- acquired UTIs over the past decade in this region [23].

Table 2: Age and gender wise distribution and frequency of UTI causes isolated from infants.

Age group	UTI Causes							
	Escherichia coli		*Pseudomonas aeruginosa*		*Klebsiella pneumoniae*		*Proteus species*	
	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)	M (%)	F (%)
< 1	-	1	-	-	-	-	-	-
1-4	10	7	1	4	-	-	-	-
5-8	4	13	-	9	1	6	-	2
9-12	5	9	1	10	-	11	6	-
Total	19	30	2	23	1	17	6	2

Table 3a: Antimicrobial potency and spectrum of 13 selected antimicrobial agents tested against most frequently occurring UTI pathogens.

Microorganism	Antimicrobial agent / % sensitive strains												
	AK	AX	AMC	AZM	B	PY	CDZ	FOX	ZOX	CL	C	CLR	DA
Escherichia coli	88	20	20	-	5	-	-	-	10	20	90	-	-
Pseudomonas aeruginosa	55	10	20	10	10	-	10	15	15	55	15	10	-
Klebsiella pneumoniae	80	-	-	25	-	10	-	-	10	5	-	10	-
Proteus species	100	60	90	10	20	55	80	95	35	75	25	55	25

AK \Amikacin, AX \Amoxicillin, AMC \Amoxicillin + Clavulanic acid, AZM \Azithromycin, , B \Bacitracin, PY \Carbenicillin, CDZ \Cefodizime, FOX \Cefoxitin, ZOX \Ceftizoxime, CL \Cephalexin, C \Chloromphenicol, CLR \Clarithromycin, DA \Clindamycin

Table 3b: Antimicrobial potency and spectrum of 13 selected antimicrobial agents tested against most frequently occurring UTI pathogens.

Microorganism	Antimicrobial agent / % sensitive strains												
	E	CN	K	L	ME	F	NOR	OFX	OX	T	P	PRL	RA
Escherichia coli	-	-	10	-	15	65	100	90	5	-	10	-	-
Pseudomonas aeruginosa	20	15	20	10	10	20	95	70	10	40	-	85	10
Klebsiella pneumoniae	-	-	-	-	-	10	100	-	-	-	15	100	10
Proteus species	10	85	10	-	30	35	95	75	70	10	55	80	70

E \Erythromycin, CN\Gentamycin, K\Kanamycin, L\Lincomycin, ME\Methicillin, F\Nitrofurantoin, NOR\Norfloxacin, OFX \Ofloxacin, OX\Oxacillin, T\Oxytetracyclin, P\Penicillin G, PRL \Piperacillin, RA\Rifampim.

These results were done according to performance standards for antimicrobial disk susceptibility tests, CLSI (formerly NCCLS). The antibiotic which not including in CLSI chart, FDA approved performance standars for antimicrobial discs obtained from drug manufatures [24].

Table 3c: Antimicrobial potency and spectrum of 8 selected antimicrobial agents tested against most frequently occurring UTI pathogens.

Microorganism	Antimicrobial agent / % sensitive strains							
	RF	SP	S	TE	TOB	TMP	SXT	VA
Escherichia coli	-	10	20	50	55	-	-	-
Pseudomonas aeruginosa	15	10	55	20	95	10	15	10
Klebsiella pneumonia	-		-	-	100	-	-	-
Proteus species	10	40	-	15	95	20	-	1

RF \Rifamycin, SP\Spiramycin, S\Streptomycin, TE\Tetracycline, TOB\Tobramycin, TMP\Trimethoprim, SXT\Trimethoprim + Sulphamethaxazole, VA\Vancomycin

CRP >20 mg/L, ESR >30 mm/hour, and WBC >15 000/mL are key findings in various studies on febrile infants [25]. The diagnostic value of these parameters for predicting serious bacterial infection in febrile infants, CRP is an acute phase reactant which opsonises invading pathogens. Levels of CRP increase within 6 hours of an inflammatory stimulus, and may rise up to 1000-fold, measurement of CRP provide direct index of acute inflammation, in contrast to CRP, the ESR is an indirect measure of the acute phase response [26].

Our investigation showed (**Table 4**) that from the 100 febrile infants with UTI, 57 had pyuria > 5 WBCs/hpf, 90 had pyuria >10 WBCs/mL, 77 had CRP >24 mg/L, 82 had ESR >35 mm/hour, and 44 had WBC >15 000/mL. Our results corroborate the findings of Crain and Dar-Shong [13, 27] whose sample was similar to ours.

Table 4: The Results of Diagnostic Test in Presence of a Positive Urine Culture.

Diagnostic Test	No.	%
Standard UA > 5 WBCs/hpf	57	57
Hemocytometer WBC Counts >10 WBCs/mL	90	90
CRP > 24 mg/L	77	77
ESR > 35 mm/h	82	82
Peripheral WBC > 15 000/mL	44	44

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