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A 5 year (2005-2009) review of antimicrobial susceptibility of clinical Klebsiella pneumoniae isolates from pediatric patients in Jordan

Mohammad Al-Shara*

Department of Pharmacology, Faculty of Nursing, Irbid National University, Irbid, Jordan

Abstract: *Aim of the Study:* The present study was conducted to investigate antimicrobial susceptibility pattern of Klebsiella pneumoniae strains isolated from clinical specimens of Jordanian pediatric patients during a five year period from 2005-2009. A total of 1023 Klebsiella pneumoniae strains were isolated from clinical specimens and tested for their susceptibility to different antimicrobial drugs. *Main findings*: Overall, high susceptibility rate was recorded for ciprofloxacin (90.5%), followed by norfloxacin (84.8%), imipenem (69.9%), nalidixic acid (66.6%), and cefixime (63.9%). Low susceptibility rate was recorded for ampicillin (16.6%), followed by amoxicillin-clavulanic acid (22.5%), tobramycin (28.6%), amikacin (31.4%), cotrimoxazole (37.3%), and aztreonam (39.3%), *Conclusion:* most of β-lactam antibiotics as well as tobramycin, amikacin, cotrimoxazole, and aztreonam, should not be used in treating infections caused by pathogenic K. pneumoniae and other related bacteria in Jordan. However, quinolone compounds and imipenem seem to be effective in treatment of infections caused by pathogenic K. pneumoniae in children.
Keywords: Antimicrobial resistant, Klebsiella pneumoniae, pediatric patients.

Introduction

Bacterial resistance has been emerging and become major public health problem worldwide. Infections results from resistant bacteria have been shown to be more frequently associated with increased morbidity and mortality than those caused by susceptible pathogens [1]. This had led to both clinical and financial implications for the treatment of infected patients [2]. Klebsiella pneumoniae is an important cause of morbidity and mortality [3]. It is a common cause of nosocomial infection causing urinary tract infections, pneumonia, and intraabdominal infections [4-5]. Many studies have demonstrated increases in antimicrobial resistance among K. pneumoniae in several countries [6-7].

Despite world-wide use of antibiotics, the distribution of the resistance is far from being uniform even in the same area [8]. Therefore, continuous surveillance is necessary to monitor changes in antimicrobial susceptibilities. Such information is important for clinician in their choice of therapy. However, there is little information on antimicrobial resistance pattern of K. pneumoniae in Jordan. Therefore, this retrospective study was conducted to determine the rate of resistance to antibiotics by K. pneumoniae strains isolated from cultures of different clinical specimens received from pediatric patients at Princess Rahmah Hospital during a five year period of 2005-2009.

Material and Methods

This study was carried out in the diagnostic Medical Microbiology Laboratory of Princess Rahmah Hospital located in Irbid, Jordan, during the year of 2005-2009. A total of 1023 bacterial isolates were identified from different clinical specimens using standard bacteriological methods. These clinical specimens included blood, urine, ear swabs and conjunctival swabs. Microbiological and antibacterial susceptibility data of this study obtained from records of diagnostic Medical Microbiology Laboratory of Princess Rahmah Hospital. These data were filled in a prepared data sheet. Antimicrobial susceptibility patterns of these isolates to antibiotics were determined using the Kirby-Bauer method of disc diffusion test [9]. The isolates were tested against the following antimicrobials; amikacin, amoxicillin-clavulanic acid, ampicillin, aztreonam, cefaclor, cefixime, cefotaxime, ceftazidime, ceftriaxone, cephlexin, ciprofloxacin, cotrimoxazole,

gentamicin, imipenem, nalidixic acid, norfloxacin, pipracillin and tobramycin. Data were analyzed using SPSS (version15 for Windows) to calculate the frequencies and cross tables. Study protocol was approved by the Ethics Committee of the Ministry of Health in Jordan (MOH, REC, 08, 0057).

Results

During a five year period (2005-2009), a total of 1023 positive K. pneumoniae cultures of pediatric patients aged below 15 years old were studied. The distribution of K. pneumoniae strains from various clinical specimens was 628 (61.4%) from urine, 354 (34.7%) from blood, 22 (2.1%) from ear swabs and 19 (1.8%) from eye swabs, (Table 1).

Overall, high susceptibility rate was recorded for ciprofloxacin (90.5%), followed by norfloxacin (84.8%), imipenem (69.9%), nalidixic acid (66.6%), and cefixime (63.9%). Low susceptibility rate was recorded for ampicillin (16.6%), followed by amoxicillin-clavulanic acid (22.5%), tobramycin (28.6%), amikacin (31.4%), cotrimoxazole (37.3%), and aztreonam (39.3%), (Table 2).

Table-1: Distribution of Klebsiella isolates in clinical specimens

Clinical specimen	Year					Total %
	2005	2006	2007	2008	2009	
Urine	107	142	132	119	128	628
Blood	69	34	61	34	156	354
Ear swab	7	6	2	5	2	22
Eye swab	3	5	3	7	1	19
Among all specimens	186	187	198	165	287	1023

Table-2: Susceptibility rate of Klebsiella isolates from children to various antimicrobials

Number (%) of Klebsiella susceptible to	2005 N= 186	2006 N= 187	2007 N= 198	2008 N= 165	2009 N= 287	Total N= 1023	Significance 2005 vs. 2009
	N (S %)	N (S %)	N (S %)	N (S %)	N (S %)	N (S %)	P-value
AMC	41 (36.5)	108 (28.7)	132 (27.2)	111 (22.5)	207 (13.5)	599 (22.5)	<0.001
AMK	68 (44.1)	42 (33.3)	65 (40.0)	42 (47.6)	171 (18.7)	388 (31.4)	<0.001
AMP	62 (9.6)	132 (3.7)	150 (10.6)	111 (7.2)	99 (57.5)	554 (16.6)	<0.001
AZT	72 (36.1)	69 (47.8)	114 (55.2)	33 (21.2)	73 (17.8)	361 (39.3)	0.013
CAZ	85 (74.1)	42 (76.1)	52 (38.4)	62 (56.4)	188 (43.0)	429 (53.8)	<0.001
CEC	65 (50.7)	36 (80.5)	101 (60.3)	115 (51.3)	113 (57.5)	430 (57.4)	0.386
CFX	45(60.0)	48 (66.6)	34 (47.0)	91 (56.0)	85 (50.5)	303 (55.7)	0.310
CF	38 (50.0)	121 (81.8)	139 (68.3)	76 (56.5)	117 (49.5)	491 (63.9)	0.964
CPR	170 (91.1)	133 (83.4)	164 (92.0)	144 (93.0)	161 (91.9)	772 (90.5)	0.807
COT	77 (38.9)	122 (45.9)	131 (33.5)	104 (38.4)	86 (27.9)	520 (37.3)	0.136
CTR	70 (41.4)	40 (20.0)	179 (62.5)	35 (17.1)	129 (37.9)	453 (45.0)	0.637
CTX	127 (64.5)	159 (72.3)	63 (26.9)	141 (56.7)	280 (41.2)	770 (54.0)	<0.001
GEN	138(63.0)	159 (68.5)	181 (61.3)	133 (59.3)	252 (43.2)	863 (57.3)	<0.001
IMP	73 (54.7)	55 (38.1)	64 (68.7)	33 (12.1)	208 (93.2)	433 (69.9)	<0.001
NAL	106 (70.7)	134 (65.5)	125 (66.4)	113 (66.3)	116 (62.9)	594 (66.3)	0.219
NOR	95 (84.2)	138 (80.4)	129 (86.0)	110 (86.3)	108 (87.9)	580 (84.8)	0.445
PIP	56 (25.0)	65 (47.6)	62 (62.9)	34 (11.7)	162 (69.1)	379 (52.7)	<0.001
TOB	64 (32.8)	54 (42.5)	79 (43.0)	38 (21.0)	152 (16.4)	387 (28.6)	0.007

Number of isolates (N), Sensitive (S), Not significant (NS)

Amoxicillin-Clavulanic acid (AMC), Amikacin (AMK), Ampicillin (AMP), Aztreonam (AZT), Ceftazidime (CAZ), Cefaclor (CEC), Cefixime (CF), Cephlexin (CFX), Cotrimoxazole (COT), Ciprofloxacin (CPR), Ceftriaxone (CTR), Cefotaxime (CTX), Gentamicin (GEN), Imipenem (IMP), Nalidixic acid (NAL), Norfloxacin (NOR), Pipracillin (PIP) and Tobramycin (TOB)

Discussion

This current study provides information regarding the distribution of pathogenic K. pneumoniae isolates and its antimicrobial susceptibility patterns in pediatric patients. Most K. pneumoniae strains isolated was from urine samples 628 (61.4%) followed by 354 (34.7%) from blood, 22 (2.1%) from ear swabs and 19 (1.8%) from eye swabs.

In this study, Klebsiella pneumoniae showed improvement in its susceptibility rate to ampicillin, cefaclor, cefixime, ciprofloxacin, imipenem, norfloxacin and pipracillin and this improvement was significant ($P<0.05$) to ampicillin, imipenem and pipracillin in comparison between the year of 2005 vs 2009. This may be because quinolone and other compounds are relatively not in common use by the population as compared to β-lactam antibiotics [12].

However, results of this study showed significant decreased ($P<0.05$) of susceptibility rates of K. pneumoniae isolates to amikacin, amoxicillin-clavulanic acid, aztreonam, ceftazidime, cephlexin, gentamicin, and tobramycin in comparison between the year of 2005 vs 2009. In addition, K. pneumoniae showed decreased of their susceptibility rates to cefotaxime, cotrimoxazole, ceftriaxone, and nalidixic acid, but that decrement was not significant ($P>0.05$). Similar findings regarding high potentials for developing resistance for pathogenic isolates of K. pneumoniae were reported [10-14]. It seems that the prevalence of antibiotic resistance of K. pneumoniae to commonly used antimicrobial drugs in Jordan has increased over the last 15 years, in comparison to previous studies [15-16]. Result of this study disagreed with previous study conducted in 2004 in Jordan which demonstrate relatively low rate of resistance [15]. At that time, Tumah [15] found that more than 90% of K. pneumoniae isolates were sensitive to above antibiotics. This increase in the resistance rate is may due to the widespread and lengthy use of these antibacterial drugs in the world including Jordan. Over a period of this study, results showed higher resistance rates of K. pneumoniae to β-lactam antibiotics compared with other studies conducted previously in Jordan [16-17] and elsewhere [18-19].

There are many possible reasons for increasing resistant rate of K. pneumoniae to common used antimicrobial drugs, including inappropriate and incorrect administration of antimicrobial agents in empiric therapies and lack of appropriate infection control strategies [19-20]**.** This problem indicates importance of performing antibiotic susceptibility testing before blind antibiotic therapy.

Conclusion

The data suggest that most of β-lactam antibiotics as well as amikacin, aztreonam, cotrimoxazole and tobramycin should not be used in treating infections caused by pathogenic K. pneumoniae and other related bacteria in Jordan. However, quinolone compounds and gentamicin seem to be effective in treatment of infections caused by pathogenic K. pneumoniae. These findings also reinforce the need for ongoing investigation to show trends in antibiotic resistance, which can help clinicians provide safe and effective empiric therapies. Moreover, resistance studies assist health authorities in the formulation of their own drug policies.

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*All correspondences to: Dr. Mohammad Al-Shara, Ph.D Pharmacology, Assistant Prof of Pharmacology, Faculty of Nursing, Irbid National University, Irbid, Jordan. E-mail ID: alshara_70@yahoo.com