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In-Vitro Activity of Third Generation Cephalosporins Against Bacterial Clinical Isolates from Pediatric Patients

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ABSTRACT

The extensive use of third generation cephalosporins in hospitals and in the community has created major resistance problems which have led to increased morbidity, mortality and healthcare costs. To evaluate the in-vitro activity of third generation cephalosporins against clinical isolates from children. A total of 3723 bacteria isolates were identified from different clinical specimens between the years of 2005-2009. Clinical specimens included blood, urine, ear swabs and conjunctival swabs using standard bacteriological methods. *E. coli* showed the highest susceptibility rate of 83.7% to cefotaxime, *K. pneumoniae* showed the highest rate of 63.9% to cefixime and *S. aureus* showed the highest susceptibility rate of 66.7% to cefotaxime. Over all bacterial isolates, the activity of tested antibiotics ranged between 72.6% to 41.6% for cefotaxime and ceftriaxone respectively. This study revealing and highlights alarming increase in resistance to commonly used third generation cephalosporin antibiotics amongst *E. coli*, *K. pneumoniae* and *S. aureus*. There is an urgent need for early detection of these isolates for better treatment outcomes. Third generation cephalosporins had poor activities against bacterial isolate in our set up.

Keywords: Third generation cephalosporins, *Escherichia coli*, *Klebsiella pneumoniae*, antimicrobial susceptibility, empiric therapy

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INTRODUCTION

An extensive use of third generation cephalosporins for treatment of bacterial infection results in an increasing resistance to these drugs which become a major public health problem all over the world. [1] Morbidity and mortality have been shown to be more frequently due to infections caused by resistant bacteria than those caused by susceptible pathogens. [2,3] In hospitals which are areas of concentrated use, bacterial resistance led to lengthened hospital stays, increased health care costs and in extreme cases, to untreatable infections. Among the large number of antibiotics being used, β-lactams agents are accounting for over 50% of all systemic antibiotics in use. [4]

The most common cause of bacterial resistance to β-lactam antibiotics is the production of both β-lactamases and Extended Spectrum β-Lactamases (ESBLs). These enzymes are commonly produced by different bacteria especially *E. coli* and *K. pneumoniae* and efficiently hydrolyze oxyimino-cephalosporins conferring resistance to third-generation cephalosporins such as cefotaxime, ceftazidime and ceftriaxone. [5]

Despite world-wide use of β-lactam antibiotics, the distribution of the enzymes responsible for resistance to oxyimino-cephalosporins and carbapenems is far from being uniform. Some hospitals in the United States seem to have no or low ESBLs, whereas in other hospitals, as many as 40% of *K. pneumoniae* isolates have been reported to be ceftazidime resistant as a result of ESBLs production. [6]

A resistance distribution pattern is far from being uniform among the different geographical areas, depending on the antibiotic consumption pattern. [7] Therefore, antibiotic susceptibility testing is very important to facilitate use of the most appropriate treatment in infected individuals.

However, there is little information on third generation cephalosporins resistance pattern in Jordan. Therefore, this retrospective study was conducted to determine the rate of resistance to third generation cephalosporins by pathogens isolated from cultures of clinical specimens received from children inpatient and outpatients at Princess Rahmah Hospital during a period of 5 years (2005-2009).

MATERIALS AND METHODS

This study was carried out in the diagnostic Medical Microbiology Laboratory of Princess Rahmah Hospital located in Irbid, Jordan, between 2005-2009. A total of 3723 bacteria 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 third generation cephalosporins (cefixime, cefotaxime, ceftazidime and ceftriaxone) antibiotics were determined using the Kirby-Bauer method of disc diffusion test. [8] Study protocol was approved by the Ethics Committee of the ministry of health in Jordan (MOH, REC, 08, 0057).

Statistical Analysis

Data were analyzed using SPSS (version15 for Windows) to calculate the frequencies and cross tabulation.

RESULTS

Tables 1-4 shows the percentage susceptibility pattern of different clinical isolates to tested antibiotics.

Over all study period, *E. coli* showed the highest susceptibility rate of 83.7% for cefotaxime, whereas the lowest susceptibility rate of 71.0% recoded for ceftazidime. *Klebsiella pneumoniae* showed low susceptibility rate to all tested antibiotics. However, the highest rate of its susceptibility of 63.9% recorded for cefixime. *S. aureus* showed also low susceptibility rate to all tested antibiotics with the highest susceptibility rate of 66.7% recorded for cefotaxime.

Among all clinical isolates during the period of study, the highest susceptibility rate of 72.6% was for cefotaxime, followed by 61.2%, 56.2%, and 41.6% for cefixime, ceftriaxone and ceftazidime respectively (Figure 1).

Table 1. Cefixime activity pattern against clinical isolates from Jordanian children in a five years period (2005-2009).

Pathogen	2005	2006	2007	2008	2009	Total	Significance 2005 vs. 2009
	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	P-value
E-coli	138 (52.8)	320 (86.5)	398 (81.1)	183 (71.0)	383 (56.9)	1422 (71.8)	0.416
Klebsiella spp	38 (50.0)	121 (81.8)	139 (68.3)	76 (56.5)	117 (49.5)	491 (63.9)	0.964
Proteus spp	11 (54.5)	22 (90.9)	21 (80.9)	1 (100.0)	16 (75.0)	71 (78.8)	0.286
Pseudo	7 (28.5)	12 (16.6)	23 (8.6)	20 (45.0)	13 (15.3)	75 (22.6)	0.508
S. aureus	21 (66.6)	58 (41.3)	123 (25.2)	79 (29.1)	139 (26.6)	420 (30.7)	<0.001
Streptococcus spp	6 (83.3)	29 (58.6)	31 (61.2)	19 (52.6)	27 (48.1)	112 (57.1)	0.125
Enterobacter	9 (55.5)	19 (47.3)	20 (65.0)	3 (0)	36 (30.5)	87 (43.6)	0.168
All pathogens	230 (53.9)	581 (77.1)	755 (66.2)	381 (56.6)	731 (48.0)	2678 (61.2)	0.11

Table 2. Cefotaxime activity pattern against clinical isolates from Jordanian children in a five years period (2005-2009).

Pathogen	2005	2006	2007	2008	2009	Total	Significance 2005 vs. 2009
	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	P-value
E-coli	414 (85.9)	400 (86.7)	29 (72.4)	389 (89.4)	290 (70.0)	1522 (83.7)	<0.001
Klebsiella spp	127 (64.5)	159 (72.3)	63 (26.9)	141 (56.7)	288 (41.2)	718 (54.0)	<0.001
Proteus spp	33 (93.9)	27 (92.5)	2 (100.0)	5 (60.0)	13 (92.3)	80 (91.2)	0.844
Pseudo	21 (42.8)	16 (50.0)	13 (100.0)	29 (89.6)	11 (36.3)	90 (66.6)	0.733
S. aureus	39 (51.2)	116 (62.9)	181 (68.5)	355 (74.9)	374 (60.9)	1065 (66.7)	0.241
Streptococcus spp	24 (70.8)	38 (86.8)	37 (91.8)	20 (85.0)	37 (94.5)	156 (87.1)	0.010
Enterobacter	19 (57.8)	26 (53.8)	13 (100.0)	4 (100.0)	30 (63.3)	92 (66.3)	0.711
All pathogens	677 (77.6)	782 (78.6)	338 (66.2)	943 (78.8)	983 (60.5)	3723 (72.6)	< 0.001

Table 3. Ceftazidime activity pattern against clinical isolates from Jordanian children in a five years period (2005-2009).

Pathogen	2005	2006	2007	2008	2009	Total	Significance 2005 vs. 2009
	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	P-value
E-coli	92 (92.3)	6 (66.6)	20 (45)	115 (74.7)	138 (73.9)	371 (77.0)	<0.001
Klebsiella spp	85 (74.1)	42 (76.1)	52 (38.4)	62 (56.4)	188 (43.0)	429 (53.8)	<0.001
Proteus spp	6 (83.3)	3 (33.3)	0	3(0.0)	4 (75)	16 (56.2)	0.779
Pseudo	22 (59.0)	8 (25)	6 (83.3)	12 (66.6)	11(54.5)	59 (57.6)	0.811
S. aureus	118 (33.8)	172 (31.9)	142 (25.3)	292 (26.0)	379 (9.4)	1103 (22.0)	<0.001
Streptococcus spp	35 (60)	51 (35.2)	12 (75)	9 (66.6)	39 (38.4)	146 (47.2)	0.066
Enterobacter	10 (70)	6 (50)	15 (86.6)	3 (33.3)	18 (55.5)	52 (65.3)	0.472
All pathogens	368 (63.5)	288 (39.9)	247 (37.2)	496 (42.3)	777 (32.5)	2176 (41.6)	< 0.001

Table 4: Ceftriaxone susceptibility pattern against gram negative and gram positive clinical isolates from Jordanian children in a five years period.

Pathogen	2005	2006	2007	2008	2009	Total	Significance 2005 vs. 2009
	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	N (%S)	P-value
E-coli	18 (66.6)	5 (0)	397 (83.8)	14 (92.8)	39 (82.0)	473 (82.4)	0.205
Klebsiella spp	70 (41.4)	40 (20.0)	179 (62.5)	35 (17.1)	129 (37.9)	453 (45.0)	0.637
Proteus spp	3 (66.6)	3 (33.3)	19 (94.7)	0	1 (100.0)	26 (84.6)	0.667
Pseudo	18 (16.6)	6 (16.6)	15 (66.6)	3 (0)	5 (80.0)	47 (38.2)	0.005
S. aureus	98 (54.0)	166 (37.9)	134 (42.5)	298 (45.9)	245 (48.1)	941 (45.4)	0.323
Streptococcus spp	36 (58.3)	47 (63.8)	8 (100.0)	9 (77.7)	20 (95.0)	120 (70.8)	0.003
Enterobacter	5 (100.0)	6 (50.0)	28 (85.7)	1 (0)	9 (77.7)	49 (79.5)	0.290
All pathogens	248 (50.4)	273 (38.8)	780 (72.0)	360 (45.2)	448 (51.3)	2109 (56.2)	0.81

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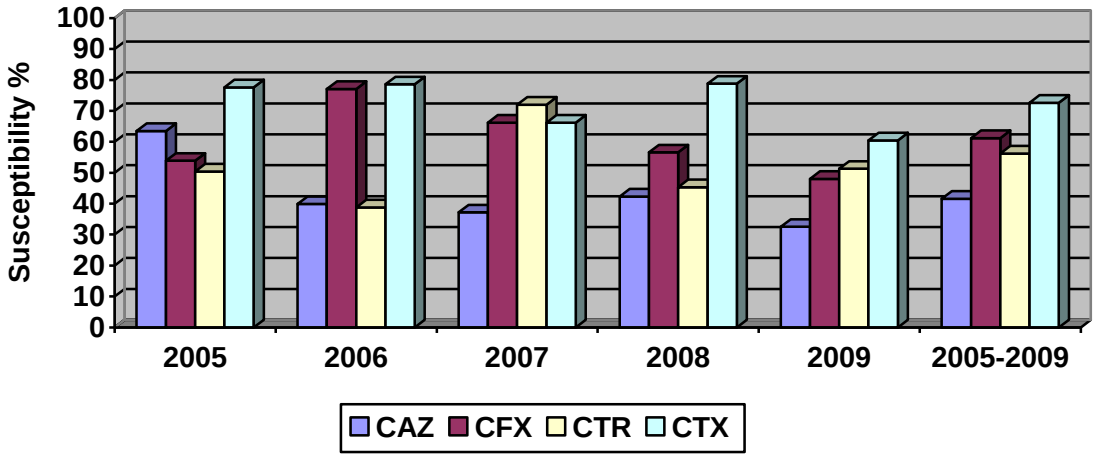
Figure 1. Susceptibility of clinical isolates to third generation cephalosporins (2005-2009).



Ceftazidime (CAZ), Cefixime (CF), Ceftriaxone (CTR), Cefotaxime (CTX)

DISCUSSION

Third generation cephalosporins proved to be high of chemotherapeutic value against different tested clinical isolates. Results of this study showed high rates of antimicrobial resistance among tested bacterial pathogens. These results are consistence with result reported elsewhere. [9,10]

Over all the period of study, these findings demonstrated that *E. coli* has susceptibility rates ranged from 83.7% for cefotaxime and 71.8% for cefixime. Susceptibility of *E. coli* to ceftazidime and cefotaxime was significantly deceased (P<0.001) in comparison between the year of 2005 and 2009, whereas the changing in the susceptibility was not significant for cefixime and ceftriaxone. This susceptibility rate was higher than that reported elsewhere. [11-13] The high susceptibility rate may due to little usage of these antibiotics for treatment of infection induced by *E. coli* in children.

K. pneumoniae also showed throughout the study period, low susceptibility rates ranged between 63.9% to 45.0% for cefixime and ceftriaxone respectively. In compression of susceptibility of *K. pneumoniae* between the year of 2005 and 2009 to tested antibiotics, these susceptibility rates showed significant decreased (P<0.001) from 64.5% to 41.2% and from 74.1% to 43.0% for cefotaxime and ceftazidime respectively, whereas decrement was not significant for cefixime and ceftriaxone. However, susceptibility rates of this study were lower than other study reported elsewhere**.** [12] This low susceptibility rate may due to extensive use of these antibiotics for treatment of infection induced by *K. pneumoniae* in the area of study.

In this study, susceptibility of *S. aureus* to tested antibiotics through out the study period was low and ranged between 66.7% and 22.0% for ceftriaxone and ceftazidime respectively. The rates of susceptibility were significantly decreased (P<0.001) from 33.8% to 9.4% and from 66.6% to 26.65 for ceftazidime and cefixime respectively in comparison between the year of 2005 and 2009. Similar findings reported low susceptibility rate of *S. aureus* to ceftriaxone [14] and to cefotaxime. [15]

To over all bacterial isolates, the activity of tested antibiotics ranged between 72.6% to 41.6% for cefotaxime and ceftriaxone respectively. However, the activity of tested antibiotics was decreased in comparison between the year of 2005 and 2009 and this decrement was significant (P<0.001) and it was from 77.6% to 60.5% for ceftriaxone and from 63.5% to 32.5% for ceftazidime.

CONCLUSION

This study revealing and highlights alarming increase in resistance to commonly used third generation cephalosporin antibiotics amongst *E. coli K. pneumoniae* and *S. aureus*. There is an urgent need for early detection of these isolates for better treatment outcomes. Third generation cephalosporins had poor activities against bacterial isolate in our set up. Therefore, in the future, continuous monitoring of susceptibility patterns

among general practice isolates is warranted not only for Third generation cephalosporins but also for all currently prescribed antibiotics.

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