

## Original Article

# In vitro ciprofloxacin resistance profiles among gram-negative bacteria isolated from clinical specimens in a teaching hospital

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## Abstract

**Objective:** To evaluate the trends of ciprofloxacin resistance pattern in commonly isolated gram-negative bacteria over time in a Saudi Arabian teaching hospital.

**Methods:** A retrospective analysis was carried out for ciprofloxacin resistance patterns of 10089 isolates of gram-negative bacteria isolated from various clinical specimens submitted to microbiology laboratories at King Fahd Hospital of the University (KFHU), Alkhobar, Saudi Arabia during the period January 2002 to August 2005.

**Results:** Increase in ciprofloxacin resistance rates in these isolates during the years 2002 and 2005 were as follows: *Escherichia coli*, 23.85 to 33.1%; *Klebsiella pneumoniae*, 15.93 to 27.55%; *Enterobacter cloacae*, 12.32 to 18.05%; *Enterobacter aerogenes*, 4.16 to 25.64%; *Pseudomonas aeruginosa* 17.05 to 39.53%, *Pseudomonas* spp., 20.58 to 58.77%; *H. influenzae*, 00.00% to 11.11% and *H. aegyptius*, 00.00% to 1.73%.

**Conclusion:** There was a gradual increase in resistance from year 2002 to 2005 in most of the gram negative isolates i.e. *E. coli*, *K. pneumoniae*, *E. cloacae*, *E. aerogenes*, *P. aeruginosa* and *Pseudomonas* spp showing that ciprofloxacin is no more a drug of choice for gram negative infections by these microbes (JPMA 60:625; 2010).

## Introduction

Over the last few decades the ever-increasing level of bacterial resistance to antimicrobials has been a cause of worldwide concern. This situation is aggravated by over the counter availability, and indiscriminate and inappropriate use of antimicrobial agents.<sup>1</sup> It is well recognized that the increased use of ciprofloxacin has led to a progressive loss of its susceptibility,<sup>2,3</sup> since its introduction for the treatment of a broad range of clinical conditions such as urinary tract infections, upper respiratory tract infections, as a prophylaxis in neutropenic patients and in poultry, resistant strains are on the increase.<sup>4,5</sup> This is particularly seen among gram-negative bacteria.<sup>6</sup> A major aspect of medical concern is the increasing ciprofloxacin resistance among *E. coli* and other

*Enterobacteriaceae*.<sup>7-10</sup>

Surveillance studies are one of the main tools for resolving the problem of antimicrobial resistance, as they enable resistance patterns to be monitored and allow early detection of any potential resistance trends.<sup>1</sup> In this study we aimed to highlight trends of resistance to ciprofloxacin among common gram negative organisms isolated in KFHU during the years January 2002 to August 2005.

## Materials and Methods

A retrospective analysis was carried out for ciprofloxacin susceptibility patterns of gram-negative bacteria isolated from various clinical specimens submitted to microbiology laboratories at KFHU, Alkhobar, Saudi Arabia

during the period from January 2002 to August 2005. Data of total of 10089 gram negative organisms [*Escherichia coli* (n=3953), *Klebsiella pneumoniae* (n=1962), *Enterobacter cloacae* (n=501), *Enterobacter aerogenes* (n=167), *Pseudomonas aeruginosa* (n=2561), *Pseudomonas spp.* (n=319), *Haemophilus influenzae* (n=258), and *Haemophilus aegyptius* (n=368)] was accessed from the hospital's computer system during the period January 2002 to August 2005. The bacterial isolates obtained on routine culture media were identified and their susceptibility testing was carried out by using the MicroScan Walk Away 96 system (Dade Behring Inc., West Sacramento, CA95691, USA). Intermediately susceptible strains were considered resistant.

## Results

Ciprofloxacin resistance of gram negative isolates recovered from specimens at KFHU during the period January 2002 to August 2005 is given in the Table. There was a gradual increase in resistance from year 2002 to 2005 in most of the gram negative isolates. For *E. coli*, resistance

*Pseudomonas spp.* This could be due to the increasing use of fluoroquinolones particularly ciprofloxacin in gram negative infections.<sup>3,7,8</sup> Similar trend was reported in another study from Saudi Arabia carried out between years 2001 and 2005.<sup>11</sup> However in our study, the rate of resistance was relatively higher but is comparable to a recent report from Saudi Arabian isolates from urinary tract infections.<sup>12</sup> This could be due to difference in trend of ciprofloxacin prescription in different healthcare settings. These results are comparable with studies from United States, France, Germany, Italy, Spain, Canada, China and Taiwan.<sup>9,13-16</sup>

*Pseudomonas spp.* and *P. aeruginosa* showed high resistance rates (59.81% and 39.53%) like other studies.<sup>17</sup> Very high resistance in *E. coli* (36.82%) and *K. pneumoniae* (27.55%) like other reports.<sup>18,19</sup> could be due to the reason that ciprofloxacin being mostly used as oral agent may lead to resistance in local faecal flora and patients acquire infection with these resistant strains. Ciprofloxacin resistance in *E. cloacae* and *E. aerogenes* has increased more in our isolates (>23% & >25% respectively) than in another study

**Table: Ciprofloxacin resistance pattern in gram-negative bacteria isolated from clinical specimens (n=10089) during the years 2002-2005.**

S.NO	Organisms	YEARS									
		2002		2003		2004		2005		2002-2005	
		TN*(NR)**	NR%	TN (NR)	NR%	TN (NR)	NR%	TN (NR)	NR%	TN (NR)	NR%
1	<i>E. coli</i>	612 (146)	23.85	1206(345)	28.07	1404(517)	36.82	731 (242)	33.1	3953 (1250)	31.62
4	<i>K. pneumoniae</i>	320 (51)	15.93	535 (94)	17.57	726 (174)	23.96	381 (105)	27.55	1962 (424)	21.61
2	<i>E. aerogenes</i>	24 (1)	4.16	31 (2)	6.45	73 (15)	20.54	39 (10)	25.64	167 (18)	10.77
3	<i>E. cloacae</i>	73 (9)	12.32	160 (33)	20.62	196 (47)	23.97	72 (13)	18.05	501 (102)	20.35
5	<i>P. aeruginosa</i>	475 (81)	17.05	677 (171)	25.25	802 (265)	33.04	607 (240)	39.53	2561 (757)	29.55
6	<i>Pseudomonas spp.</i>	34 (7)	20.58	129 (39)	30.23	107 (64)	59.81	49 (19)	38.77	319 (129)	40.43
7	<i>H. aegyptius</i>	11 (0)	0	115 (2)	1.73	173 (3)	1.73	69 (0)	0	368 (5)	1.35
8	<i>H. influenzae</i>	28 (0)	0	77 (11)	14.28	63 (1)	1.58	90 (10)	11.11	258 (22)	8.52

Key: \*TN: Total number during the year; \*\*NR: Number resistant.

rates were 23.85, 28.07, 36.82 and 33.1% during the years 2002, 2003, 2004 and 2005 respectively. Resistance rates in other isolates during the same years respectively were as follows: *K. pneumoniae*, 15.93, 17.57, 23.96 & 27.55%; *E. cloacae*, 12.32, 20.62, 23.97 & 18.05%; *E. aerogenes*, 4.16, 6.45, 20.54 & 25.64%; *P. aeruginosa*, 17.05, 25.25, 33.04 & 39.53% and *Pseudomonas spp.*, 20.58, 30.23, 59.81 & 38.77%. None of the isolates of *H. aegyptius* and *H. influenzae* was resistant during the year 2002. However, there was slight increase (1.73%) in resistance of the former and fluctuation in the later (14.28, 1.58 & 11.11%) during the years 2003-2005.

## Discussion

There was a gradual increase in resistance from year 2002 to 2005 in most of the gram negative isolates i.e. *E. coli*, *K. pneumoniae*, *E. cloacae*, *E. aerogenes*, *P. aeruginosa* and

(<10%)<sup>20</sup> during the same time period which again can be attributed to variable prescription practices. Emergence of ciprofloxacin resistance in *H. aegyptius* and *H. influenzae* is also of concern. In 2002 none of these isolates was resistant like another study from Saudi Arabia,<sup>21</sup> however fluoroquinolone non-susceptible *H. influenzae* isolates are reported.<sup>22</sup> A high resistance (14.28%) in *H. influenzae* during the year 2004 is of particular concern.

During the time period lapsed after this study, ciprofloxacin resistance must have increased further as has been reported in a recent study where more than 80% of multidrug resistant gram negative rods were resistant to ciprofloxacin.<sup>10</sup> Our study shows that ciprofloxacin can no more be used as empirical therapy in infections due to *E. coli*, *K. pneumoniae*, *E. cloacae*, *E. aerogenes*, *P. aeruginosa* and *Pseudomonas spp.* It is essential that those concerned be alerted to the possibility of a trend towards further increased

resistance to ciprofloxacin, so that the judicious use of ciprofloxacin and its alternatives can be considered particularly in areas of high fluoroquinolone resistance rates like ours amongst gram-negative bacteria.<sup>23</sup>

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