ORIGINAL ARTICLE

Burden of extensively drug-resistant and pandrug-resistant Gram-negative bacteria at a tertiary-care centre

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Abstract

The emergence of resistance to multiple antimicrobial agents in Gram-negative bacteria is a significant threat to public health, as it restricts the armamentarium of the clinician against these infections. The aim of this study was to determine the burden of extensively drug-resistant (XDR) and pandrug-resistant (PDR) Gram-negative bacteria at a tertiary-care centre. Antimicrobial susceptibility testing of 1240 clinical isolates of Gram-negative bacteria obtained from various clinical samples during the study period was carried out by the Kirby-Bauer disc diffusion method. Minimum inhibitory concentration of all antibiotics including tigecycline and colistin was determined by Vitek-2 automated susceptibility testing system. Out of 1240 isolates of Gram-negative bacteria, 112 isolates (9%) were resistant to all the antibiotics tested by Kirby-Bauer disc diffusion method. This finding was corroborated by Vitek-2. In addition, Vitek-2 found that 67 isolates were resistant to all antibiotics except tigecycline and colistin. A total of 30 isolates were susceptible to only colistin, and four isolates were susceptible to only tigecycline. It was also found that six isolates (excluding five isolates of *Proteus* spp.) were resistant to both colistin and tigecycline. Thus, 101 (8.1%) out of 1240 isolates were XDR and 11 isolates (0.9%) were PDR. The findings of this study reveal increased burden of XDR and PDR Gram-negative bacteria in our centre. It also highlights the widespread dissemination of these bacteria in the community. This situation warrants the regular surveillance of antimicrobial resistance of Gram-negative bacteria and implementation of an efficient infection control program.

Keywords: Colistin, extensively drug-resistant (XDR), Gram-negative bacteria, pandrug-resistant (PDR), tigecycline, Vitek-2
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Introduction

Of late, the medical community worldwide has been witness to an increase in infections due to Gram-negative bacteria, which are resistant to many classes of antibiotics [1]. These infections are an important cause for prolonged hospitalization, leading to increased treatment costs and poor patient outcome in the form of increased morbidity and mortality [2]. These resistant pathogens were earlier considered to be primarily nosocomial pathogens, but it is now evident that they have spread to the community [3]. The emergence of resistance to multiple antimicrobial agents in pathogenic bacteria has become a significant threat to public health, as there are fewer, or sometimes even no, effective antimicrobial agents available for infections caused by these bacteria [4].

In the medical jargon to date, there is no consensus on the definitions and use of terms such as 'multidrug resistant' (MDR), 'extensively drug resistant' (XDR) and 'pandrug resistant' (PDR), which depict resistance in multidrug-resistant organisms [4]. A proposition for defining these resistant bacteria was discussed in a joint program by European Centre for Disease Prevention and Control (ECDC) and the US Centers for Disease Control and Prevention (CDC). They formulated few definitions and defined XDR bacteria as 'isolates being non-susceptible to at least one agent in all but 2 or fewer antimicrobial categories listed in the Clinical and Laboratory Standards Institute (CLSI) guidelines' and PDR bacteria as 'isolates

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being non-susceptible to all agents in all antimicrobial categories for each bacterium' [4].

This study was carried out with an aim to determine the burden of XDR and PDR Gram-negative bacteria at a tertiary-care centre in Pune, India.

Materials and methods

This study was carried out from July to September 2014 at a large tertiary-care centre. A total of 1240 nonrepetitive clinical isolates of Gram-negative bacteria were identified from various clinical specimens received in the microbiology laboratory with the help of conventional phenotypic methods.

Antimicrobial susceptibility testing was carried out by Kirby-Bauer disc diffusion method, and the results were interpreted according to CLSI guidelines [5].

Minimum inhibitory concentration (MIC) for all the isolates which were resistant to all the antibiotics by disc diffusion method was determined by Vitek-2 automated susceptibility testing method.

Results

A total of 1240 nonrepetitive clinical isolates of Gram-negative bacteria were identified by conventional phenotypic methods from various clinical samples received in the microbiology laboratory of a tertiary-care centre.

The most commonly isolated Gram-negative bacteria was *Escherichia coli* (625/1240), followed by *Klebsiella pneumoniae* (269/1240), *Pseudomonas aeruginosa* (172/1240), *Acinetobacter baumannii* (123/1240), *Proteus* spp. (40/1240), *Enterobacter* spp. (6/1240) and others (5/1240).

Out of these 1240 isolates of Gram-negative bacteria, 112 isolates (9%) were resistant to all the antibiotics tested by Kirby-Bauer disc diffusion method. The distribution of these resistant isolates is listed in Table 1. The most common isolate found to be resistant to all antibiotics tested was *P. aeruginosa,* followed by *K. pneumoniae, A. baumannii, E. coli* and *Proteus* spp.

The most common sample from which these 112 isolates were obtained was urine (37.5%), followed by wound swab/pus (22.3%), tracheal aspirates (17.9%), blood (7.1%), cerebrospinal fluid (7.1%), central line tip (4.5%) and other miscellaneous samples (3.6%). The sample-wise distribution of these resistant isolates is shown in Fig. 1.

The ward-wise distribution of isolates is shown in Fig. 2. Most of the resistant isolates were obtained from acute wards (42.9%) and intensive care units (ICUs) (29.5%), followed by other wards (23.2%) and the outpatient department (OPD) (4.4%).

TABLE 1. Species distribution of extensively resistant and pandrug-resistant Gram-negative bacteria by disc diffusion method (n = 112)

Sample	Organism	Total isolates	Resistant isolates	%
1.	*Escherichia coli*	625	18	2.9
2.	*Klebsiella pneumoniae*	269	32	11.9
3.	*Pseudomonas aeruginosa*	172	34	19.8
4.	*Acinetobacter baumannii*	123	19	15.4
5.	*Proteus* spp.	40	5	12.5
6.	*Enterobacter* spp.	6	2	33.3
7.	*Raoultella ornithinolytica*	1	1	100
8.	*Hafnia alvei*	1	1	100
9.	*Salmonella typhi*	1	—	—
10.	*Stenotrophomonas maltophilia*	1	—	—
11.	*Serratia marcescens*	1	—	—

MIC of all antibiotics was determined by Vitek-2 automated susceptibility testing system using GN-AST cards. It was found that 67 isolates were resistant to all antibiotics except tigecycline and colistin. A total of 30 isolates were susceptible to only colistin, of which 29 were *P. aeruginosa* and one was *A. baumannii.* Four isolates were susceptible to only tigecycline, out of which two were *K. pneumoniae* and two were *A. baumannii.* A total of six isolates were resistant to both colistin and tigecycline, out of which three were *P. aeruginosa,* two were *K. pneumoniae* and one was *Hafnia alvei.* As *Proteus* spp. are intrinsically resistant to tigecycline and colistin, testing for these antibiotics against *Proteus* spp. was not done by Vitek-2. Thus, 101 (8.1%) of 1240 isolates were XDR, and 11 isolates (0.9%) were PDR. The species distribution of XDR and PDR Gram-negative bacteria is shown in Table 2.

The most common sample from which PDR isolates were obtained was urine (6/11), followed by tracheal aspirate (3/11) and pus (2/11). These PDR isolates were mainly obtained from ICUs (6/11) and acute wards (5/11). No PDR isolate was obtained from other wards or OPD.

Discussion

Antimicrobial resistance is a worldwide problem that knows no international boundaries and can spread between continents [6]. Emergence of resistance to multiple antimicrobial agents in pathogenic bacteria has become a significant threat to public health, as there are fewer, or sometimes even no, effective antimicrobial agents available for infections caused by these bacteria [4]. Of late, terms such as 'multidrug resistance' have been used in medical literature to describe isolates of *Mycobacterium tuberculosis* resistant to rifampicin and isoniazid. A group of international experts came together in a joint initiative of the ECDC and CDC to deliberate and describe different patterns of resistance found in healthcare-associated,