



## OCCURRENCE OF GRAM-NEGATIVE BACTERIAL PATHOGENS THAT ARE MULTIDRUG-RESISTANT (MDR), EXTENSIVELY DRUG-RESISTANT (XDR), AND PAN-DRUG-RESISTANT (PDR) IN AN INDIAN TERTIARY CARE HOSPITAL

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### Abstract

**Background:** One of the top 10 worldwide public health hazards to humanity, according to WHO, is AMR. The main forces behind the spread of bacteria that are resistant to antibiotics are misuse and overuse of antibiotics. The goal of the current study was to create a successful antimicrobial stewardship programme for tertiary care hospitals establishing incidence of MDR, XDR and PDR.

**Materials and Methods:** This retrospective study was conducted from 1st January 2021 to 31st October 2022. Laboratory data were collected from the medical record section.

**Results:** Of the total clinical sample received 7633; pathogenic bacteria were isolated from 2422 [32%] clinical samples of which 1778 [23%] were gram-negative bacteria.

The most prevalent microorganism was *Escherichia coli* 768 [43%], followed by *Klebsiella pneumoniae* 474 [27%], *Pseudomonas aeruginosa* 238 [13%], and *Acinetobacter* spp. 91 [5%],

*Citrobacter* spp. 91 [5%], *Enterobacter* spp. 74 [4%], *Proteus* spp. 28 [2%]. 84 [5%] strains were Carbapenemase producers. 705 [40%] strains were ESBL producers predominantly from UTI and sepsis infections caused by *E. coli* and *Klebsiella pneumoniae*.

**Conclusion:** *E. coli* followed by *Klebsiella pneumoniae* were the most prevalent reported microorganisms. The rapid rise in MDR cases is regarding and accentuates the essentials for sustained surveillance, accurate diagnostic microbiological laboratory capacity, earlier diagnostic tests, and robust infection prevention and control.

**Keywords:** MDR, XDR, PDR, AMR, gram negative bacteria

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## 1. Background

WHO has declared that AMR is one of the top 10 global public health threats facing humanity. Misuse and overuse of antimicrobials are the foremost drivers in the progress of drug-resistant pathogens. AMR has been developed among pathogens isolated from urinary tract infections, sepsis, sexually transmitted infections, and some forms of diarrhea, signifying that we are running out of current antibiotics.<sup>1</sup> The current study was conducted to frame an active antimicrobial stewardship program in the tertiary care hospital. Standard criteria for multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan-drug-resistant (PDR) bacteria have been recommended by the European Centre for Disease Control (ECDC) and the Centres for Disease Control and Prevention (CDC), Atlanta. According to recommendations, acquired non-susceptibility to at least one agent in three or more antimicrobial groups constitutes multidrug resistance (MDR). Pan drug-resistant (PDR) is defined as being non-susceptible to all agents in all antimicrobial categories, whereas extensively drug-resistant (XDR) is defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories.<sup>2,3</sup> In order to determine the prevalence of MDR, XDR, and PDR bacterial isolates in a tertiary care hospital in Central India, this short-term study was started.

## 2. Materials and Methods

A waiver has been taken to conduct this study by the Institutional Ethics Committee. This study was conducted from patient samples that were collected for routine diagnostic purposes. We follow a blanket consent policy in our hospital for participation in the study and use of the patient data for research and educational purposes. No separate sample was collected for the study purpose.

### Study design:

This retrospective study was conducted from 1st January 2021 to 31st October 2022. Demographic and clinical data were collected from the medical record section. The bacterial strains isolated from clinical samples of urine and blood were identified by automated BD Phoenix.<sup>1</sup> The clinical specimens of urine and blood from indoor patient departments (IPD) along with ICU only were counted in the study. Identification and antibiotic susceptibility test of bacterial strains was done by automation bd phoenix [8] as per Clinical Laboratory Standard Institute

(CLSI) guidelines<sup>[9]</sup>. NMIC 500 ID and AST panel were used for Gram-negative bacilli (GNB) including antibiotics like amikacin, gentamicin, cefazolin, cefoxitin, ceftriaxone, cefuroxime, cefepime, ampicillin, piperacillin, tazobactam, aztreonam, cotrimoxazole, fosfomycin, nitrofurantoin, imipenem, meropenem, ertapenem, ciprofloxacin, levofloxacin, minocycline, tetracycline, ceftazidime, and colistin, respectively.<sup>4,5,6</sup> For routine Quality Control of antibiotic susceptibility test, *S. aureus* ATCC 25923, *E. coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853 were used. MDR, XDR, and PDR strains were identified as per criteria given by ECDC and CDC<sup>[1,2,7]</sup>. Extended Spectrum  $\beta$ -lactamases (ESBL) producing strains were detected by combined disk method using ceftazidime (30  $\mu$ g) and ceftazidime plus clavulanic acid (30  $\mu$ g plus 10  $\mu$ g) [10]. An increase in diameter of  $\geq 5$  mm with ceftazidime plus clavulanic acid as compared to ceftazidime disk alone was considered positive for ESBL detection. Carbapenemase producers given by bd phoenix were also confirmed by conventional methods.

## 3. Results

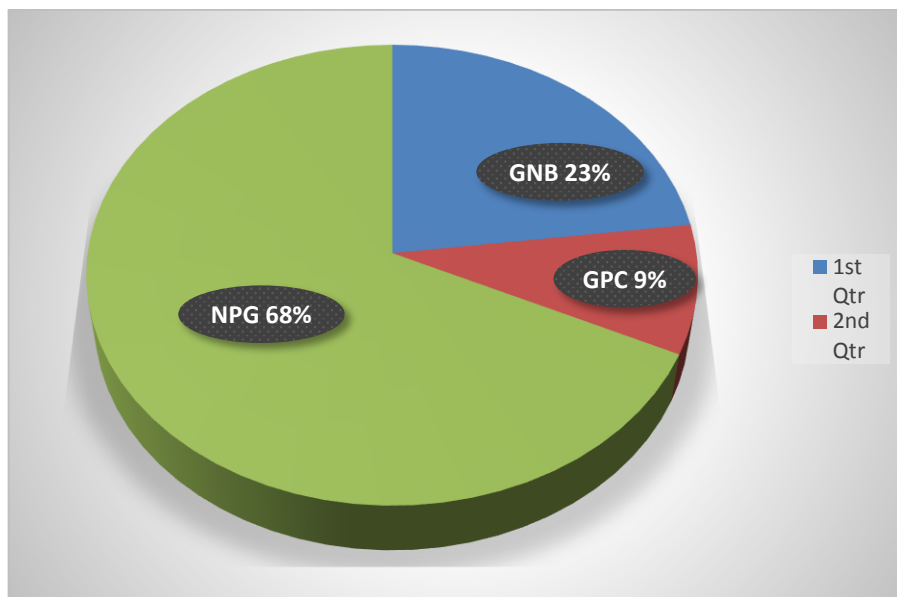
Of the total clinical sample received 7633; pathogenic bacteria were isolated from 2422 [32%] clinical samples of which 1778 [23%] were gram-negative bacteria.

The most prevalent microorganism was *Escherichia coli* 768 [43%], followed by *Klebsiella pneumoniae* 474 [27%], *Pseudomonas aeruginosa* 238 [13%], and *Acinetobacter* spp. 91 [5%],

*Citrobacter* spp. 91 [5%], *Enterobacter* spp. 74 [4%], *Proteus* spp. 28 [2%]. 84 [5%] strains were Carbapenemase producers. Predominantly, *E. coli*, *Klebsiella pneumoniae*, and *Acinetobacter* spp. were isolated from samples received from UTI and sepsis. 705 [40%] strains were ESBL producers largely from UTI and sepsis infections caused by *E. coli* and *Klebsiella pneumoniae*...

Around 74.2% of gram-negative bacteria were MDR, 16.70% were found to be XDR while PDR organisms were significantly low.

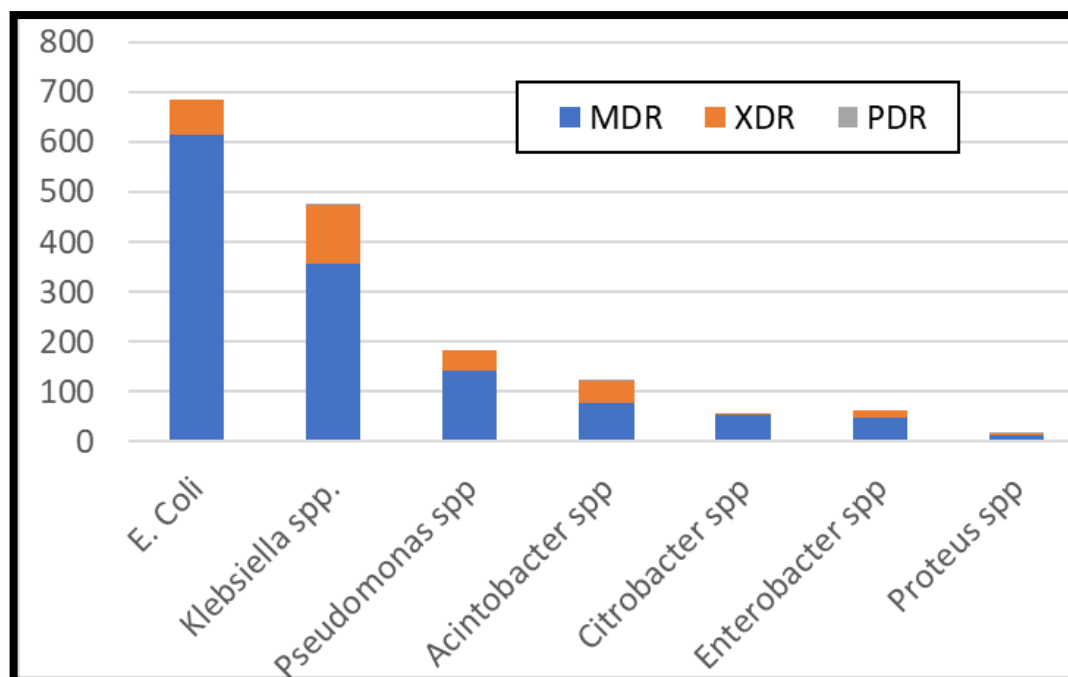
Incidence of Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) isolated (N=7633)



Total GNB =1778 (32%), Total GPC= 644 (9%), NPG= No Pathogen grown

Table -2 Proportion of MDR, XDR, and PDR among gram-negative clinical isolates of ICU and wards (n=1778)

bacteria	Total no	MDR	XDR	PDR
E. coli	768	615 (80%)	69 (9%)	0
Klebsiell spp.	474	355 (75%)	118 (25%)	3 (0.5%)
Pseudomonas spp	238	142 (60%)	42 (18%)	0
Acintobacter	91	77 (85%)	44 (49%)	4 (4%)
Citrobacter	91	54 (60%)	4 (5%)	0
Enterobacter	74	48 (65 %)	15 (32%)	0
Proteus	28	12 (45%)	5 (20%)	1 (4%)
other	14	2	0	0
total	1778	1321 (74.2%)	297 (16.70%)	8 (0.44%)



Bar diagram showing the proportion of MDR, XDR, and PDR among gram-negative clinical isolates of ICU and wards (n=1778) (n=1778)

#### 4. Discussion

MDR, PDR, and XDR bug infections were primarily seen in ICU patients. Patients who have protracted hospital stays, lengthy catheterizations, and central lines are constantly at danger of developing resistant illnesses.<sup>9,10,11,12,13,14</sup> MDROs continue to cause clinical and financial problems for patients and healthcare providers. The problem is that germs are building up resistance at a rate that is far faster than the new medicine that has been introduced to the market<sup>[15]</sup>. Concerning public health, MDROs are regarded as superbugs with a limited number of available treatments. According to Barbara Soule, Practise Leader for Infection Prevention and Control Services at Joint Commission Resources, "Patients who contract an infection with MDROs always have a higher risk of a protracted illness and fatality. When compared to patients who do not have an MDRO infection, the cost of care for such patients can be added. *E. coli*, *Klebsiella pneumoniae*, and *Acinetobacter* spp. were primarily isolated from samples of sepsis and UTI. The majority of the 705 [40%] strains that produced ESBLs came from *E. coli* and *Klebsiella pneumoniae*- and UTI-related sepsis illnesses. . Our findings complemented those of other studies. According to Hyun M and Lee JY, *E. coli* and *Klebsiella pneumoniae* were the two most common MDROs in their investigation<sup>[16]</sup>. Since there were more *E. coli* strains isolated overall (768) than there were *Klebsiella pneumoniae* strains, the percentage of MDR *E. coli* bacteria was higher in this investigation. In our study, there was a somewhat greater frequency of medication resistance than in a similar study conducted in a tertiary care hospital, where people from different socioeconomic strata visit for medical care. Most individuals receive medication with incorrect dosages without seeking guidance from medical professionals. The short duration of the experiment and involvement of only one centre at a tertiary institution make this study limited. . A multicenter study involving all types of healthcare facilities for at least a year would be necessary to reflect the trend of illnesses brought on by MDR, XDR, and PDR strains of bacteria in the area. There is a dearth of information about MDR, XDR, and PDR in healthcare systems around the world, including India. Until and unless antibiotic resistance is diagnosed along with its incidence, the strategies for controlling antibiotic resistance cannot be properly applied in the healthcare system. Drug restrictions must be applied strictly in order to prevent antibiotic abuse, overuse, and over-the-counter sales. Following that, it is imperative to conduct screenings, monitor antibiotic use, and prevent the spread of MDROs by adhering to accepted infection control practises.

#### 5. Conclusion

The most common microbes found were *Klebsiella pneumoniae* and *E. coli*, respectively. The sharp increase in MDR cases highlights the need for effective infection prevention and control, accurate diagnostic microbiological laboratory capacity, earlier diagnostic testing, and ongoing surveillance. In order to minimise the threat of antimicrobial resistance, which is a current global concern, we hereby accomplish that time finding and careful checking of MDR, XDR, or even PDR bacterial strains must be implemented by all clinical microbiology laboratories.

**Conflict of Interests:** The publication of this paper does not include any conflicts of interest.

**Finances:** Neither internal nor external funding was provided for this study. Data have been produced as part of an organization's everyday operations.

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