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Original Research Article

Incidence density rate of multidrug-resistant organism (MDRO) at a tertiary care teaching hospital: A retrospective cross-sectional study

Rupal Patel[1]*, **Pinal Joshi**[1], **Naimika Patel**[1], **Chirag Modi**[1]

[1]*Dept. of Microbiology, Pramukhswami Medical College, Bhaikaka University, Anand, Gujarat, India*

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ABSTRACT

Background: Multidrug-resistant organisms (MDROs) has become a major public health concern. Rise of MDROs and their negative consequences on patient's survival and health care costs need the assessment of their burden and implementation of practices to control their emergence and spread. There is a lack of literature mentioning incidence density rates (IDR) of various MDRO infections in Indian hospitals. Therefore, the study was conducted to determine the infection IDR and trend of various MDROs at a tertiary care teaching hospital. It will serve as a benchmark data for similar facilities using the same surveillance definitions and methodology.

Materials and Methods: A retrospective cross-sectional study was conducted using culture data of ten years (January 2014 to December 2023) at Shree Krishna Hospital, Karamsad. MDRO studied included Methicillin-resistant *Staphylococcus aureus* (MRSA), V*ancomycin-resistant Enterococci* (VRE), *Carbapenem-resistant Enterobacterales* (CRE), Multidrug-resistant (MDR) *Acinetobacter* spp. and MDR *Pseudomonas aeruginosa*.

Results: A total of 7311 MDRO were detected from 1321793 in-patients, showing the overall IDR of 5.53 per 1000 patients-days. CRE (n = 3056, 42%) was the most common MDRO. The overall IDR per 1000 patient-days of MRSA, VRE, CRE, MDR- *Acinetobacter spp*., and MDR- *P. aeruginosa* was 0.81, 0.23, 2.31, 1.29 and 0.89 respectively. Overall MDRO IDR has increased from 4.20 to 8.77 from 2014 to 2023. An increasing IDR was observed for MRSA (0.57 to 1.48) and MDR- *P. aeruginosa* (0.43 to 1.60). Around 80% of the *Acinetobacter spp*. were MDR as compared to other MDRO.

Conclusions: MDROs have been identified as a significant problem at our institute showing an increasing trend. We recommend following stringent infection control practices including isolation protocols as well as adherence to hospital antibiotic policy to reduce the burden of MDROs.

1. Introduction

MDROs are defined as microorganisms that are non-susceptible to one or more classes of antimicrobial agents. As per WHO, carbapenem-resistant *Acinetobacter baumannii* (CRAB) and *Pseudomonas aeruginosa*, third-generation or carbapenem-resistant *Enterobacteriaceae*, vancomycin-resistant *Enterococcus* spp. and methicillin-resistant *Staphylococcus aureus* organisms are critical and needs urgent attention.[1,2] MDROs infections are more commonly seen in critically ill patients with prior antimicrobial exposure or who have comorbidities that lead to poor clinical outcomes and death.[3] Also many infants in the country are now born with infections caused by resistant strains and these greatly increased infant mortality rates. The Center for Disease Dynamics, Economics and Policy (CDDEP) reported that amongst MDROs, MRSA is rapidly rising worldwide.[4,5] In India, prevalence of MDROs ranges

* *Corresponding author*.
E-mail address: drrplpatelmp@gmail.com (R. Patel).

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from 30% to 60%.[6] Prevalence of extended-spectrum beta-lactamase (ESBL) gram-negative bacilli (GNB) ranges from 19% to 60% and carbapenem-resistant GNB ranges from 5.3% to 59%.[7] With a limited treatment options for MDRO, concerns for these infections are increasing and MDRO infections often lead to increased length of stay, costs, and mortality. It is a global health problem that requires urgent action for effective antimicrobial stewardship interventions.[1,2] Without adherence to recommendations for hand hygiene and use of gloves, health care personnel (HCP) transmit MDROs to patients in great extent. Thus, strategies to increase adherence to standard precautions and monitor the trends are identified as important components of MDRO control programs. Preventing infections will reduce the burden of MDROs in healthcare settings.[2]

There is a lack of screening and reporting for MDRO infections in Indian hospitals. Therefore, the objective of the present study was to determine the MDRO infection incidence density rate (IDR) and trend of MDRO infections at our hospital. It will also provide a benchmark for similar facilities using the same surveillance definitions and methodology.

2. Materials and Methods

The study was conducted after the approval of the Institutional Ethics Committee. This was a retrospective cross-sectional study, carried out at the Microbiology laboratory of Central Diagnostic Laboratory (CDL), an NABL-accredited laboratory of Shree Krishna Hospital and Pramukhswami Medical College, Bhaikaka University, Karamsad. The culture data from January 2014 to December 2023 was analyzed to determine the MDRO IDR per1000 patient-days and trend of MDRO infections which included *Methicillin-resistant Staphylococcus aureus* (MRSA), V*ancomycin-resistant Enterococci* (VRE), *Carbapenem-resistant Enterobacterales* (CRE), Multidrug-resistant (MDR) *Acinetobacter* spp. and MDR *Pseudomonas aeruginosa*. All clinical isolates from all age groups were included in the study. Participants in whom the same isolates were previously isolated from culture and were suggestive of persistent infection were excluded from the study.

All the clinical specimens such as urine, sputum, endotracheal & tracheal aspirate, broncho-alveolar lavage, pus, blood, and sterile body fluids (pleural fluid, cerebrospinal fluid, ascitic fluid etc..) received for culture and antimicrobial susceptibility test were processed as per the standard protocol. Conventional culture methods and the BacT/ALERT® 3D Microbial Detection System (BioMerieux, France) were used and the isolates were processed for identification and antimicrobial susceptibility tests by the Vitek 2 Compact system (BioMerieux, France) as per the CLSI guidelines.[8]

The following definitions were used to consider MDRO and were calculated per 1000 patients-days.[9]

1. MRSA: *Staphylococcus aureus* cultured from any specimen that tested oxacillin-resistant, cefoxitin-resistant, or methicillin-resistant by standard susceptibility testing methods were considered as MRSA.
2. VRE: *Enterococcus faecalis, Enterococcus faecium*, or *Enterococcus spp*. that was resistant to vancomycin, by standard susceptibility testing methods were considered as VRE.
3. CRE: *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Klebsiella aerogens* or *Enterobacter spp*. resistant to imipenem, meropenem, doripenem, ertapenem by standard susceptibility testing methods were considered as CRE.
4. MDR-*Acinetobacter spp*. & MDR *Pseudomonas aeruginosa (P. aeruginosa): Acinetobacter spp*. & *P. aeruginosa* isolates non-susceptible (specifically, either resistant or intermediate) to at least one agent in at least 3 antimicrobial classes of the following 6 antimicrobial classes: Aminoglycosides (Amikacin, Gentamicin, Tobramycin) Carbapenems (Imipenem Meropenem Doripenem), Fluoroquinolones (Ciprofloxacin, Levofloxacin), β-lactam/β-lactam β-lactamase inhibitor combination (Piperacillin-tazobactam), Cephalosporins (Cefepime, Ceftazidime, Cefoxitin, Ceftriaxone), Sulbactam (Ampicillin-sulbactam) were considered as MDR- *Acinetobacter* & MDR *P. aeruginosa*.
5. Overall MDRO IDR (cases/per 1000 patient-days) = Total MDRO during the observation period / total numbers of inpatient days during the observation period *1000. Similarly, IDR of MRSA, VRE, CRE, MDR-*Acinetobacter spp*. & MDR *P. aeruginosa* was calculated per 1000 patient-days.

2.1. Data collection and analysis

The data of all culture-positive samples from which MDRO has been isolated was collected from the Laboratory & hospital information system. Data were analyzed using Microsoft® Excel for Mac version 16.79.2 (23112723).

3. Results

A total of 7311 MDRO were detected from 1321793 in-patients, showing the overall IDR of 5.53 per 1000 patients-days. CRE (n = 3056, 42%) was the most common MDRO (Figure 1). The overall IDR per 1000 patient-days of MRSA, VRE, CRE, MDR- *Acinetobacter spp*., and MDR-*P. aeruginosa* has been shown in Table 1. Overall MDRO IDR has increased from 4.20 to 8.77 from 2014 to 2023 (Figure 2). An increasing IDR was observed for MRSA and MDR- *P. aeruginosa* isolates (Figures 3, 4, 5, 6 and 7). As

per Figure 6, around 80% of the *Acinetobacter spp*. were MDR as compared to other MDRO.

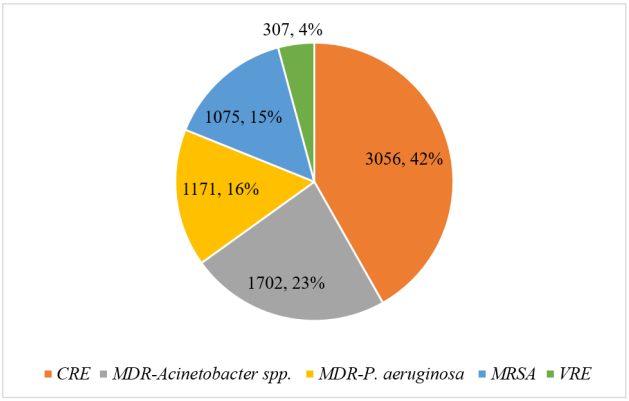

Figure 1: % Distribution of various MDRO (n=7311)

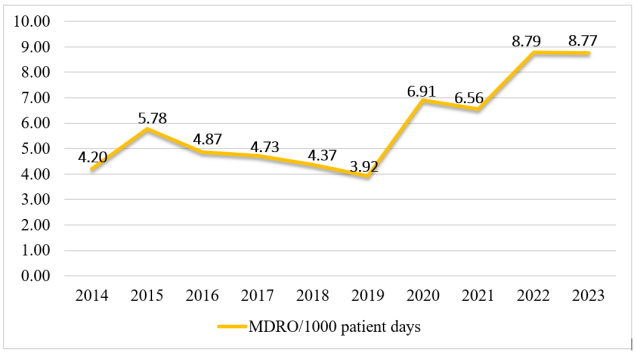

Figure 2: Year-wise trend of MDRO/1000 patient-days

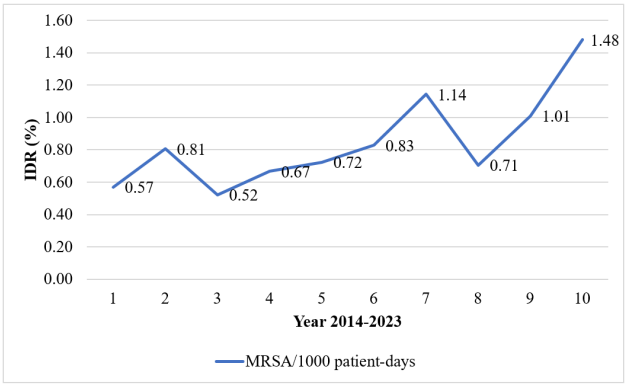

Figure 3: Year-wise trend of MRSA

4. Discussion

Globally, it has been observed that infections caused by antimicrobial-resistant organisms is emerging nowadays. It represents a serious health problem for both healthcare

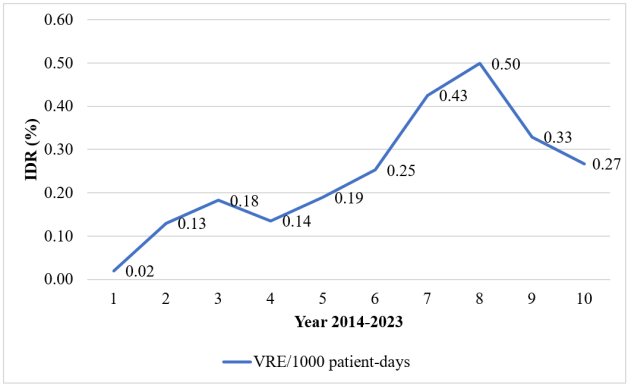

Figure 4: Year-wise trend of VRE

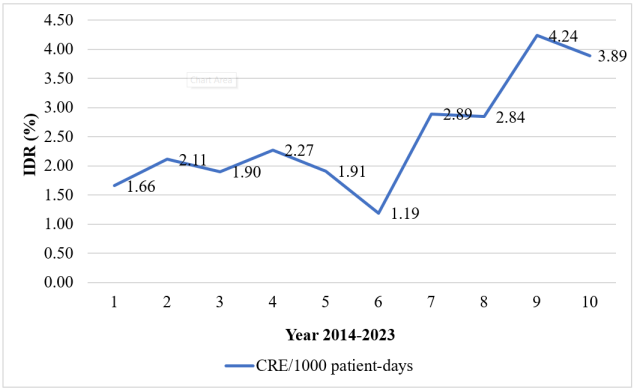

Figure 5: Year-wise trend of CRE

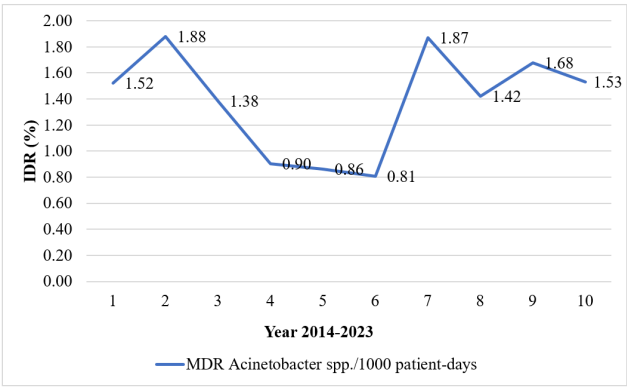

Figure 6: Year-wise trend of MDR *Acinetobacter spp.*

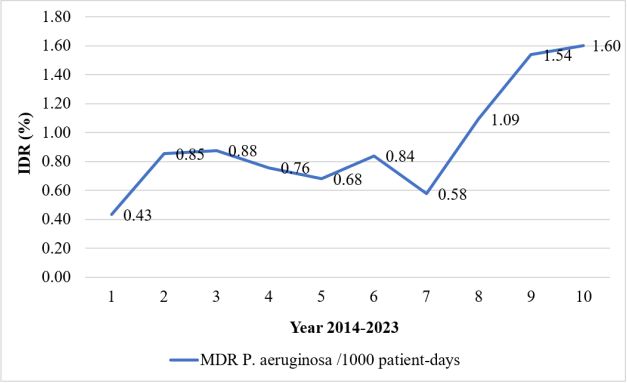

Figure 7: Year-wise trend of MDR *P. aeruginosa*

Table 1: Overall incidence density rate (IDR) of MDROs per 1000 patient-days (2014-2023)

Type of MDROs	Overall incidence density rate (IDR)
Methicillin-resistant Staphylococcus aureus (MRSA)	0.81
Vancomycin-resistant Enterococcus spp. (VRE)	0.23
Carbapenem-resistant Enterobacterales (CRE)	2.31
MDR - *Acinetobacter spp.*	1.29
MDR - *P. aeruginosa*	0.89

practitioners and patients. There are various risk factors for acquiring infection with MDROs such as lack of knowledge regarding organisms and their antimicrobial susceptibility pattern, rampant use of unreasonable fixed drug combinations, long-term use of antimicrobial therapy, poor infection control practices, prolonged length of hospital stay, invasive procedures, and colonization. MDR bacteria can cause various types of infections such as pneumonia, urinary tract, wound infections, and septicemia and are associated with an increase in mortality and morbidity.[5,10–12] One large, multicentre observative cohort study provided data on the morbidity & mortality of healthcare associated infections (HAIs) with multidrug-resistant bacteria in Germany and found that 1.6 per 1000 patients suffered a HAI with an MDRO and 0.1 per 1000 patients died as a result of it.[13] Therefore, monitoring incidence density rate & trend analysis of various MDROs is important for the control of infection and for implementing the institutional antimicrobial stewardship program in India.

In the present study, overall MDRO infection IDR was 5.53 per 1000 patient-days which was lower than the published studies where MDRO were detected in 26,499 of all in-patients (37.1 per 1000 in-patients).[13] In our study, Hospital acquired (HAI) MDRO infection rate has not been analyzed separately. However, published studies mention varied rates of HAI MDRO infection IDR ranging from 0.97 - 4.8 per 1000 in-patients.[13–15] Prevalence of CRE was most common followed by MDR- *Acinetobacter spp.* in the present study. Similar to this, Carbapenem resistant *Klebsiella pneumoniae* (CRKP) was responsible for 35.40% of HAIs caused by MDROs.[15]

4.1. MRSA

During the study period, we observed increase in the IDR of MRSA from 0.57 to 1.48 per 1000 patient-days. However, it is lower than the findings of the study where overall MRSA colonization and/or infection was 16.5/1000 patients-days and 0.5/1000 patient-days for HAI MRSA.[13] Contrary to this, a recent study reported an overall stable and rather decreasing MRSA IDR in both ICU & non-ICU settings indicating geographic disparities, variations and complex factors influencing MRSA rates.[16] Published studies across India shows that the trend of MRSA is increasing from 26.14% to 85%.[2,6,17] The variations in prevalence could be due to different geographical areas, and the study methodology. A surveillance study conducted by Wattal et al, reported that the prevalence of MRSA was 78% in their study. It could be because of the high usage of cephalosporins and quinolones.[2] Lohan et al, found the prevalence of MRSA rising from 28% to 35.1% among patients undergoing surgery followed by admission to ICUs. This increasing trend is due to the carriage of MRSA by HCWs & patients, use of indwelling devices, diversity in mecA gene, poor compliance to hand hygiene, lack of surveillance and lack of compliance to care bundle.[17] However, the risk factors for acquiring the MRSA were not analyzed in the present study.

4.2. VRE

In the present study, IDR of VRE isolates has increased from 0.02 to 0.27 per 1000 patient-days at our institute. However, it is lower than the findings of the study where overall VRE colonization and/or infection was 6.3/1000 patients-days.[13] A recent study reported increase in VRE rates from 0.25 to 0.63 per 1000 patient-days. Disruption of certain infection control measures and inappropriate use of vancomycin and third-generation cephalosporins may contribute to this phenomenan.[16] Similar to our findings, a published study mentioned the prevalence of VRE from 0.4% to 35.5% around the world.[10,17] In Asian regions, the prevalence rate of VRE ranges from 1% to 27.70% including in India.[17,18] Such high prevalence could be due to, organisms being transmitted to humans through animal food as well as the fecal-oral route through contaminated water and food as many mammals and birds have reservoirs of enterococci, exposure to the broad-spectrum antibiotic, length of hospital stays, and a breach in hospital infection control.[2,18]

4.3. CRE

Carbapenems are used to treat infections caused by ESBL-producing organisms. A new class of carbapenemases emerged in 1996.[2] The increased prevalence of CRE has been associated with high mortality and is a global public health problem.[19] In the present study, IDR of CRE isolates increased from 1.66 to 3.89 per 1000 patient-days and were the most common MDRO at our institute. Similar to our findings, incidence of CRE has increased in published studies.[6,16,19] However, lower carbapenem resistance has also been reported by a published study due to adherence to hospital antibiotics stewardship programme.[20]

4.4. MDR- Acinetobacter spp.

Hospital-acquired & community-acquired infection caused by *Acinetobacter baumannii* is a major challenge to the healthcare system as this organism is becoming resistant to a large group of antibiotics although some strains show resistance to all antibiotics and contribute to increased morbidity and mortality.[21,22] Many outbreaks were reported globally by the MDR strain of *Acinetobacter spp*. As per the CDC report of 2013, each year approximately 7000 infections and 500 deaths are caused by MDR *Acinetobacter*. Infections caused by carbapenem-resistant strains have been associated with high death rates.[23] The prevalence of MDR *Acinetobacter spp*. from 29% up to 74% was mentioned by different published studies.[22,23] A recent study also observed that ICU & Non-ICU had very significant increases in CRAB BSI IDR. The global rise in CRAB during the pandemic is a matter of concern.[16] However, we didn't observe any change in the trend in MDR *Acinetobacter spp*. (1.52 to 1.53 per 1000 patient-days) during the present study. Around 80% of the *Acinetobacter spp*. were MDR as compared to other MDRO in the present study. Similar to this, *A. baumanni* isolates detected during the study period were almost resistant to all the drugs being tested.[14]

4.5. MDR- P. aeruginosa

In the US, published data suggest that 13 - 19% of hospital-acquired infections were caused by MDR- *P. aeruginosa* each year amongst them the estimated mortality was 46.1%. In the present study, we found that the IDR of MDR- *P. aeruginosa* increased from 0.43 to 1.60 per 1000 patient-days**.** Similar to this, a significant increase (187%) in carbapenem-resistant *P. aeruginosa* (CRPA) BSI IDR was observed in non-ICU during the study period.[16] Concordance to our findings, published studies show that the rate of MDR- *P. aeruginosa* has increased in the U.S (4 to 14%), and Italy (2.1 to 4.1%).[24] Other published studies showed a very high prevalence of 76.8% MDR- *P. aeruginosa* in burns patients which is a cause of concern.[25] Whereas the low prevalence, 9%, 14% & 19.5%, of MDR- *P. aeruginosa* was also mentioned by published studies.[6,10,26]

As the spread of MDRO is the biggest threat, urgent drug-resistant bacterial countermeasures are needed. Among the drug-resistant bacteria, CRE and CRAB are some of the most important drug-resistant bacteria to deal with, and the outline of the infectious diseases caused by such bacteria will be useful for their control in future.[27] To prevent of spread of MDRO, contact precautions, single room isolation and dedicated specific staff should be given a consideration to patients with multiple drug-resistant organisms (MDROs) in ICUs. However, isolation and cohorting strategies cannot be implemented in all cases; especially in open-plan ICUs.[28] One semi-experimental study found that the comprehensive multi-model strategies including behavioral aspects of health care personnel, continual training programs, regular feedback, and environment control reduced the incidence of HAIs and the HAIs caused by MDROs in rehabilitation units.[15] One Health approach, as defined by the World Health Organization, is the strategy that involves the collaboration of multiple sectors to improve public health outcomes. Whole-genome sequencing (WGS) studies can be a useful tool for understand the spreading dynamics of MDRO and can help in limiting their spread. The analysis of resistome and virulome by WGS, can help the infection control team to strengthen the surveillance mechanisms.[29]

Our study is one of the very few studies to establish infection incidence density rates & trends of various MDRO among inpatients in a tertiary care hospital. There are some limitations of our study. Being a retrospective study, we couldn't study location-wise and organism-wise distribution of MDRO which might have been useful in taking site-specific appropriate infection control measures to prevent the spread of such organisms.

5. Conclusions

MDROs have been identified as a significant problem at our institute showing an increasing trend. We recommend following stringent infection control practices including isolation protocols as well as adherence to hospital antibiotic policy to reduce the burden of MDROs.

6. Author Contributions

Authors have made substantial contributions to the conception, design of the work, the acquisition, analysis & interpretation of the data and drafting the work and substantively revising it. All authors have met the ICMJE's requirements for authorship. The paper represents their honest efforts, and that they are able to independently validate the accuracy of the data presented.

7. Sources of Funding

None.

8. Data Availability Statement

The study did not report any data.

9. Conflicts of Interest

The authors declare no conflicts of interest.

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Author biography

Rupal Patel, Professor https://orcid.org/0000-0003-4809-5494

Pinal Joshi, Ex. Resident Doctor

Naimika Patel, Assistant Professor https://orcid.org/0000-0002-7579-3135

Chirag Modi, Professor https://orcid.org/0000-0002-2281-9573

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