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INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals

ISSN 2349-7203



Human Journals

Research Article

July 2022 Vol.:24, Issue:4

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Surveillance of Multi-Drug Resistant Bacteria Over 3 Years in the Nephrology Department of a Tertiary Care Hospital, India: A Cross-Sectional Study



IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
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ISSN 2349-7203

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Submitted: 24 June 2022
Accepted: 29 June 2022
Published: 30 July 2022

Keywords: Multi-drug resistant bacteria, Antimicrobial resistance, Infections, Gram-positive bacteria, Gram-negative bacteria

ABSTRACT

Antimicrobial resistance has become a challenge in modern-day medical practice and poses a significant risk to both the patient and public health as a whole. Surveillance of multi-drug resistant bacteria in a healthcare setting is a necessity to have an optimum treatment outcome and less of treatment failures. Antibiotic misuse and overuse resulted in an increased incidence of MDR bacteria. Our aim was to study the prevalence, distribution, and antimicrobial susceptibility pattern of MDR bacteria in patients admitted to the Nephrology department from a tertiary hospital in India. The cross-sectional study was conducted in the department of Nephrology of a tertiary care hospital in South India, and carried out in in-patients in whom culture test were done. Among the 246 patients with culture isolated, we found out a higher rate for MDR organisms with 82.11% (n=202). An increasing trend of resistance from 77.45% in 2018 to 88.46% in 2020 was observed during the 3 consecutive years. Multi-drug resistance was more prevalent in Gram-negative organisms (82.44%) and also MDR infections have shown a more chance for causing mortality. MDR infections are associated with increased socioeconomic burden due to increased need for treatment and observed increased mortality. So strategies like Antibiotic Stewardship and continuous surveillance should be done to control the phenomenon.



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INTRODUCTION

Over the last decade, the incidence of severe infections with antibacterial-resistant Gram-positive and Gram-negative bacteria has increased, and these infections now pose a serious threat to global public health. Infections with MDR strains are associated with increased morbidity and mortality, and extended length of hospital stay¹. The irrational use of antibiotics in the day to day life has led to the emergence of MDR organisms. It is also associated with an increased financial burden on patients. Identifying the clinical characteristics, prevalence and distribution of infections caused by MDR bacteria is essential for effective treatment².

MECHANISM OF ANTIBIOTIC RESISTANCE

Antibiotic resistance occurs when potentially harmful bacteria change in such a way that the effectiveness of the antibiotic is canceled or diminished³. The antibiotic resistance mechanism of most bacteria is acquired by altering the target gene. These encoded genes can lead to lytic enzyme production, altered membrane permeability, efflux action, and concealment from antibiotic effects. According to the Centers for Disease Control and Prevention (CDC), antibiotic resistance is responsible for about 2 billion infectious diseases and more than 20,000 deaths, costing \$ 55 billion annually in the United States⁴.

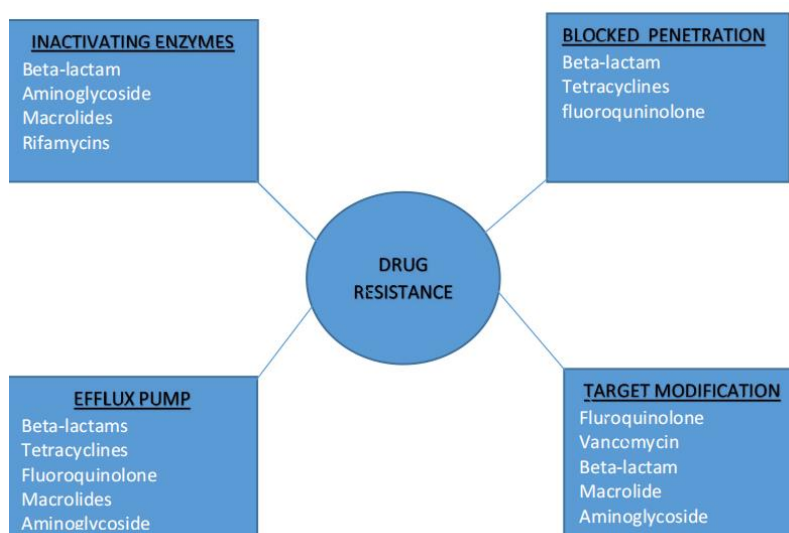


Figure No. 1: Mechanism of Antibiotic Resistance

Gram-positive and Gram-negative bacteria are ubiquitous but pose a unique threat to in-patients with weak immunity. Gram-positive bacteria cause major problems and are the focus of many eradication efforts, but Gram-negative bacteria are now classified as a more serious threat by the CDC because they are developing dangerous resistance⁵. Gram-negative bacteria that are often associated with antibiotic resistance include *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Acinetobacter baumani*, and *Enterobacter* species. The most common Gram-positive bacteria found include MRSA, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Staphylococcus hemolyticus*¹.

RISK FACTORS

Risk factors associated with infection with the MDR pathogen (including the MDRGNB and ESKAPE groups) include age, gender, current hospital stay for 5 days, and previous antibiotic therapy (last month before the current infection), but not in the last 3 months), patient comorbidities (CKD, chronic respiratory illness, CHF, cancer, diabetes requiring insulin therapy or oral anti-diabetes before infection, myocardial infarction) and general medical conditions⁶.



CONTRIBUTING FACTORS

Factors that contributed to the persistence and spread of MDR Gram-negative and gram-positive infections include:

- Misuse of the existing antimicrobial agents in the population. This has led to the development of an adaptive mechanism for bacterial resistance.
- Lack of good infection control practices.
- Lack of good antibiotic stewardship programme, including the use of multiple broad-spectrum drugs, helped maintain a cycle of increased resistance¹.

The effects of multidrug-resistant infections can be determined by analyzing clinical outcomes, hospital mortality, and length of ICU or length of hospitalization⁷. Rates of resistance are much higher in critically ill patients. Multidrug resistance further increases the risk of death due to sepsis⁸. The emergence of infections by these organisms and increased drug resistance among them requires careful monitoring of the antimicrobial susceptibility profiles of these organisms⁹. The study aimed to determine the prevalence and change in

pattern of MDR organisms in association with the epidemiology features in nephrology department. Thus surveillance of antimicrobial susceptibility is fundamental to combat the emergence of resistance.

METHODOLOGY

This is a cross-sectional study done from records of adult patients who have come to the Nephrology department during 2018-2020 and it was a retrospective analysis for 6 months. This study was conducted at the Department of Nephrology and Microbiology at Kochi Lourdes Hospital, a tertiary care hospital. Patient data was gathered retrospectively, in which the demographics of the patient, reason for admission, lab parameters, culture and sensitivity reports, antibiotics prescribed and outcomes of therapy were included in a specially designed data collection form. The collected data was compiled in Microsoft Excel and displayed in tables and graphs. The data were tabulated, analyzed and compared to related studies. Multi-drug resistant organisms have been described as having *in vitro* resistance to more than one antimicrobial tested. Data were reviewed for obtaining the resistance trends, frequency and prevalence of MDR organisms.

RESULTS AND DISCUSSION

In our study, during the study period, 246 patients from the Nephrology department whose culture and sensitivity test done were taken and assessed. The total patients were distributed as 102 in 2018, 75 in 2019 and 69 in 2020. Among them, a significantly higher number of isolates were found to be multi-drug resistant, representing 82.11% (n=202).

MDR ORGANISMS

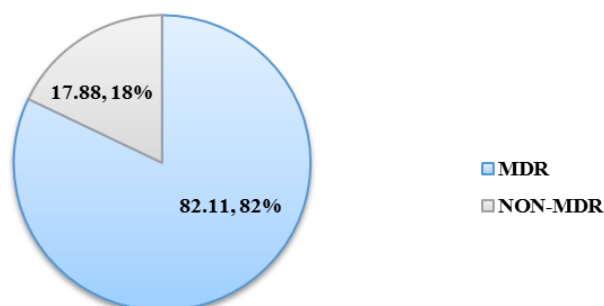


Figure No. 2: MDR and Non-MDR Organisms Isolated in 3 Years

Guobin Su *et al* in 2018 identified in their study that patients with impaired renal functions had high risk for acquiring MDR infections¹⁰.

The location wise analysis showed that MDR organisms were mostly seen in wards (57.42%) than ICU (42.57%). Age wise distribution of MDR organisms showed that they were frequently isolated in all age categories and among them, the highest MDR isolates were seen in 28-37 age category with 88.88% and lowest with 18-27 year group with 78.57%. All the age categories and MDR organisms found are represented in Figure 3.

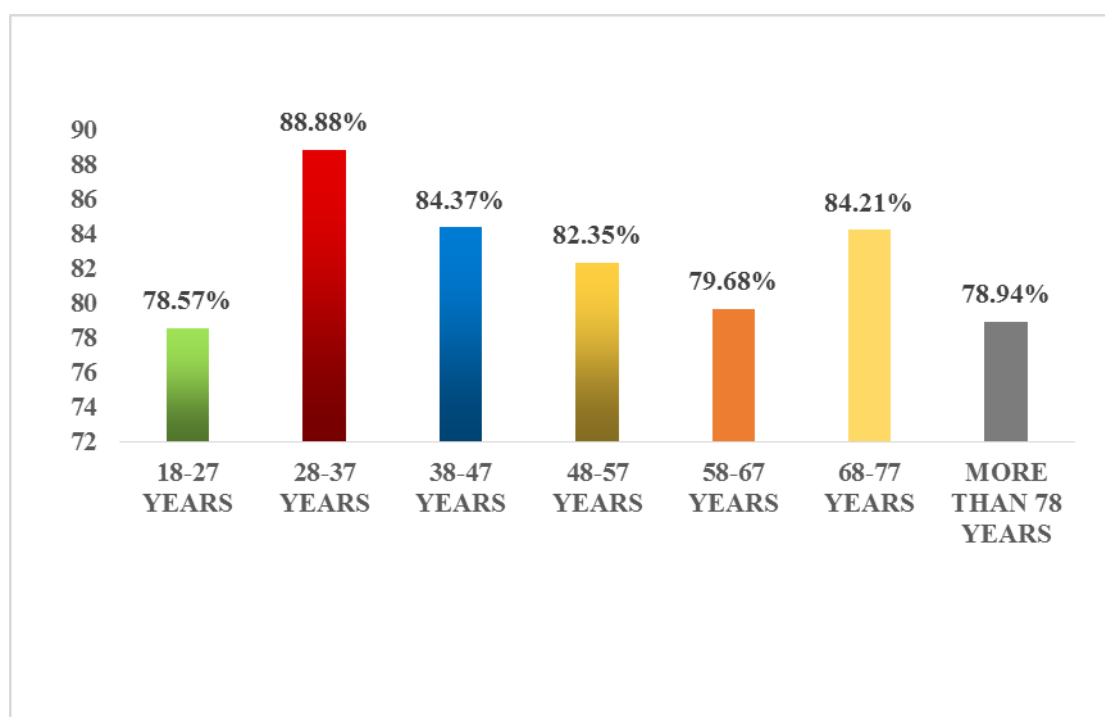


Figure No. 3: Age Wise Distribution of MDR Organisms

In the 3 years under consideration (2018-2020), an increasing trend of resistance were seen with 77.45% (n=79), 82.66% (n=62) and 88.4% (n=61) MDR organism infections in 2018, 2019 and 2020 respectively.

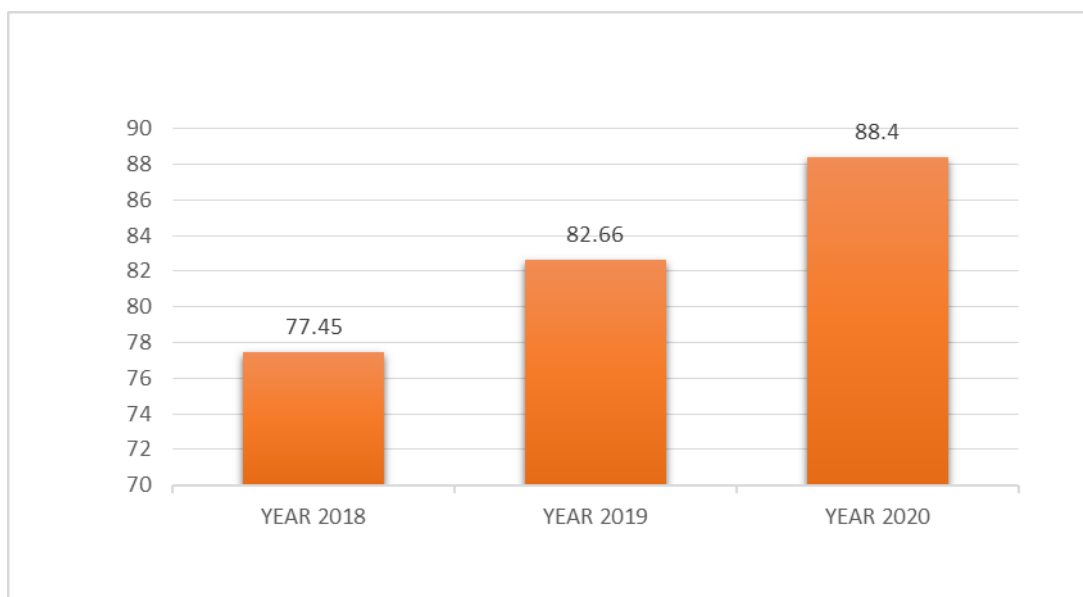


Figure No. 4: Year Wise Isolation of MDR Organisms

In a similar 10 year pattern study of MDR organisms conducted by Giammanco *et al* in 2017, 23%-63% increase in multi-drug resistance of Gram-negative organisms was observed¹¹.

MDR Gram Positive and Gram Negative Organisms

Among the gram negative organisms (n=188), 82.44% (n=155) were found as MDR organisms and among the gram positive organism (n=58), 81.03% (n=47) were multidrug-resistant. By analyzing the cumulative results, gram negative organisms have shown more multidrug resistance than that of gram positive isolates.

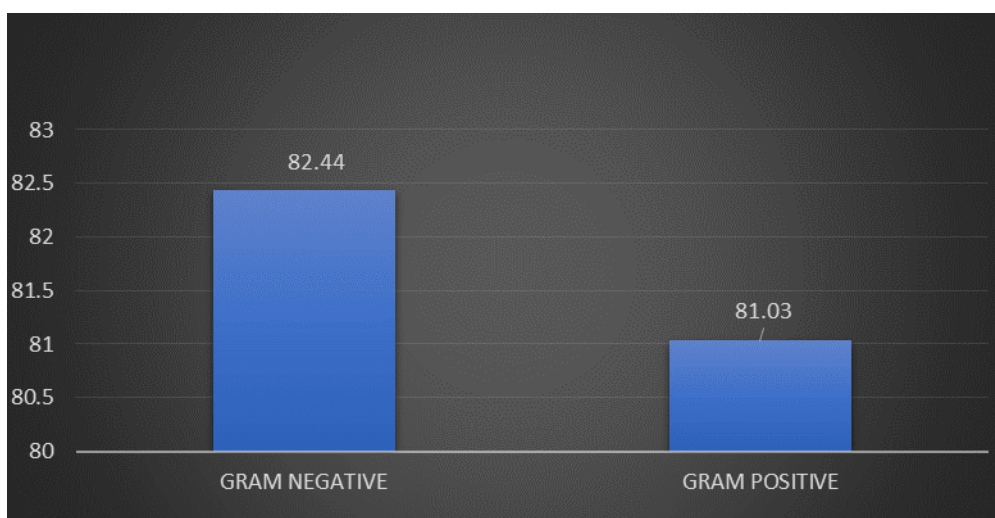


Figure No. 5: Gram-Positive and Gram-Negative MDR Organisms

Our findings were similar to that conducted by Vasudevan *et al* in 2014, showing increase in resistance among Gram-negative bacteria¹².

Organism Wise Multi-drug Resistance

In our study, 23 different organisms were isolated and the major and frequently isolated were *E. coli* (21.16%), followed by *Klebsiella pneumoniae* (15.87%) and then *Pseudomonas aeruginosa* (6.12%). Rate of MDR isolates obtained for different organisms are depicted in Table 1.

In case of *Staphylococcus aureus* (MRSA), *Enterococcus faecium*, *Elizabethkingia meningoseptica*, *Staphylococcus haemolyticus*, *Enterobacter aerogenes*, *Enterobacter cloacae* ssp *cloacae*, Enterococci, *Proteus mirabilis*, *Acinetobacter junii*, *Klebsiella pneumoniae* spp *ozaenae*, Methicillin resistant *Staphylococcus epidermidis*, *Shewanella putrefaciens* and *Streptococcus pyogenes*, all the obtained isolates were found to be multidrug resistant (100%).

Analysis of major organisms like *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Staphylococcus epidermidis* shown that 93.42%, 89.47%, 42.85%, 42.85%, and 91.66% of respective isolates shown multi-drug resistance. Least MDR isolates were obtained for *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Table No. 1: MDR Isolates of Different Organisms

ORGANISMS	MDR ISOLATES (in %)
<i>ESCHERICHIA COLI</i>	93.42
<i>KLEBSIELLA PNEUMONIAE</i>	89.47
<i>STAPHYLOCOCCUS EPIDERMIDIS</i>	91.66
<i>STAPHYLOCOCCUS AUREUS</i> (MRSA)	100
<i>PSEUDOMONAS AERUGINOSA</i>	42.85
<i>STAPHYLOCOCCUS AUREUS</i>	42.85
<i>ENTEROCOCCUS FAECIUM</i>	100
<i>ELIZABETHKINGIA MENINGOSEPTICA</i>	100
<i>ENTEROCOCCUS FAECALIS</i>	83.33
<i>BURKHOLDERIA CEPACIA</i>	75
<i>STAPHYLOCOCCUS HAEMOLYTICUS</i>	100
<i>ENTEROBACTER AEROGENES</i>	100
<i>ENTEROBACTER CLOACAE</i> SSP CLOACAE	100
ENTEROCOCCI	100
<i>PROTEUS MIRABILIS</i>	100
<i>ACINETOBACTER BAUMANNII</i>	50
<i>ACINETOBACTER JUNII</i>	100
<i>KLEBSIELLA PNEUMONIAE</i> SPP OZAENAE	100
METHICILLIN RESISTANT <i>STAPHYLOCOCCUS EPIDERMIDIS</i>	100
RALSTONIA SPP	50
<i>SERRATIA MARCESCENS</i>	50
<i>SHEWANELLA PUTREFACIENS</i>	100
<i>STREPTOCOCCUS PYOGENES</i>	100

In a similar study conducted by S. Esposito *et al* in 2017, found that *Enterococcus faecium*, *Staphyococcus aureus*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter* species shown higher rates of multi-drug resistance¹³.

MDR Organisms Found in Deceased Patients

Among the deceased patients (n=14) under study, 78.57% (n=11) were infected with multi-drug resistant organisms and MDR *Klebsiella pneumoniae* is found to be the major culprit for mortality representing 47.36% of total organisms found in deceased patients. The presence of organisms with multi-drug resistance in death patients shows that MDR organisms are a major risk factor for mortality in the Nephrology department.

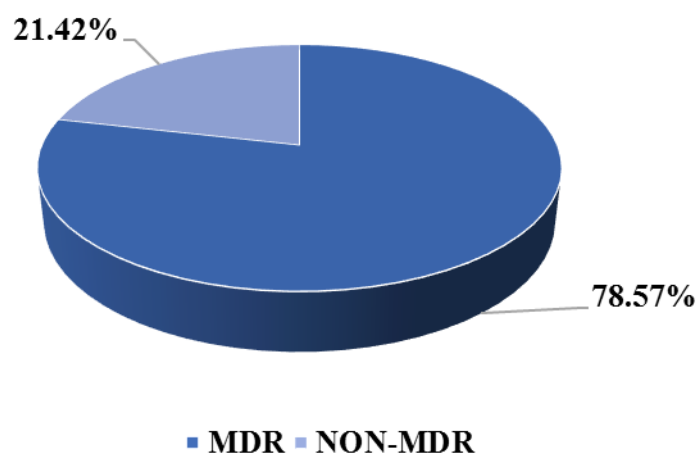


Figure No. 6: MDR Organisms Isolated in Deceased Patients

In a study by Ibrahim ME *et al*. Since 2012, they have concluded that MDR bacteria are a major cause of treatment failure in infectious diseases, leading to increased duration and severity of illness, increased mortality and increased medical costs¹⁴.

CONCLUSION

The prominent proportion of MDR isolates showed an increasing trend during three consecutive years, and an increase in the prevalence of MDR strains of Gram-negative bacteria was also observed. Therefore, MDR infections are associated with a steadily increasing socio-economic burden due to increased need for treatment and observed increased mortality. So strategies like Antibiotic Stewardship and continuous surveillance should be done to control the phenomenon.

ACKNOWLEDGEMENT

We express our sincere thanks to the most respected guide Sr. Binu Jose Veliath, Assistant Professor, Department of Pharmacy Practice, St Joseph's College of Pharmacy, Cherthala, and our consultant guide Dr. Binu Upendran, HOD Nephrology department, Lourdes hospital, Ernakulam for the inspiring guidance, valuable suggestions, effective criticisms, and constant support. We express our sincere gratitude to all who supported and helped in the completion of the research. We believe that all persons who have directly or indirectly contributed to this study, whom we have not mentioned personally, are aware of our deep appreciation.

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