

# Microbiological Profile of Significant Multi-Drug Resistant Organisms Isolated in a Tertiary Care Centre, Kerala, India

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## ABSTRACT

Emergence of bacterial antimicrobial resistance (AMR) is a major concern across the globe. Infections with multidrug resistant organisms (MDRO's) increase the morbidity and mortality in addition to financial costs, especially in vulnerable patients. Knowing the profile of MDRO's in a particular region or institution helps in optimal and timely antibiotic therapy, which is a key factor in avoiding the selection pressure exerted on microorganisms. In this study, microbiological profile of significant MDRO's isolated over a period of two years were analysed retrospectively. 58% of the total isolates were classified as MDRO's. Intensive care units (ICU's) contributed to a significantly higher number of MDRO's than other departments ( $p < 0.001$ ). Methicillin resistance was seen in 54% of the *Staphylococcus aureus* isolates. Carbapenem resistance was encountered widely amongst members of the genus enterobacteriaceae (approximately 40% isolates of *Klebsiella* spp. and *Enterobacter* spp.) and *Acinetobacter* spp. (78%). This study emphasizes the fact that AMR burden is high in low- and middle-income countries (LMIC's) and that a concerted effort on the part of legislators, medical community and general public is required to address the issue.

**Keywords:** Antimicrobial resistance, MDRO profile, carbapenem resistance

## INTRODUCTION & BACKGROUND

Antimicrobial resistance (AMR) is the ability of bacteria to thrive in the presence of antimicrobial agents that are normally active against them. This resistance is mediated by diverse resistance genes that evolve as a result of selection pressure exerted by the appropriate and/or inappropriate use of antimicrobial agents<sup>(1-3)</sup> or it may be intrinsic<sup>(4)</sup>. Both gram positive bacteria and gram negative bacteria are affected by the emergence and rise of AMR. In the strictest sense, multidrug resistant organisms (MDROs) are labelled as such because of their *in vitro* resistance to more than one antimicrobial agent. The resistance is interpreted using the clinical breakpoints provided by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and/or by the Clinical and Laboratory Standards Institute (CLSI)<sup>(5)</sup>.

Antibiotic resistant infections, particularly those caused by MDROs present a major threat to global public health. This resistance, whether intrinsic or acquired has a significant bearing on the pathway of clinical management of infected or colonized patients<sup>(4)</sup>. Infections with MDROs in critically ill patients can increase the mortality, hospitalization costs and length of hospital stays. Analysis of the

burden of resistance have been understudied in low and middle income countries (LMICs) even though the impact of this burden is disproportionately high in the same regions<sup>(3,6-8)</sup>

The situation in India is no different from other LMICs. Rising incomes and improved access to antibiotics has led to indiscriminate and inappropriate use of the same<sup>(9)</sup>. In studies from different parts of the country, prevalence of MDROs range from 30% to 60% of all isolates<sup>(10,11)</sup>. The first step towards addressing this problem is to develop a robust antimicrobial stewardship programme and antibiotic policy which would enhance clinical outcomes, reduce non-judicious use of antibiotics and minimize adverse effects associated with the use thereof<sup>(12)</sup>. An institutional and department-wise antibiogram and MDRO profile is necessary for the same.

Here we conducted a study to assess the microbiological profile of significant MDROs isolated from patient samples received at the Bacteriology laboratory of Government Medical College Kozhikode. Another aim of the study was to deduce a department-wise profile of MDROs on which an antibiotic policy can be based. Approval was obtained from Ethical Committee and Institutional Research Committee for the same.

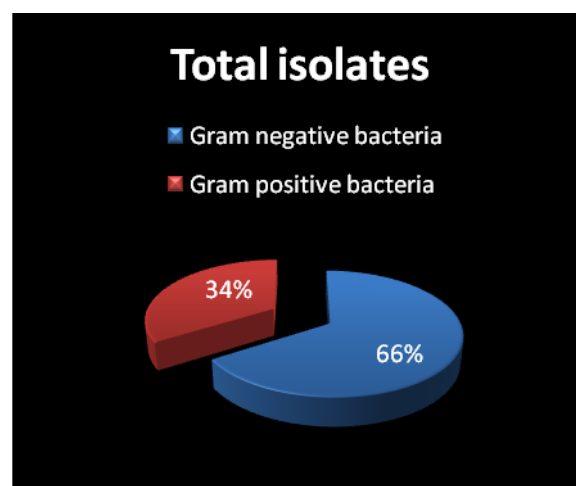
## MATERIALS AND METHODS

A two year retrospective study including all samples received for culture at the bacteriology laboratory was done.

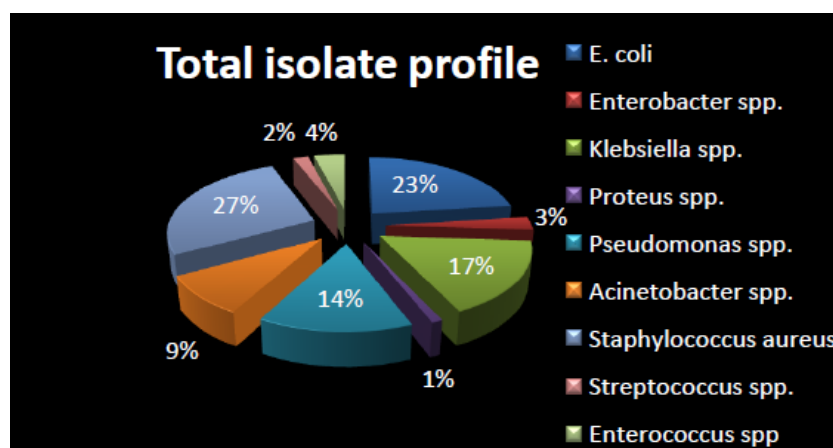
MDROs were defined as per international consensus<sup>(5)</sup> and all MDROs for which at least 30 isolates were present were included in the study. The minimum sample size was calculated as 600, anticipating a prevalence rate of 40% based on previous studies and to detect the prevalence with 4% precision. Resistance data collected from the laboratory, and stored in the WHONET programme was retrieved and analysed. The analysis was done by dividing the locations of origin of samples into three (medical, surgical and intensive care) departments

## RESULTS

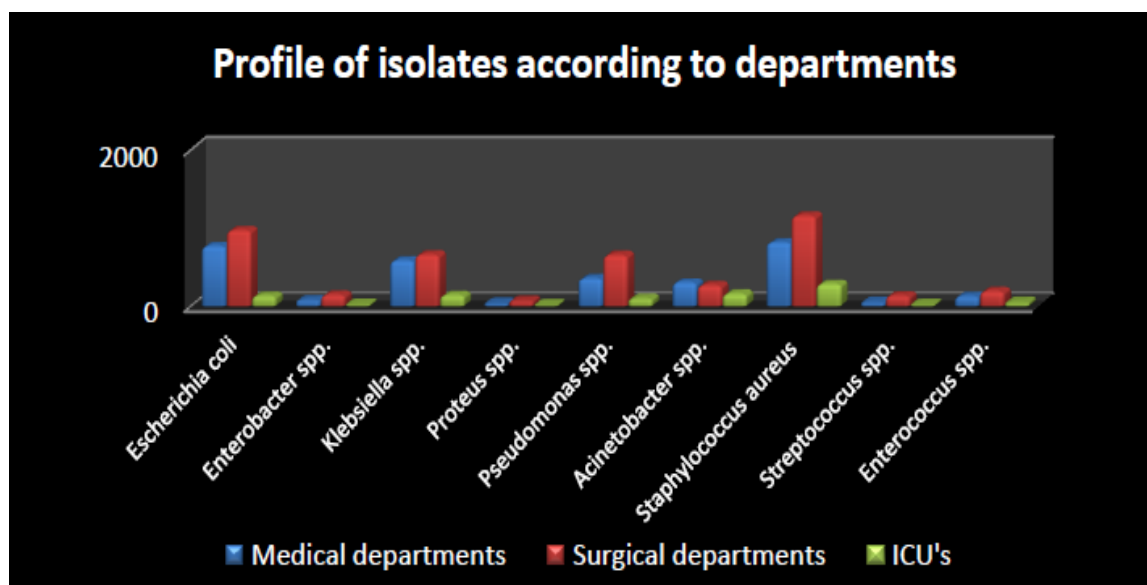
A total of 8173 significant bacterial isolates were included in the study, of which gram negative and gram positive organisms were 66% (n=5384) and 34% (n=2789) respectively



Isolate profile across all departments is as follows



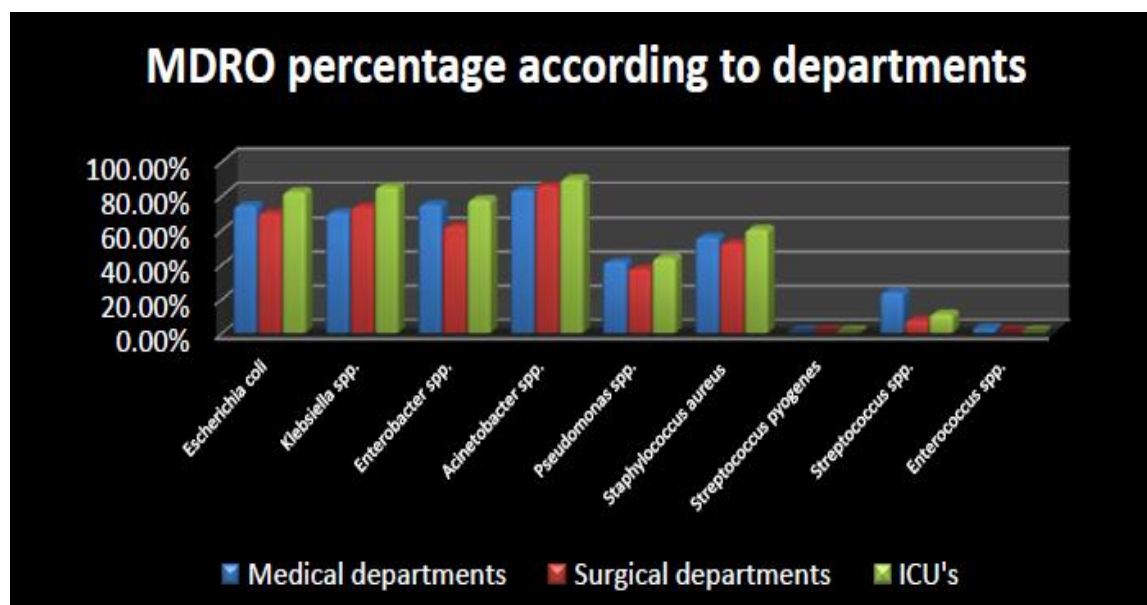
Profile of isolates from ICU's, and medical and surgical departments are as follows.



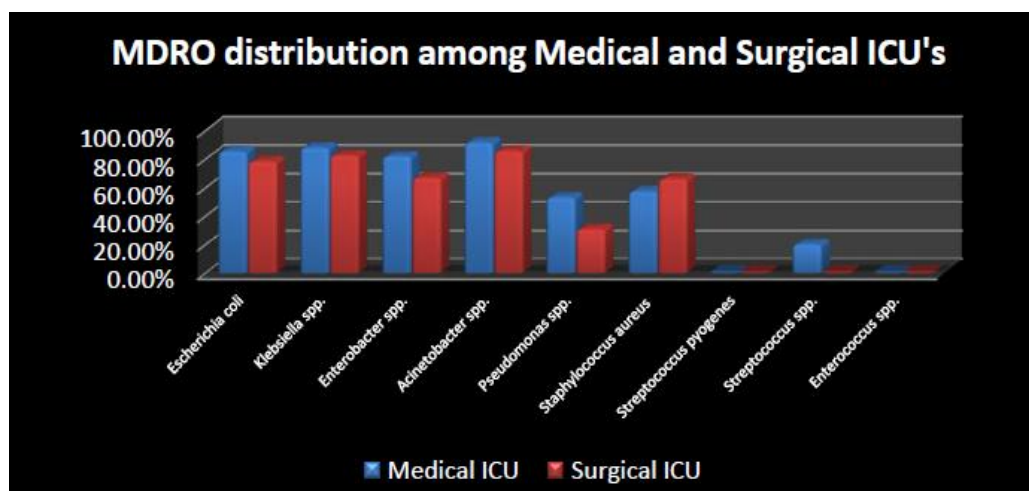
MDRO's among gram positive and gram negative bacteria were determined according to resistance data in accordance with international consensus<sup>(5)</sup>. Of the total isolates 58% (n=4745) were MDRO's. *Proteus spp.* was excluded from the list as the numbers of isolates were not statistically significant after discounting intrinsic resistance.

Amongst different MDRO's the predominant ones were *Escherichia coli* (28%), methicillin resistant *Staphylococcus aureus* (26%), *Klebsiella spp.* (21%), *Acinetobacter spp.* (13%) and *Pseudomonas spp.* (9%). Of the total isolates of *Staphylococcus aureus*, 53.8% (n=1208) were Methicillin resistant (MRSA).

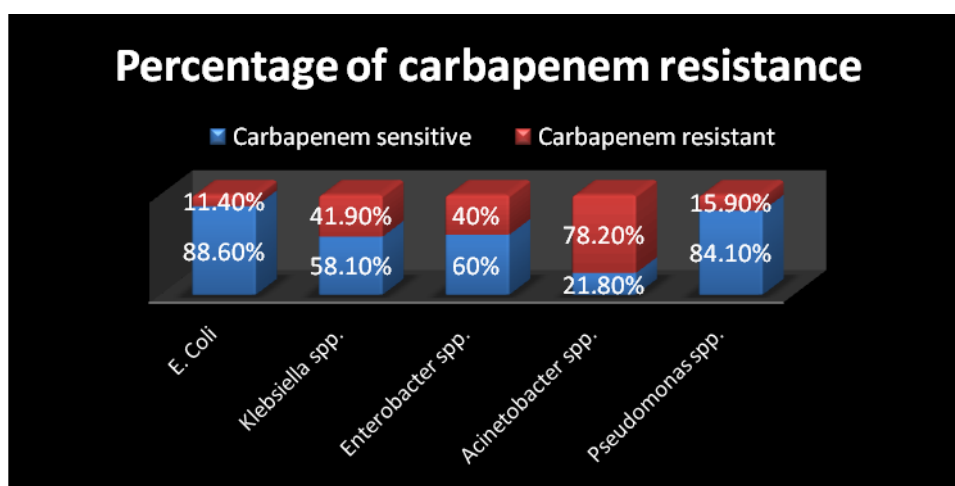
Department-wise percentage of different MDRO's is as follows.



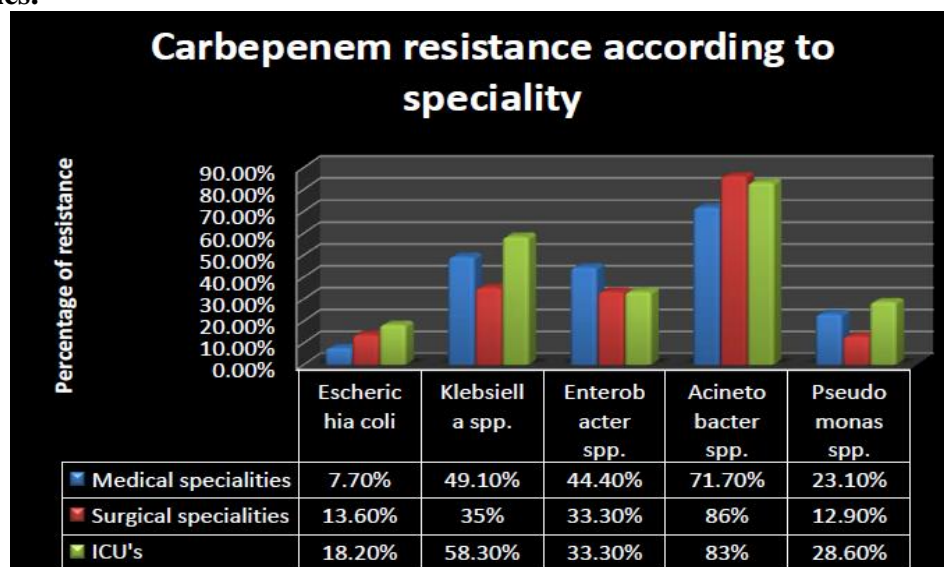
### MDRO distribution among medical and surgical ICU's



Carbapenem resistance amongst isolates of *Escherichia coli*, *Klebsiella spp.*, *Enterobacter spp.*, *Acinetobacter spp.* and *Pseudomonas spp.* are shown below



Distribution of carbapenem resistant strains between ICU's, and medical and surgical specialities.



## DISCUSSION

In this study, we sought to assess the microbiological profile of significant isolates including MDRO's which will in turn be useful in drafting the institutional antimicrobial stewardship programme. A total of 8173 significant isolates were included in the study in which there is a predominance of gram negative bacteria (66%). Different studies from across the world also show a gram negative predominance amongst significant isolates<sup>(13-16)</sup>. Compared to medical specialities, surgical specialities contributed to a significant numbers of *Staphylococcus aureus* isolates in this study. This could be because staphylococcal infections commonly involve skin and soft tissues, and such cases are usually handled by the surgical specialities.

In the present study, 58% percent of the total isolates were MDRO's and amongst them, the predominant ones were *E.coli* (28%), Methicillin resistant *staphylococcus aureus* - MRSA (26%), *Klebsiella* spp. (21%), *Acinetobacter* spp. (13%) and *Pseudomonas* spp. (9%). Between different specialities, the percentage of MDRO's was significantly higher ( $p < 0.001$ ) in ICU's than other areas. This could be because of increased selection pressure for microorganisms due to the use of multiple antibiotics in such a setting. Prevalence of MDRO's range from approximately 25% in studies from high income countries to 80% in that from low and middle income countries<sup>(11,17,18)</sup>.

Of all the isolates of *staphylococcus aureus* included in this study, 54% were MRSA. The prevalence of MRSA around the globe has been rising over the years. This rise is steeper in LMIC's than in the developed world. Studies in Africa and the middle east shows that MRSA prevalence has increased from 16% to approximately 50% in some areas<sup>(19,20)</sup>. In India, the prevalence of MRSA is higher in south India than other regions<sup>(21,22)</sup>. This could be due to increased access to healthcare system and subsequent over usage of antibiotics.

Carbapenem resistance profile was analysed between isolates of *E.coli*, *Klebsiella* spp., *Enterobacter* spp. *Acinetobacter* spp. and *Pseudomonas* spp. It shows that up to 40% isolates of *Klebsiella* and *enterobacter* spp. and 78% isolates of *acinetobacter* spp. were carbapenem resistant. This trend of increasing carbapenem resistance is evident from studies across the world and India<sup>(17,23,24)</sup>. One study from north India<sup>(24)</sup> reports that amongst enterobacteriaceae, higher percentage of carbapenem resistance was seen in *klebsiella* isolates when compared with *E.coli* (54% and 16%). The same findings were also seen in the present study (42% for *Klebsiella* spp. as opposed to 11% in *E.coli*). Another worrying factor is the high rate of carbapenem resistance seen in isolates of *Acinetobacter* spp. in this study. This is not an isolated phenomenon as evidenced in studies published from both high and low income countries<sup>(17,23,25,26)</sup>. *Acinetobacter* spp. is characterized by rapid development of drug resistance to wide variety of antibiotics, indicating a high adaptability to the selective pressure from extensive use of antibiotics<sup>(8)</sup>.

## CONCLUSION

The menace of MDRO's is prevalent across both the high income countries and low and middle income countries. The burden of the same and associated medical, social and financial costs are disproportionately higher in LMIC's. Wide prevalence of carbapenem resistance amongst isolates is to be viewed seriously as higher treatment options are limited, expensive and has increased therapy related morbidity and mortality. This problem can only be tackled by a multi-pronged approach involving:(a) implementation of government legislature to regulate unrestricted use of antibiotics in both humans and animals (b) development of a robust antimicrobial stewardship programme at the local hospital level ensuring the reduction in selection pressure which drives microbial adaptation (c)

capacity building in infection prevention and control practices leading to efficient screening, isolation and disinfection in healthcare environments to contain clonal dissemination of MDRO's.

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**Conflict of Interest:** The authors declare that they have no conflict of interest

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**Ethical Approval:** Approved

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