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Resistance in Gram Negative Organisms: A Need for Antibiotic Stewardship

Areena Hoda Siddiqui[1]* and Poonam Verma[2]

[1]Department of Microbiology, Career Institute of Medical Sciences& Hospital, Lucknow, India.
[2]Department of Biotechnology, IFTM University, Moradabad, India.

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Antibiotic resistance is increasing in Gram Negative organisms. It is important to know the antibiogram of the hospital to start empirical therapy. It can serve as a reference to clinician looking for information on antibiotic resistance. A retrospective analysis of the isolates obtained from January 2016 to December 2016 was performed. Samples were processed as per CLSI guideline. A total of 718 isolates were obtained. These were analysed for the prevalence of MDR/XDR/PDR. It was found that XDR isolates are prevalent in our teaching hospital. The study showed an emergence in pan drug resistant isolates. The knowledge of local antibiogram along with strong antibiotic stewardship program can help in guiding antibiotic therapy.This reduces antibiotic pressure among organisms and hence development of resistance.

Keywords: Extensive Drug Resistance, Multidrug Resistant Organism, Pan Drug resistance.

Multi Drug Resistant Organisms (MDRO) is on rise. This situation is worse in Intensive care unit ICUs where the patients are put on high end antibiotics which lead todevelopment of resistant isolates. With the dictum "hit wise hit nice" it becomes necessary to choose right empirical antibiotic to treat the patients.

The cost of health care for patients with resistant infections is higher than care for patients with non-resistant infections due to longer duration of illness, additional tests and use of more expensive drugs[1]. Over-use and misuse of antibiotics in animals and humans is contributing to the rising threat of antibiotic resistance. Some types of bacteria that cause serious infections in humans have already developed resistance to most or all of the available treatments, and there are very few promising options in the research pipeline[2,3].

* To whom all correspondence should be addressed.
E-mail: drareenahoda@rediffmail.com

It is therefore important for any hospital to know the prevalence of various organisms, their sensitivity pattern so that right antibiotic can be initiated and a strong infection control and antibiotic stewardship program. The golden hour within which the treatment has to be initiated as defined by Sepsis guideline is 1 hour[4]. The early the treatment initiated the lesser is mortality rate. There is an increase in mortality rate 7% with each hour delay[5]. Therefore this study was done to know the prevalence of antibiotic resistance and antibiogramin Gram Negative organisms in ICU s of our teaching hospital. Patients admitted here have always previous exposure to other healthcare facilities.

MATERIAL AND METHODS

This is a retrospective study where all the isolates obtained in the year 2016 were analysed. The samples included in the study for analysis are urine, blood , respiratoryculture and samples

from skin and soft tissue infections. All the isolates were tested against high end antibiotics. Clinical samples were processed as per CLSI guideline using cystein lysine electrolyte deficient (CLED) agar, MacConkeyAgar (oxoid) and pre-prepared Blood Agar & Chocolate Agar plates from BD. Body fluids were processed on solid medium as well as liquid medium. Blood culture sets

Table 1. Showing classification used for the isolates

Resistance type	Definition
MDR	Bacteria resistant to at least 3 classes of drugs-beta lactum and beta lactum inhibitor combinations, aminoglycosides (amikacin, gentamicin, netilmicin), fluoroquinolones (ciprofloxacin, levofloxacin, norfloxacin in urine)
XDR	Resistant to carbepenems (imipenem , meropenem) along with above
PDR	Bacteria resistant to almost all classes of antibiotics including polymyxins

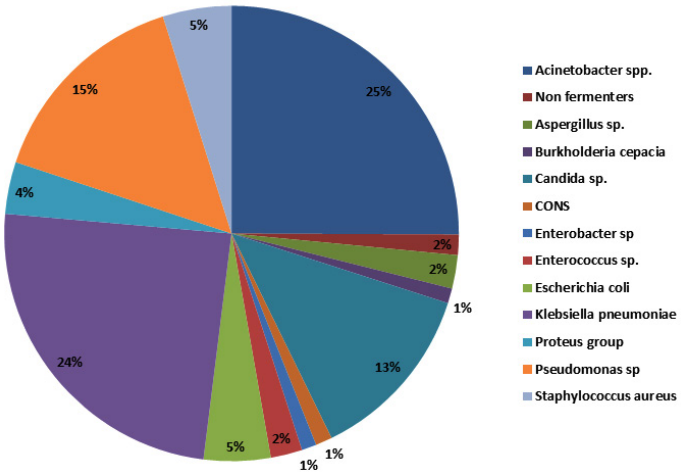

Fig.1. Showing isolates from Respiratory sample

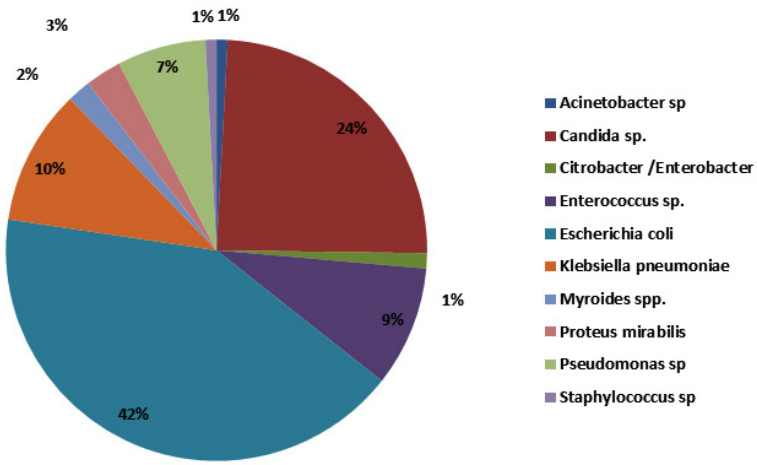

Fig. 2. Showing isolates from Urine sample

were processed on brain heart infusion(BHI) broth. Clinical isolates were further tested for identification & susceptibility testing by manual methods. Manual sensitivity was performed on Mueller Hinton Agar (BD) using antibiotic discs from BD. CLSI M-100-S23 was followed susceptibility testing. The isolates included for this study are *Acinetobacter*, *Pseudomonas*, *E coli, Klebsiella sp*. These isolates were defined as multidrug resistant, extensively drug resistant, pan drug resistant (MDR, XDR, PDR) as per following classification (Table 1). Antibiotic susceptibility testing was done and data evaluation was done against Carbapenems(Imipenam, Meropenem), tigecycline, Minocycline, Polymixins.

Table 2. Showing Prevalence of MDR/XDR/PDR in Respiratory isolates

	Acinetobacter-110(%)	*Pseudomonas*-53(%)	*Klebsiella*-98(%)	*E coli*-13(%)
MDR	0	0	1(1.02)	0
XDR	78(70.90)	45(84.9)	44(44.89)	4(30.76)
PDR	1(0.9)	0	6(6.1)	0

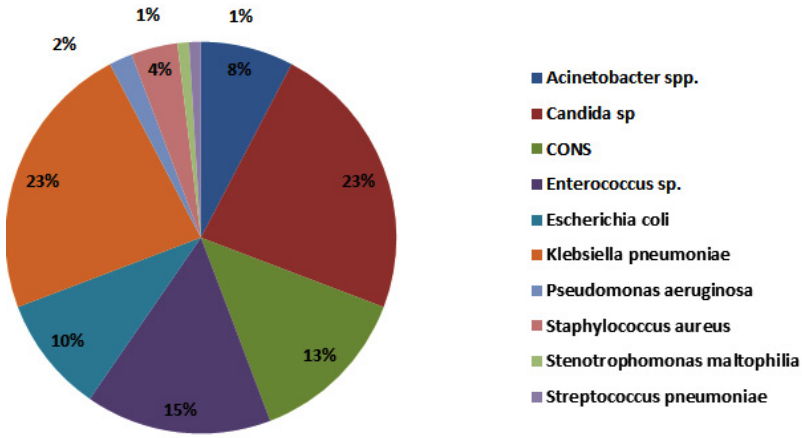

Fig. 3. Showing isolates from Blood sample

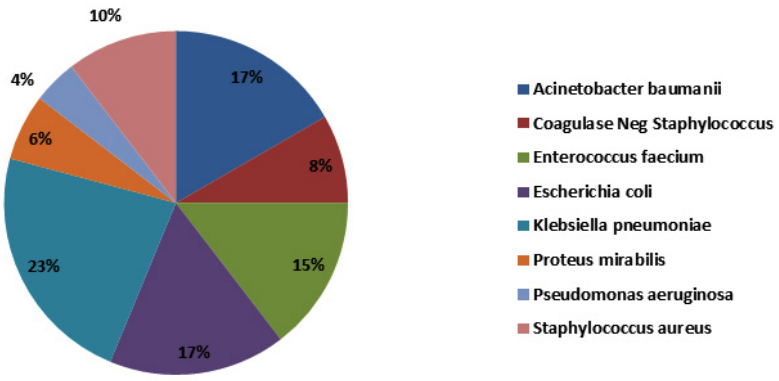

Fig. 4. Showing isolates from Skin and Soft Tissue Infection samples

RESULTS

A total of 718 isolates were obtained from 3892 samples submitted to our lab. Prevalence of various isolates in the four categories of samples are shown in Fig. 1 (Respiratory isolates), Fig.2 (Urine Isolates), Fig. 3 (Blood Isolates), Fig.4 (skin and soft tissue infections)

Data revealed that *Klebsiella*sp is more prevalent in our hospital. MDR/XDR/PDR among Acinetobacter, Pseudomonas, Klebsiella and E coli from the mentioned samples are summarized in the table 2,3,4,5. PDR isolates are more commonly seen in *Klebsiella* sp. followed by *Pseudomonas*sp and *Acinetobacter* sp. Carbapenem resistance is seen more commonly in *Acinetobacter* sp. Thus the

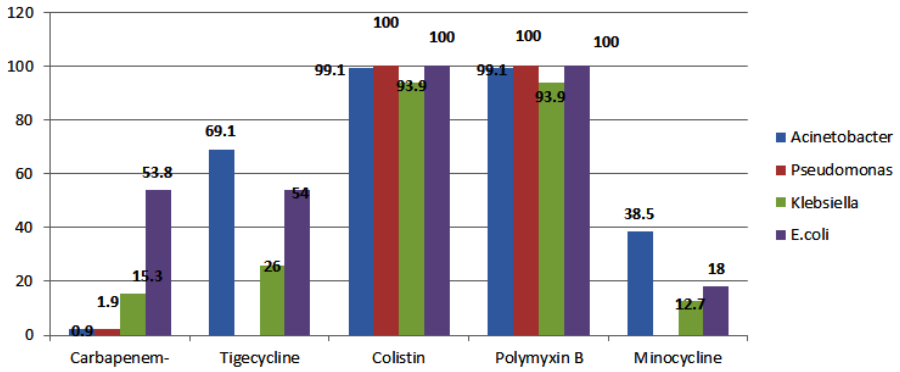

Fig. 5. Sensitivity pattern in Respiratory isolates (%)

Table 3. Showing Prevalence of MDR/XDR/PDR in Urine isolates

	Acinetobacter- 2(%)	*Pseudomonas*- 8(%)	*Klebsiella*- 7(%)	*E coli*- 26(%)
MDR	0	0	0	0
XDR	2(100)	6(75)	6(85.71)	10(38.46)
PDR	0	1(12.5)	1(14.28)	0

Table 4. Showing Prevalence of MDR/XDR/PDR in Blood isolates

	Acinetobacter- 8(%)	*Pseudomonas*- 3(%)	*Klebsiella*- 24(%)	*E coli*- 11(%)
MDR	0	0	0	0
XDR	7(87.57)	1(33.33)	12(50)	4(36.36)
PDR	0	0	2(8.33)	0

Table 5. Showing Prevalence of MDR/XDR/PDR in Skin and Soft Tissue Infection isolates

	Acinetobacter- 8(%)	*Pseudomonas*- 2(%)	*Klebsiella*- 11(%)	*E coli*- 8(%)
MDR	0	0	0	0
XDR	7(87.57)	2(100)	9(81.81)	3(37.5)
PDR	0	0	0	0

prevalence of XDR isolate is more in our teaching hospital. Sensitivity of the isolates obtained from four categories of samples is shown in Fig 5,6,7,8. Data revealed that Polymixins followed by tigecycline antibiotic have good sensitivity against all the isolates.

DISCUSSION

The study we can conclude that PDR isolates are emerging. It is more commonly seen in the Klebsiellasp followed by *Pseudomonas* sp. and *Acinetobacter* sp.[6] Carbapenem resistance

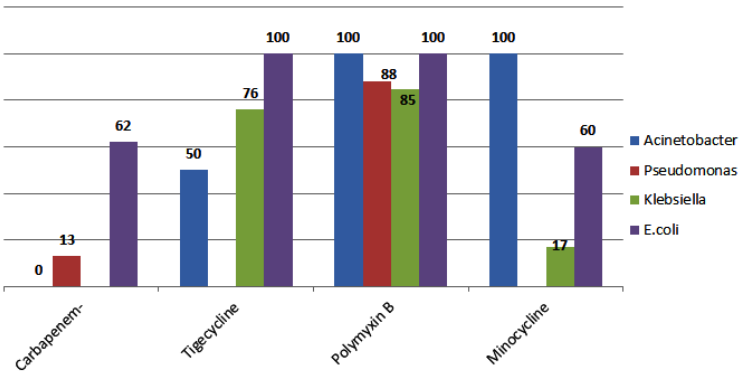

Fig. 6. Showing Sensitivity pattern in Urine isolates (%)

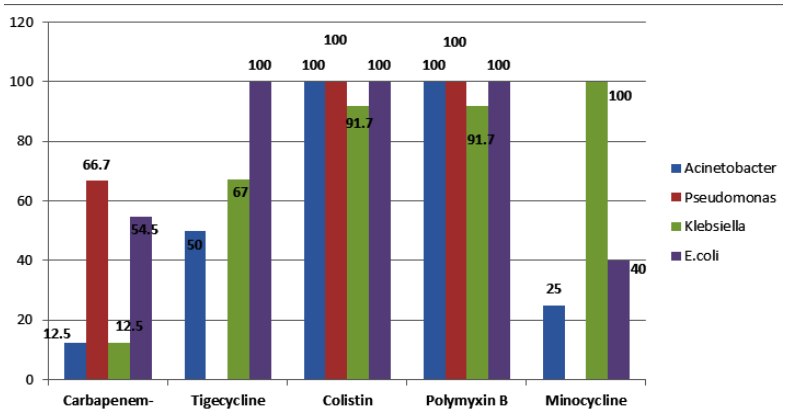

Fig. 7. Showing Sensitivity pattern in Blood isolates (%)

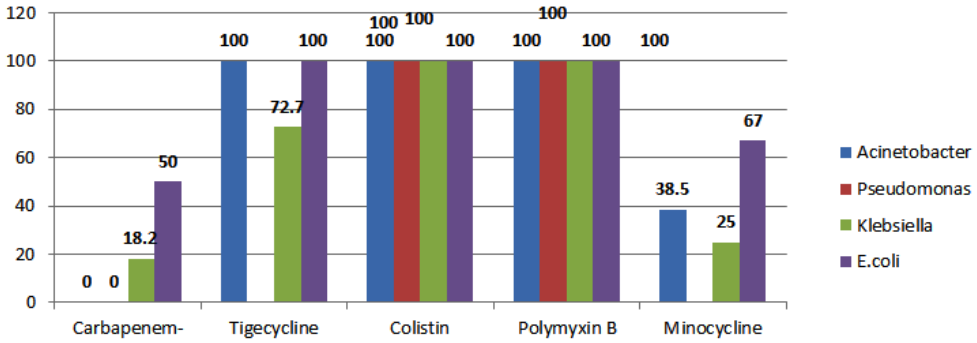

Fig. 8. Showing Sensitivity pattern in Skin and Soft Tissue Infection isolates (%)

is more commonly seen in Acinetobacter sp. In these situations it becomes very challenging to treat the patient. These can pose a serious threat to the patient as well as treating physician. Emergence of PDR can be attributed to inadvertent use of antibiotics[7]. These result in prolong length of stay, increase cost to the patient, increase in morbidity and mortality[8]. Various strategies have been described and implemented to overcome resistance[9].

It is warranted that as soon as the patient is admitted in the emergency; proper clinical evaluation as well as tests must be ordered. These tests should include at least routine cultures.[4,10] The recent diagnostic modalities help in early identification and sensitivity of the isolates. Pro inflammatory markers can aid in diagnosis where culture reports are not available.[11,12] It is recommended that Antibiotic must be de-escalated once microbiological culture reports are available.[4]

Treatment of colonization is another cause for emergence of resistant strains. It is always wise to rule out colonization from infection. Studies have revealed that suppression of normal flora may lead to overgrowth of resistant micro-organisms. These resistant microorganisms may spread within the body,cause infection to the same patient or to other patients.[13] A strong antibiotic stewardship can help in minimizing injudicious antibiotic usage and hence development of resistant strains.

Nosocomial Infection screening along with best infection control practices (hand hygiene, contact isolation, standard precautions, cleaning and disinfecting of environment) can reduce transmission of multidrug resistant organisms.

CONCLUSION

Antibiotic resistance is a global emergency It is a serious threat to us. Various strategies to combat resistance and prevent spread are laid down which need to be implemented.

Healthcare organization should support in implementation of these strategies at root level. Strict regulations to restrict over the counter use of medication can help in reducing this menace.

Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard deûnitions for acquired resistance Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard deûnitions for acquired resistance Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard deûnitions for acquired resistance Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard deûnitions for acquired resistance Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard deûnitions for acquired resistance

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