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Study of Antibiotic Sensitivity and Resistance Pattern of Bacterial Isolates in Intensive Care Unit Setup of a Tertiary Care Hospital

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Abstract: ***Objective**: To evaluate the antibiotic sensitivity and resistance pattern in an intensive care unit (ICU) setting of a tertiary care hospital. **Materials and methods**: A cross-sectional, retrospective study was conducted for a period of 1 year in 2019 on a total of 195 patients who were admitted to ICU of tertiary care hospital. The culture and sensitivity pattern of clinical isolates from blood, urine, sputum, endotracheal tube (ET) aspirate, catheter sites, and wound swabs were analyzed. Positive cultures were segregated and their antibiotic sensitivity testing was performed under the guidelines of clinical and laboratory standard institute (CLSI). **Results**: Of the total 195 ICU admissions, cultures were sent for 167 cases. Of which 127 patients were culture positive and 40 cases were culture negative. Isolated bacteria were mostly gram-negative bacilli, of which Escherichia coli was (18.6%), Acinetobacter (14.5%), Klebsiella (11.6%), Pseudomonas (9.8%), and Proteus (1.74%). Among the gram-positive organisms, coagulase negative staphylococcus (CoNS) (15.6%) was most commonly isolated followed by Streptococcus (2.32%). Fungal growth was also seen in 26 (15.11%) samples. Samples that grew organisms were blood (n = 48), sputum (n = 17), urine (n = 39), ET aspirate (n = 40), pus (n = 11), catheter (n = 4), ear swab (n = 2), and stool (n = 1). **Conclusion**: Gram-negative bacterial infections are increasing in ICUs, leading to inappropriate selection of antibiotics. Hence, antibiotic sensitivity and resistance pattern in a hospital setup has to be studied so as to guide the treating consultant to initiate empirical antibiotics in critical cases.*

Keywords: Antibiogram, Antibiotic, Culture, Intensive care unit, Resistance, Sensitivity

1. Introduction

Antibiotics have served as the corner stone of modern medicine. Emergence of antibiotic resistance is a worldwide public health problem and a threat to mankind.[1] In India, the burden of infectious disease is highest among the world; and recent reports showed the inappropriate and irrational use of antimicrobial agents against the diseases led to increase in the development of antimicrobial resistance (AMR).[2] Besides poor financial conditions, inadequate infrastructure, high burden of disease, and unregulated sales of cheap antibiotics have amplified the crisis of AMR in India.[3, 4]

Bacterial infections are a frequent cause of hospitalization, and particularly nosocomial infections are more common in critical care settings.[5] Globally the emergence of antibiotic resistance and limited availability of treatment options present an increasing challenge for the management of bacterial infections worldwide. Rate of nosocomial infections range from 5% to 30% among ICU patients. The increased risk of infection is associated with severity of patient illness, length of exposure to invasive devices and procedures, increased patient contact with healthcare personnel, and length of stay in hospital. Over the past 15–20 years, infection control practices and new antimicrobial development have primarily targeted control and treatment of infections caused by gram-positive organisms.[6-9] Recently the incidence of infections caused by gram-negative bacteria in ICU has risen, and the lack of available treatment options against some multi-drug-resistant (MDR) strains is alarming. Infections caused by MDR gram-negative organisms are associated with high morbidity and mortality.[10] Hence, careful adherence to infection control and infection treatment guidelines helps to improve patient outcome and reduce hospital cost. In this study, we analyze the pattern of antibiotic sensitivity and resistance based on the results of various cultures of microbial specimens from admitted patients. Information obtained may be crucial as a reference for pathogen identification and selection of empirical antibiotic therapy in our ICU setup.

2. Materials and Methods

Retrospective observational study conducted in a teaching tertiary care hospital in one year in 2019, a total of 195 adult patients admitted to ICU in this study period were included. Patients in whom cultures were not sent for testing were excluded. Data were collected from MRD of the hospital including patient identity, diagnosis, comorbidities, source of infection, results of microbial culture, antibiotic sensitivity and resistance pattern, antibioticuse, duration of stay in hospital, and clinical outcome. Of the total 195 ICU admissions, cultures were sent for 167 cases, of which 127 patients were culture positive and 40 cases were culture negative. In few cases, culture sample was sent from more than one site based on patient's clinical requirement. Isolated bacteria were mostly gram-negative organisms like *E. coli* (18.6%), *Acinetobacter* (14.5%), *Klebsiella* (11.6%), *Pseudomonas* (9.8%), and *Proteus* (1.74%). Among the gram-positive organisms, CoNS(15.6%) was mostcommonly isolated followed by *Streptococcus* (2.32%). Fungal growth was also seen in 26 (15.11%) samples. Specimens on which grew organisms were blood (n = 48), sputum (n = 17), urine (n = 39), ET aspirate(n = 40), pus (n = 11), central venous catheter tip (n = 4), ear swab(n = 2), and stool (n = 1).

3. Results

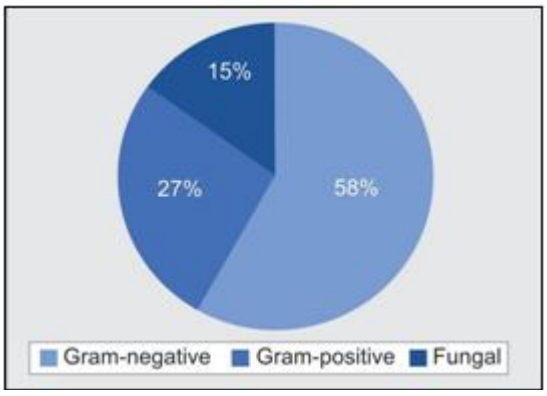
During the study period, a total of 195 cases were admitted to the medical ICU, of which 165 cases were sent for culture and sensitivity. A total of 127 cases had growth of organisms, which were tested for sensitivity pattern by

standard laboratory methods, remaining 40 cases were culture negative. Among the culture grown cases, 100 samples were gram-negative and 46 were gram-positive organisms and 26 were positive for fungal growth as depicted in Figure 1.

The positive isolates are obtained from the following samples: blood (*n* = 48), sputum (*n* = 17), urine (*n* = 39), ET aspirate (*n* = 40), pus (*n* = 11), catheter (*n* = 4), stool (*n* = 1), ear swab (*n* = 2), and vaginal swab (*n* = 1) (Fig. 2). CoNS is the most frequent isolate from blood culture, *E. coli* and fungal growth from urine culture, and *Klebsiella* and *Acinetobacter* from ET secretions.

E. coli (18.6%) was the most common organism isolated, followed by *Acinetobacter* (14.5%), *Klebsiella* (11.6%), *Pseudomonas* (9.8%), and *Proteus* (1.74%). Among the gram-positive organisms, CoNS (15.6%) was the most common organism followed by *Streptococcus* (2.32%). In all, 26 samples, i.e., (15.11%) were positive for fungal growth (Table 1).

E. coli was most sensitive to colistin (96.8%), followed by tigecycline (78.12%), nitrofurantoin (71.8%), imipenem (68.75%), and meropenem (68.75%) (Fig. 3). Similarly Figures 4 to 6 depict sensitivity pattern of *Pseudomonas* and *Klebsiella*, respectively. *Acinetobacter* showed highest sensitivity to colistin (68%) followed by tigecycline (64%) (Fig.7). Staphylococcus showed 100% sensitivity to tigecycline and nitrofurantoin. Similarly Table 2 depicts the sensitivity pattern of other isolated organisms. *E. coli*, *Acinetobacter*, *Pseudomonas*, *Proteus*, and *Enterobacter* showed resistance to cephalosporins and piperacillin–tazobactam. Resistance to colistin was observed more in *Proteus*, and CoNS *Staphylococcus* showed 100% resistance to vancomycin and clindamycin, as depicted in Table 3.



4. Discussion

Antibiotic resistance is an emerging problem in critically illcases, which affects prognosis and survival of the patients. Italso results in prolonged stay in hospital, increasing the cost oftreatment.[11–13]

In our study, of the 167 cases sent, 76% were culture positive compared to 46.4% by Chakravarthi et al.[14] Among these, gram- negative accounted for 58%, gram- positive were 27%, and fungal growth was yielded in 15% of samples (Fig.1).

Samples sent for culture were blood (*n*=48), urine (*n*=39), ET aspirate (*n* = 40), central venous catheter tips (*n* = 4), sputum (*n*=17), and pus (*n*=11) (Fig.2).

The most common organisms isolated. This is comparable to other studies where gram- negative organisms were most commonly isolated.[10] Among gram- positive, CoNS was the most common organism isolated (15.6%). Fungal growth was also seen in 15.11% samples (Table1).

In Asian countries including India, most of the isolates obtained from ICU patients are gram-negative organisms such as *E.coli*, *Klebsiella*, and *Acinetobacter* followed by gram-positive organisms like *Staphylococcus* comparable to our study.[15–17]CoNS was the most common organism isolated in blood culture, i. e., (43.75%), followed by *E.coli* and *Pseudomonas*, this is comparable to studies done by Vanitha Rani et al., [18] Javeed et al.,[19] Jain et al.,[20] Rajeevan et al.,[21] and Shrestha et al.[22]

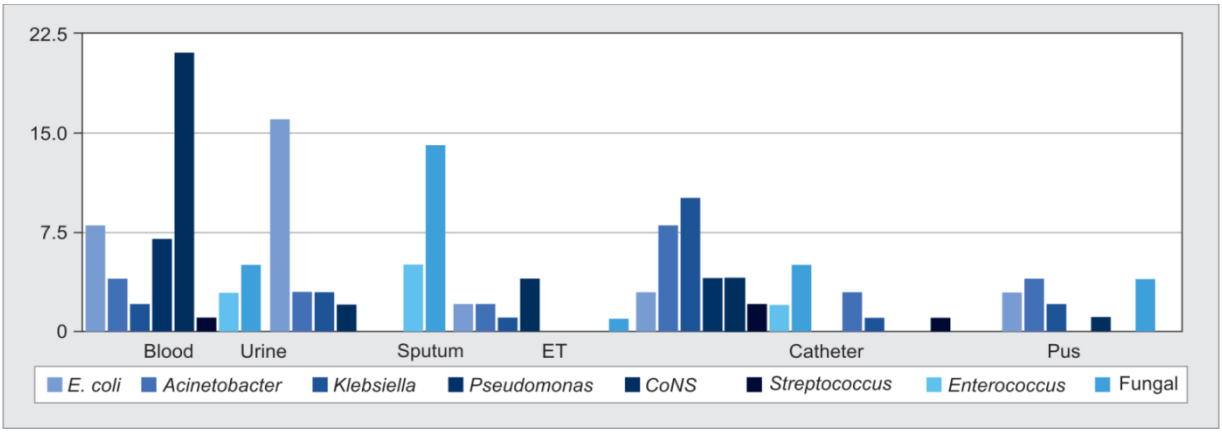


Figure 2: Type of culture sample and organism isolated

Table 1: Frequency of organisms isolated

No.	*Organisms*	*Frequency*
1	*Escherichiacoli*	32(18.6%)
2	*Acinetobacter*	25(14.5%)
3	*Klebsiella*	20(11.6%)
4	*Pseudomonas*	17(9.8%)
5	Coagulase negative *Staphylococcus*	27(15.6%)
6	*Enterococcus*	13(7.5%)
7	*Proteus*	3(1.74%)
8	*Staphylococcus*	2(1.16%)
9	Nonfermenting gram-negative *Bacillus*	3(1.74%)
10	*Streptococcus*	4(2.32%)
11	Fungal	26(15.11%)
	Total	127(100%)

E.coli (41%) was commonly isolated from urine, followed by fungal growth and *Acinetobacter*. In other studies such as Bajaj et al.[23] and Sheth et al.,[24] *Klebsiella* was commonly isolated from urine culture. Fungal urinary tract infection has become a significant nosocomial problem over the past decade;[21] however, laboratory yield of yeast in urine and its significance may be difficult to differentiate from colonization and infection.[24–27]

Klebsiella was commonly isolated from ET aspirate culture (27.5%) followed by *Acinetobacter* and *Pseudomonas*. In most other studies done in respiratory ICU, *Acinetobacter* was commonly isolated followed by *Klebsiella* and *Pseudomonas*.[28–30.]

E.coli showed highest resistance to ceftazidime, cefepime, and ceftriaxone (62.5%). This was identical to the study by Hsu et al., [31] Mangaiarkkarasi et al.,[32] and Oteoetal.(Fig.8).[33]

Acinetobacter showed high resistance to cephalosporins (96%) followed by piperacillin–tazobactam (84%) as also reported by Chakraverti et al.(Fig.9).[14]

Klebsiella showed high resistance to cephalosporins (65%), amikacin, gentamicin and meropenem (60%), imepenem (45%), and colistin (20%). The resistance of *Klebsiella* to cephalosporins was also observed in other studies by Sheth et al., [24] Javeed et al. (Fig.10).[19] *Pseudomonas* showed the highest resistance to antipseudomonal drugs such as ceftazidime (76.4%), piperacillin–tazobactam (64.7%),

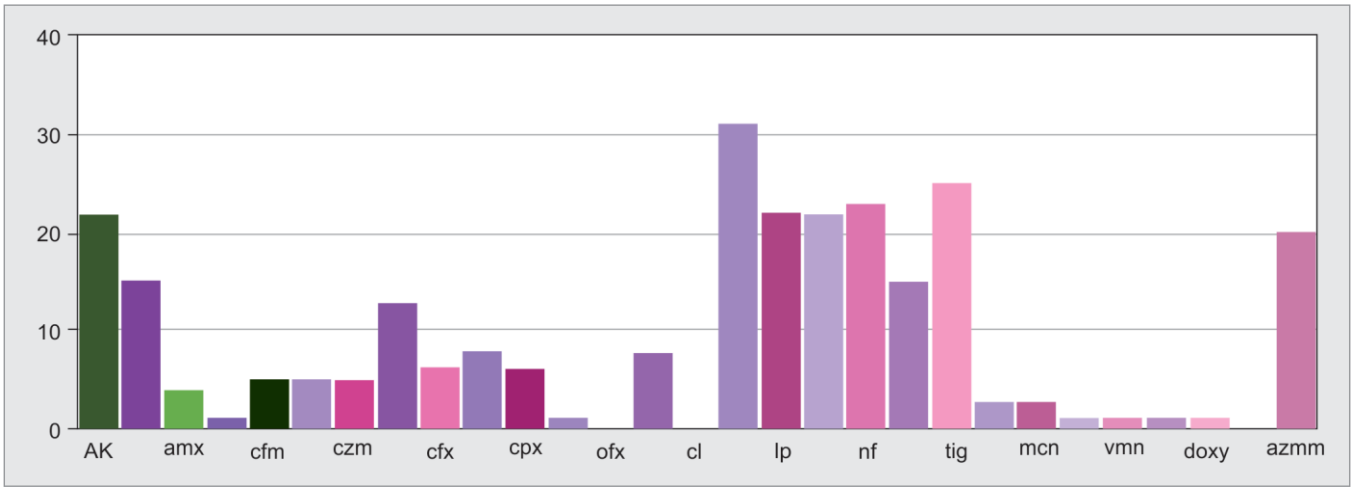


Figure 3: *Escherichiacoli*- sensitivity pattern

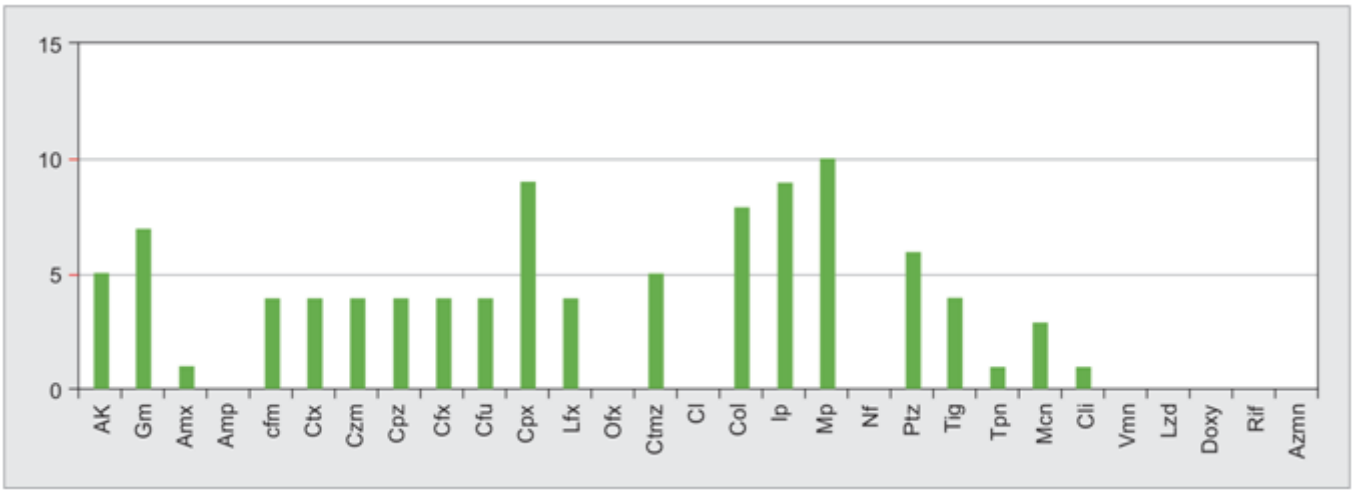


Figure 4: *Pseudomonas*-sensitivity pattern

Table 2: Antibiotic- sensitivity pattern of isolates

	E.coli	*Acineto*	*Kleb*	*Pseud*	*CoNS*	*Entero*	*Prot*	*Strepto*	*Staph*
Ak	**68.75**	4	40	29.4	19.2	38.4	33.3	50	50
Gm	46.87	12	40	41.1	50	23.07	33.3	75	50
Amx	12.5	0	10	5.88	19.2	53.8	33.3	0	0
Amp	3.12	0	0	0	26.9	0	0	0	0
Cfm	15.62	4	25	23.5	26.9	15.3	0	75	50
Ctx	15.62	4	25	23.5	26.9	15.3	0	75	50
Ctzm	15.62	4	25	23.5	26.9	15.3	0	75	50
Cfpz	40.6	4	25	23.5	26.9	15.3	0	75	50
Cxm	18.7	4	25	23.5	26.9	15.3	0	75	50
Cfu	25	4	25	23.5	26.9	15.3	0	75	50
Cpx	18.7	8	20	52.9	30.7	23.07	0	25	50
Lfx	3.12	0	0	23.5	34.6	0	0	0	0
Ofx	0	0	0	0	0	0	0	0	0
Ctmx	25	8	25	25	**42.3**	23.07	0	50	50
Cl	0	0	0	0	**42.3**	0	0	0	0
Col	**96.8**	**68**	**70**	**47.05**	19.2	23.07	0	50	50
Ip	**68.75**	24	**45**	**52.9**	19.2	38.4	**33.3**	50	50
Mp	**68.75**	28	30	**58.8**	23.07	30.7	**33.3**	25	50
Nf	**71.8**	0	0	0	61.5	23.07	0	0	**100**
Ptz	46.87	16	0	35.2	15.3	30.7	33.3	0	50
Tig	**78.12**	**64**	**55**	23.5	69.2	**76.9**	0	25	**100**
Tpn	9.37	0	15	5.88	76.9	61.5	0	0	50
Mcn	9.37	40	10	17.6	57.6	15.3	0	NT	50
Cli	3.12	0	5	5.88	**57.6**	30.7	0	**75**	0
Vmn	3.12	0	5	0	**61.5**	**76.9**	0	**75**	50
Lzd	3.12	0	0	0	**57.6**	**84.6**	33.3	**75**	50
Doxy	3.12	0	0	0	**50**	15.3	0	0	50
Rif	0	4	0	0	42.3	23.07	0	0	50
Aznm	62.5	0	0	0	0	0	0	0	0

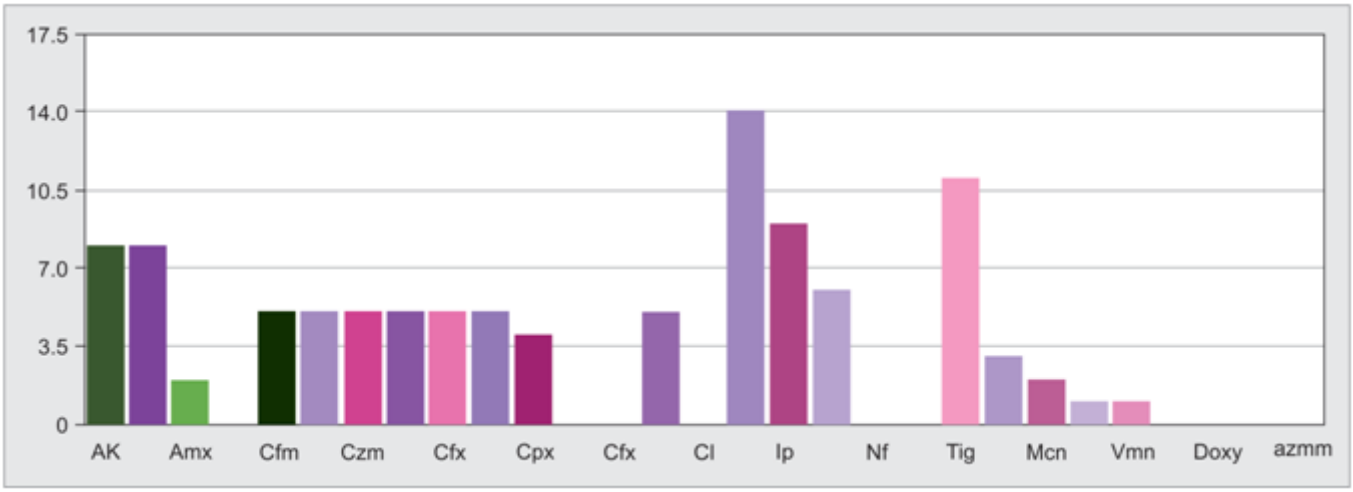


Figure 5: *Klebsiella*-sensitivity pattern

Table 3: Antibiotic- resistance pattern of isolates

	E.coli	*Acineto*	*Kleb*	*Pseudo*	*CoNS*	*Entero*	*Proteus*	*Strepto*	*Staph*
Ak	18.75	0	60	**70.5**	**80.7**	61.5	66.6	50	50
Gm	21.8	0	60	58.8	50	76.9	66.6	25	50
Amx	37.5	0	**90**	**94.1**	**80.7**	61.5	66.6	0	0
Amp	37.5	0	0	0	0	0	0	0	0
Cfm	62.5	96	65	76.4	73.06	0	**100**	25	50
Ctx	**62.5**	**96**	**65**	**76.4**	73.06	**84.6**	**100**	25	50
Ctzm	**62.5**	**96**	**65**	**76.4**	73.06	**84.6**	**100**	25	50
Cfpz	43.7	**96**	**65**	**76.4**	73.06	**84.6**	**100**	25	50
Cxm	56.2	**96**	**65**	**76.4**	73.06	**84.6**	**100**	25	50

Cfu	46.8	**96**	**65**	**76.4**	73.06	**84.6**	**100**	25	50
Cpx	21.12	**92**	**70**	47.05	69.2	76.9	66.6	75	50
Lfx	15.62	0	0	76.4	57.6	0	0	0	0
Ofx	15.62	0	0	0	0	0	0	0	0
Ctmx	40.6	**92**	65	70.5	57.6	76.9	66.6	50	50
Cl	12.5	0	0	0	57.6	0	0	0	0
Col	3.12	32	20	52.9	**80.7**	76.9	**100**	**50**	50
Ip	21.8	12	45	47.05	**80.7**	61.5	66.6	**50**	50
Mp	18.75	**72**	60	41.1	73.06	69.2	66.6	**75**	50
Nf	6.25	0	0	**100**	42.3	76.9	66.6	**100**	0
Ptz	40.6	**84**	0	64.7	**84.6**	69.2	66.6	**100**	50
Tig	0	36	35	**76.4**	30.7	23.07	100	75	0
Tpn	15.62	0	75	**94.1**	23.07	38.4	**100**	**100**	50
Mcn	0	60	0	**82.35**	34.6	**84.6**	**100**	Not	50
Cli	12.5	0	0	**100**	34.6	69.2	**100**	25	**100**
Vmn	12.5	0	85	94.1	38.4	23.07	100	25	**100**
Lzd	12.5	0	90	100	42.3	15.3	66.6	25	50
Doxy	12.5	0	90	100	50	**84.6**	0	**100**	50
Rif	15.62	0	90	100	19.2	76.9	0	**100**	50
Aznm	12.5	0	0	0	0	0	0	0	0

Ak, amikacin; Amx, amoxicillin; Amp, ampicillin; Gm, gentamicin; Cfm, cefepime; Ctx, ceftriaxone; Czm, ceftazidime; Cpz, cefaperazone; Cfx, cefexime; Cfu, cefuroxime; Cpx, ciprofloxacin; Lfx, levofloxacin; Ofx, oflaxacin; Ctmz,cotrimoxazole; Cl, clarithromycin;Col,colistin;Ip,imepenem;Mp,meropenem; Nf, nitrofurantoin; Ptz, piperacillin–tazobactam; Tig, tigecycline; Tpn, tiecoplanin; Mcn, minocycline; Cli, clindamycin; Vmn, vancomycin; Lzd, linezolid;Doxy, doxycycline; Rif, rifampicin; Aznm, aztreonam; NT, not tested; *E. coli*, *Escherichia coli*; *Acinito*, *Acinetobacter*; *Kleb*, *Klebsiella*; *Pseud*, *Pseudomonas*; *Entero*, *Enterococcus*; *Prot*, *Proteus*; *Strepto*, *Streptococcus*; *Staph*, *Staphylococcus*

The bold values indicate the rate of emergence of antibiotic resistant organisms to our basic antibiotics and need for higher antibiotics and also some multidrug resistant organisms. Its time to stay Alert!!!

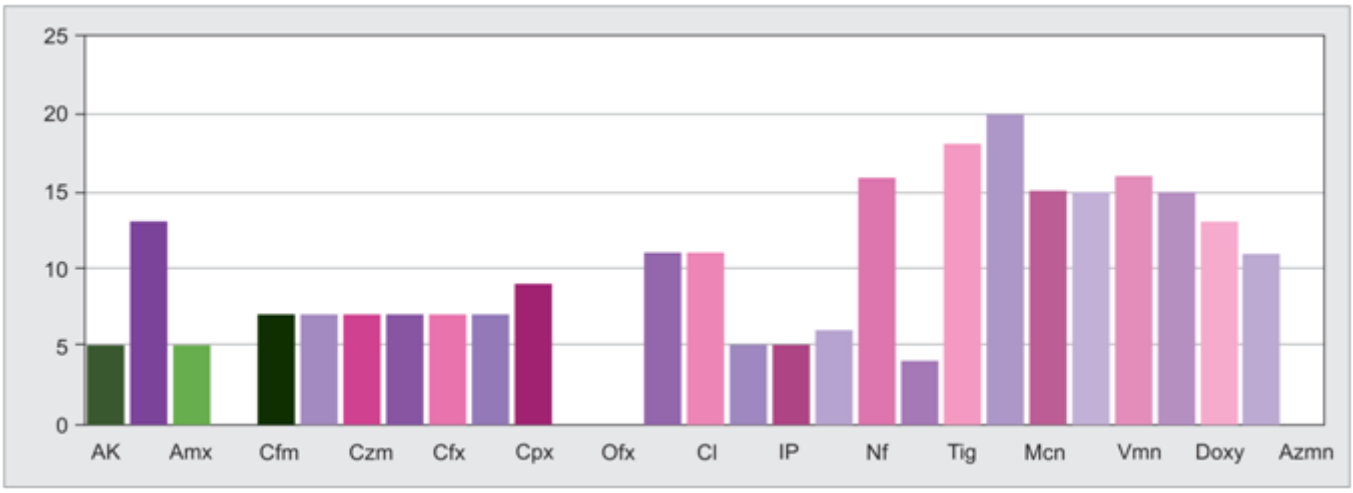


Figure 6: CoNS-sensitivity pattern

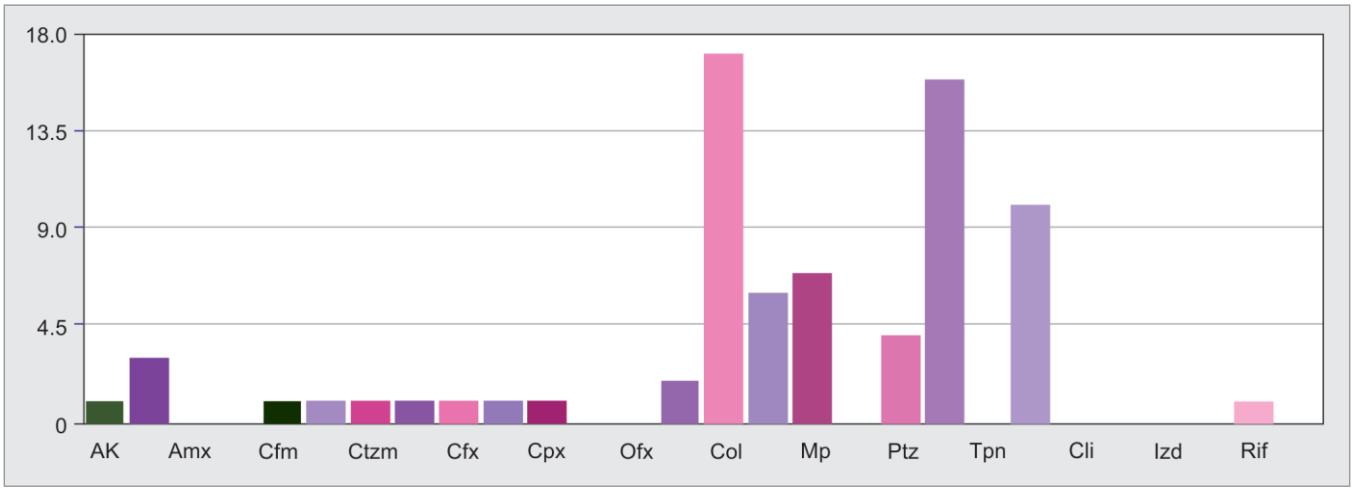


Figure 7: *Acinetobacter*- sensitivity pattern

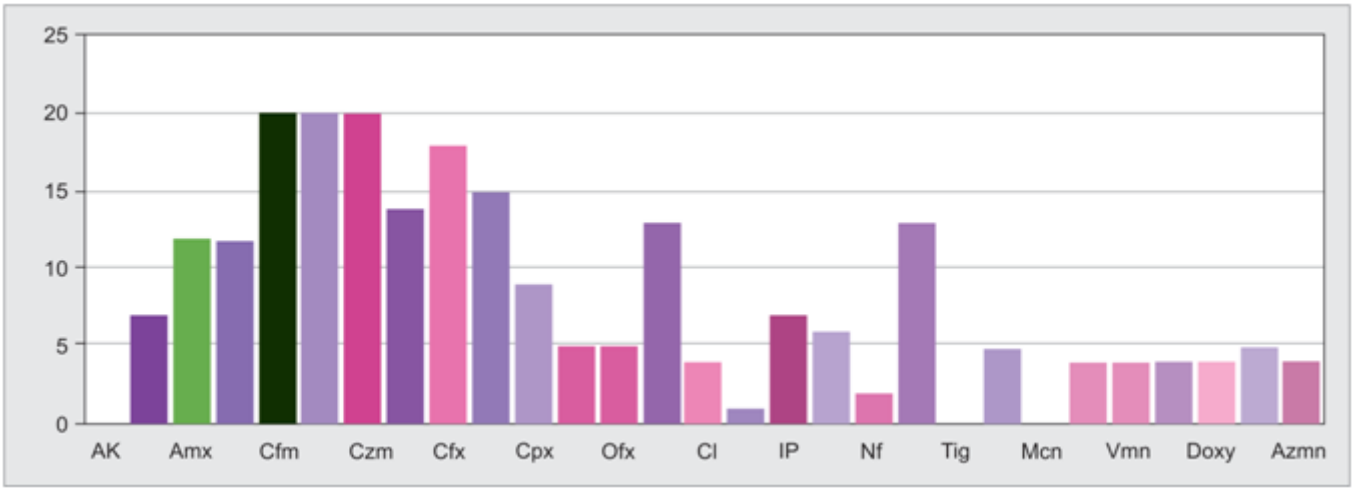


Figure 8: *Escherichiacoli*-resistance pattern

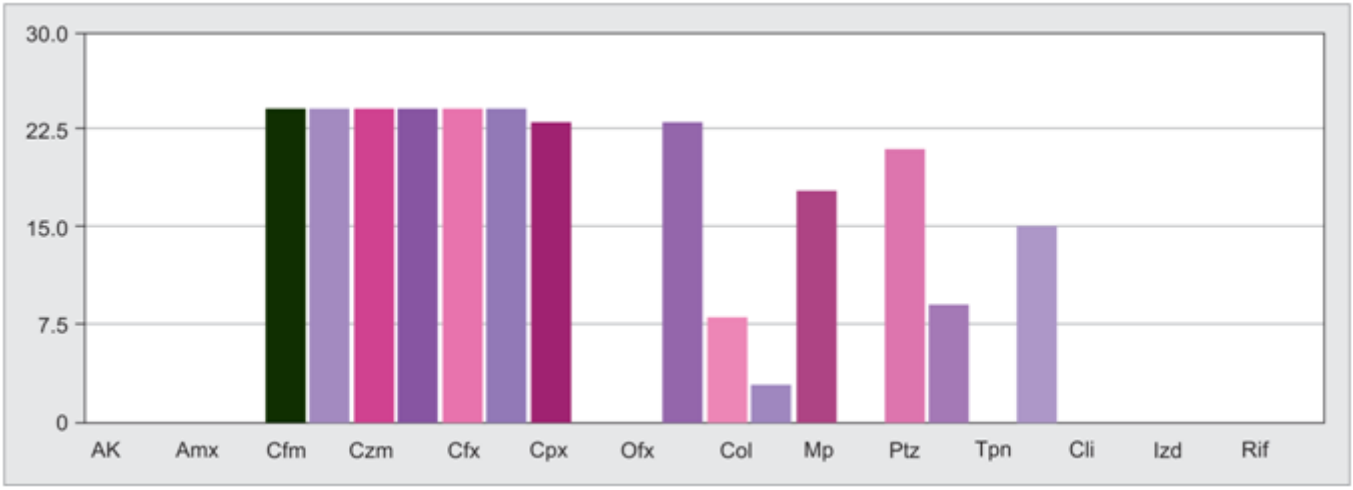


Figure 9: *Acinetobacter*- resistance pattern

amikacin (70.5%), gentamicin (58%), imepenem (47%), and meropenem (41.1%). It also showed high resistance to colistin, i.e., (52%), this pattern of resistance was observed by Mohanasundara metal.[34](Fig.11).

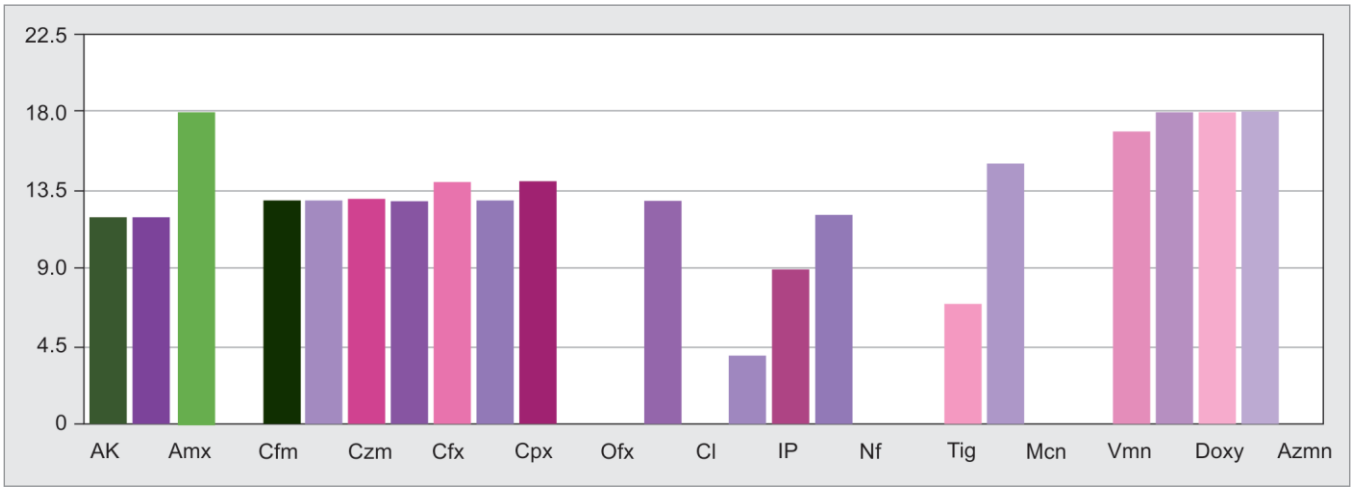


Figure 10: *Klebsiella*- resistance pattern

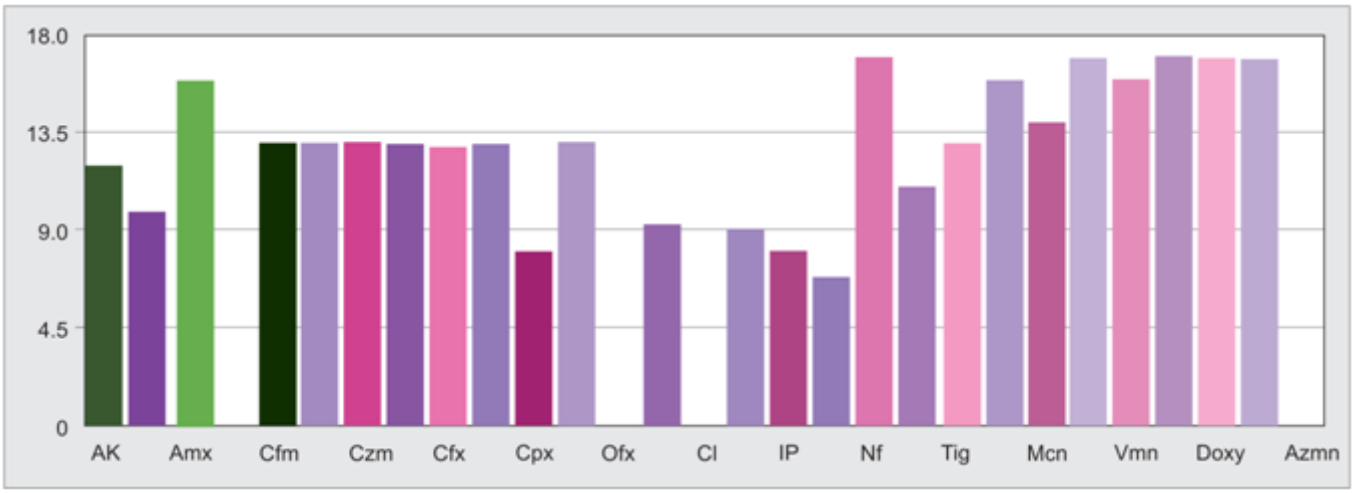


Figure 11: *Pseudomonas*- resistance pattern

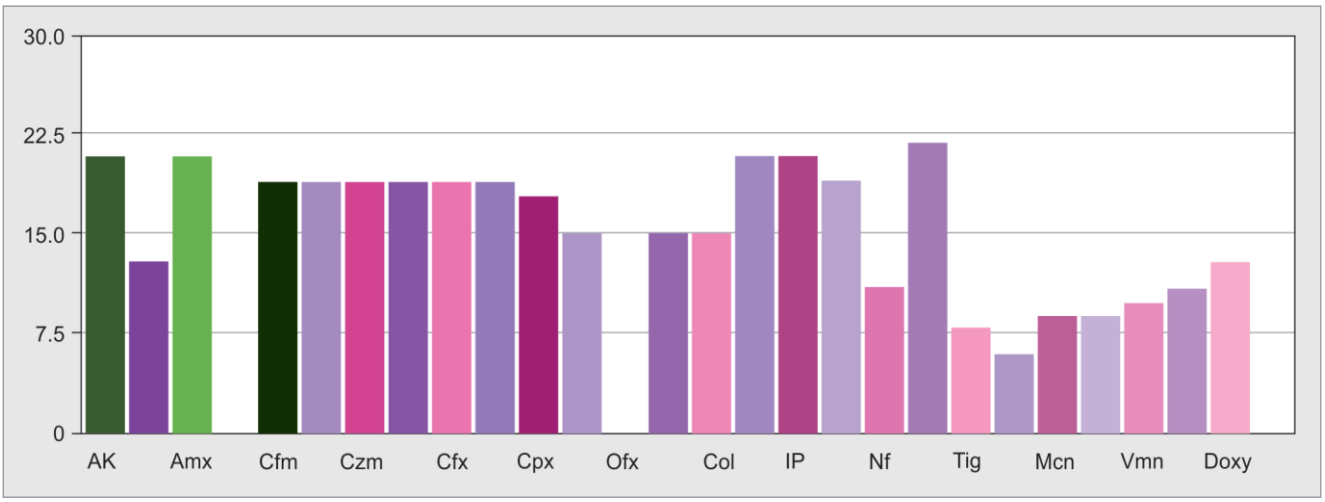


Figure 12: CoNS-resistance pattern

Enterococcus showed highest resistance to cephalosporins (84.6%), amoxicillin (61%), cotrimoxazole, andcolistin (76%). Streptococcus showed 100% resistance to piperacillin–tazobactam and teicoplanin. *Staphylococcus* showed 100% resistance to vancomycin and clindamycin (Fig. 12). In our study the most common organisms isolated from patients in ICU were gram-negative isolates such as *E. coli*, *Acinetobacter*, *Klebsiella*, *Pseudomonas*, and *Proteus* which showed highest resistance to second- and third-generation cephalosporins followed by piperacillin– tazobactam.

Piperacillin–tazobactam has been the mainstay of empirical antibiotic therapy followed by carbapenems in severely ill ICU patients. Indian guidelines by Indian Council of Medical Research (ICMR) also recommend the use of β-lactam with β-lactamase inhibitor such as piperacillin–tazobactam as empirical antibiotic therapy in critically ill

patients. In our study, we observed significantly high resistance to piperacillin and tazobactum, i.e., around 40–80% in both gram-negative and positive infections, in the obtained culture and sensitivity reports.

Carbapenem-resistant Enterobacteriaceae including *Klebsiella*, *E. coli*, and *Acinetobacter* has emerged with increasing prevalence over the past decade, which is also evident in our study where *E. coli* showed around 68% sensitivity to carbapenems, whereas *Acinetobacter* showed only 24%, *Klebsiella*30–45%, and *Pseudomonas* 50–55%.

This may be due to the prior antibiotic usage, prior severe gram-negative infections, inappropriate course of antibiotics, and patients coming with severe sepsis and septic shock as ours is a tertiary care hospital.

With the emergence of these multidrug-resistance organisms, older medications such as colistin has been revived. Even in our study, we observed good sensitivity of gram-negative isolates to colistin, where *E. coli* showed 96.8% sensitivity, *Acinetobacter* 68%, *Klebsiella*70%, and *Pseudomonas* 47%.

But few pan-drug-resistant isolates were also identified in our study, which were resistant to all drugs including carbapenems, colistin, and minocycline. Emergence of such pan-drug-resistant organisms are threat to mankind and do makes us think what next.

Probably at this stage, a local antibiogram has to be drawn in every ICU setup, at least quarterly, for better clinical decision-making regarding initiation of empirical antibiotics with antibiotic stewardship program, which are beneficial in preventing the emergence of MDR and extremely drug resistant organisms. Most important in this is the use of broad-spectrum empirical antimicrobials with an aggressive de-escalation strategies to minimize collateral damage to current and future patients. Emphasis should also be laid on the use of sterile techniques while inserting devices, hand hygiene and use of gowns and gloves in ICU to prevent nosocomial infections and better patient response and clinical outcome.

5. Conclusion

Antibiotic resistance is a major upcoming problem in today's clinical practice, increasing the challenges to treating consultants as well as huge financial burden to patient bystanders. Gram-negative-resistant infections are increasing in our ICU setups, leading to increased morbidity and mortality. Hence, timely antibiogram and antibiotic stewardship programs have to be conducted for a better understanding of the type of organism, their sensitivity and resistance pattern, so as to initiate empirical antibiotics in emergency conditions. Also equal emphasis has to be given for de-escalation of antibiotics whenever indicated, so as to prevent further misuse of antibiotics and increase the resistance of these organisms. Better usage of available drugs lead to better preservation of stores for future generation.

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