Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

Sushitha U[1], Faisal Imran[2], Mohammad Jaffar Sadiq[3]*, P Vaasanthi[1], Tajmullah Ahmed[4], Kanishk Gupta[4], Nehmat Ghaboura[3] and Nain Tara Bukhari[5]

[1]*Raghavendra Institute of Pharmaceutical Education and Research, Ananthapuramu, Andhra Pradesh, India*
[2]*Batterjee Medical College, North Obhur, Jeddah, Kingdom of Saudi Arabia*
[3]*Department of Clinical Pharmacology, Batterjee Medical College, North Obhur, Jeddah, Kingdom of Saudi Arabia*
[4]*Department of Dental Sciences, Batterjee Medical College, North Obhur, Jeddah, Kingdom of Saudi Arabia*
[5]*Department of Microbiology, University of Karachi, Pakistan*

*Corresponding Author: Mohammad Jaffar Sadiq, Department of Clinical Pharmacology, Batterjee Medical College, North Obhur, Jeddah, Kingdom of Saudi Arabia.

Abstract

Aim: The study was aimed to identify the resistance pattern of the microorganisms in the patients admitted in the ICU.

Methods and Material: It is a prospective, observational study carried out for a period of twelve months (November 2013-November 2014). The patient's demographic data was collected from their case sheet and medical history, and clinical isolates were collected from analysed and processed samples.

Statistical Analysis: The results were tabulated and explained through descriptive analysis.

Results: Regarding gender more male patients were admitted in ICU as compared to female patients, with predominant age group of 46 - 60 years. *E. coli* and *Corynebacterium* were largely resistant microorganisms isolated when checked for antibiotics sensitivity test.

Conclusion: Study suggested that antibiotics should not be used as empirical treatment to avoid emergence of multi drug resistant strains, and physicians should be trained to focus on laboratory investigation based treatment in cases where antimicrobial therapy is needed instead of irrational and illogical combination of antibiotics. High antibiotic resistant strains from clinical isolates are alarming and need investigation.

Keywords: ICU; Antimicrobials; Resistance Pattern; Microorganisms

Abbreviations

ICU: Intensive Care Unit; Co: Colistin; Amik: Amikacin; Chlor: Chloramphenicol; Cotri: Cotrimoxazole; Cipro: Ciprofloxacin; Cef: Ceftriaxone; PT: Piperacillin/Tazobactam; Azi: Azithromycin; Me: Meropenem; Amo: Amoxicillin/Clavulanate; Ampi: Ampicillin; Ge: Gentamicin; Doxy: Doxycycline; Vanco: Vancomycin; Peni: Penicillin-G; Clin: Clindamycin; Clo: Cloxacillin; S: Streptomycin; L: Linezolid

Introduction

Antimicrobials are the chemotherapeutic agents that inhibit the growth of microorganisms [1]. Antimicrobial agents misuse has led to emergence of resistance among microorganisms. To reduce the antimicrobial resistance either we have to decrease the use or increase the rationality towards their use, but it is difficult and not efficient way of controlling resistance [2].

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

284

Most of the microbial infections ends up putting the patient in the Intensive Care Units (ICU) of a medical facility and among those Nosocomial infections are most common [1]. Further use of mechanical ventilators increases the risk of infection at ICU settings [4]. Nosocomial infections most commonly acquired by the body through urinary tract while other common ways of entry include surgical wounds, the respiratory tract and the blood stream [5]. Because of this antimicrobial resistances is one of the emerging serious clinical issue in the cases taken into ICU [3]. In recent years, efforts have been focused on rationalizing the management of the available antimicrobial agents rather than on reducing its total use [2]. Emergence of resistance among microorganisms can be reduced by optimal choice of selection of medication with proper doze and duration of treatment. Strict regulation and monitoring can bring down the antimicrobial resistance in microorganisms. Audit and continuous surveillance of studies including the antimicrobial sensitivity patterns in ICUs may prove an important factor in reducing the increasing incidence of resistance against the available active agents [3].

Materials and Methods

Setting and design

A prospective, observational study was planned and performed from November 2013 till November 2014 in an ICU of a secondary care referral hospital, situated at resource challenged settings of South India.

Data Collection

Patient's demographic details, like infection detail, pathogen bio data with its sensitivity pattern were recorded from patient history and examination of patient case sheets. The organism's isolates were obtained from the clinical samples i.e. blood, urine, sputum, pus, peritoneal fluid, wound swab, tissue etc. Descriptive statistical analysis was employed which represents the results in percentages and assists in the explanation of the obtained data.

Isolation and Identification

Pathogens were identified after culture and verified by biochemical tests. Antimicrobial sensitivity patterns were obtained through Kirby Bauer disc diffusion method following CLSI guidelines [6-11].

A three-step identification procedure was employed in the identification of the organisms, which includes serological identification tests, biochemical identification tests followed by the staining techniques through which confirmation of the microorganism, the results are expressed in the form of graphs from images 01 to 09.

Results

The study was conducted for a period of 12 months, 111 patients were recruited and included in to the study after getting the informed consent of the patient willing to join the study. Basic demographic details of the patients were shown in table 1. Males to female ratio showed that more female patients were admitted. Predominant age group varies between 46 - 60 years.

Age in years	Male (%)	Female (%)	Overall (%)
15 - 30	12 (15.4)	18 (34)	30(22.9)
31 - 45	22 (28.2)	15 (28.3)	37 (28.3)
46 - 60	30 (38.5)	16 (30.2)	46 (35.1)
61-75	13 (16.6)	4 (7.5)	17 (13)
≥ 76	1 (1.3)	0 (0)	1 (0.7)
Total	78 (100.0)	53 (100.0)	131

Table 1: Demographic distribution of study participants.

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

285

A total of 295 clinical samples including different fluids were sent for microbial culture and sensitivity test. Microbial growth was obtained more from 1st sample as compared to repeated samples as shown in table 2.

Contents (microbial culture sensitivity response)	First Culture (N = 246)	Repeat Culture (N = 28)	Repeat Two (N = 7)	Repeat Culture ≥ Three (N = 14)
Positive response	80 (32.5%)	16 (57.2%)	3 (42.8%)	4 (28.6%)
Negative response	166 (67.5%)	12 (42.8%)	4 (57.2%)	10 (71.4%)
Total	246 (100%)	28 (100%)	7 (100%)	14 (100%)

Table 2: Growth of organisms at different points of cultures.

The methodology of identification of the microorganisms is explained schematically basing on the three different criteria of their identification features including serological tests, biological tests and staining techniques. The detailed methods are explained in the table 2, which is made self-understandable.

Gram-negative isolates were more as compared to Gram-positive organisms. *E. coli* was commonly isolated and identified, whereas among Gram-positive organisms *Corynebacterium* was predominantly identified. High rate of isolation of pathogens were obtained from sputum samples followed by pus, blood, tissue, urine, peritoneal fluid, wound swab and ascetic fluid samples. It was found that poly infecting organisms were present in single sample table 2.

The detailed information of the commonly prescribe antimicrobial sensitivity patterns against Gram-negative microorganisms, out of which most of the Gram-negative microbes showed high resistance levels against commonly prescribe antimicrobial agents. Whereas, *Proteus penneri* was sensitive to all antimicrobial agents used (Table 3) and the Gram-positive microbes showed high level of resistance against ciprofloxacin and other commonly prescribe antimicrobial agents (Table 4). The sensitivity pattern of infectious microorganisms is mentioned against commonly prescribe antibiotics were explained further in the figures 1 to 9.

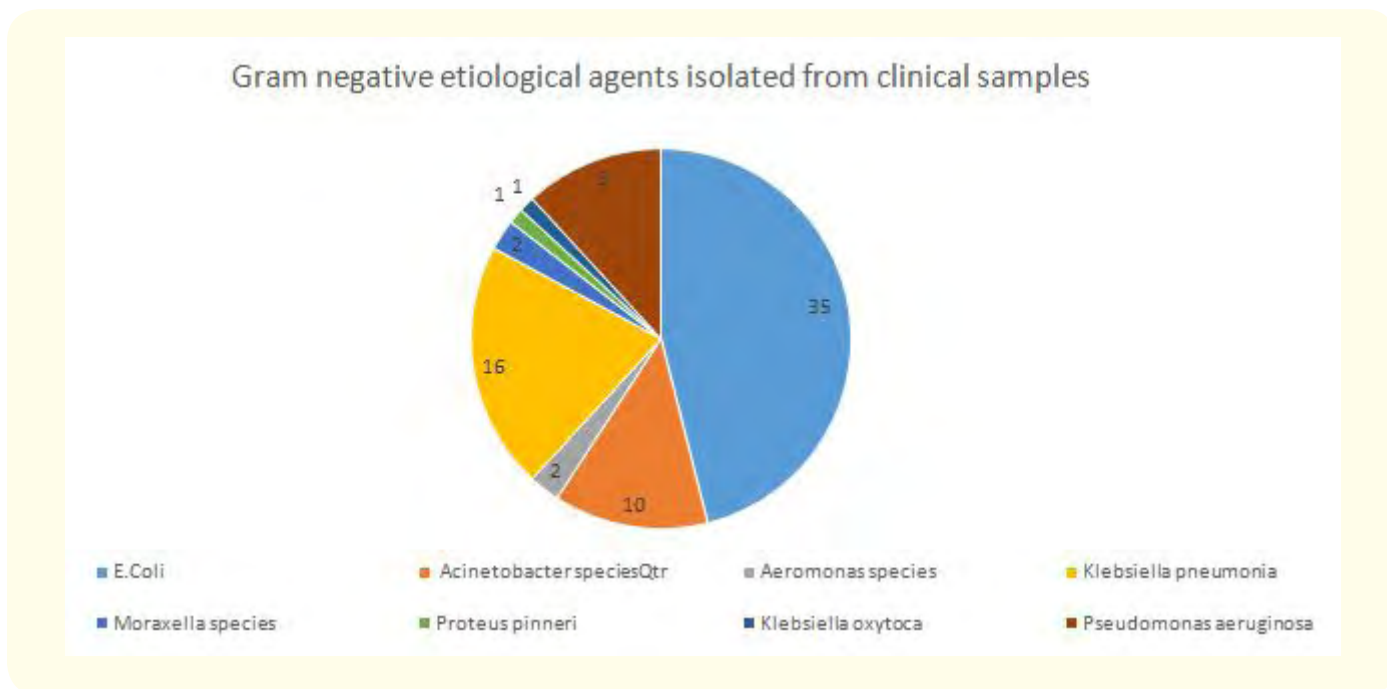| Isolated microorganism	Sensitivity	Intermittent	Resistance
E. coli	Co(13), Amik(29), Chlor(32), Cotri(8), Cipro(3), Cef(4), PT(3), Me(30), Amo(1), Ge(12)	Amik(2), Ge(10)	Amik(3), chlor(2), Cotri(26), cipro(31), cef(24),PT(28), Az(5), Me(4), Ampi(34), Amo(32), Ge(12)
Unidentified Gram-negative bacteria	Amik(1), Chlor(1), Cotri(1), Cipro(1), Cef(1), PT(1), Me(1)		Co(1), Amo(1), Ampi(1), Ge(1)
Pseudomonas aeruginosa	Co(3),Amik(2), Chlor(1), Cotri(1), Cipro(3), PT(4), Me(5), Ge(4)	Cipro(3), Me(1)	Amik(3), Cipro(1), PT(3), Me(1), Ge(2)
K. Pneumonia	Co(3), Amik(8), Chlor(12), Cotri(7), Cipro(6), Cef(3), PT(1), Me(12), Ampi(1), Ge(7)	Cipro(2)	Amik(6), Chlor(3), Cotri(4), Cipro(4), Cef(8), PT(12), Amo(14), Ampi(7), Ge(6)
Moraxella Sp	Co(1), Cotri(2), Cipro(2), Amo(2)		Amik(2), Chlor(2), Cef(2), PT(2), Ampi(2), Ge(2)
Proteus penneri	Co(1), Amik(1), Chlor(1), Cotri(1), Cipro(1), Cef(1), PT(1), Me(1), Amo(1), Ampi(1), Ge(1)		
K. Oxytoca	Chlor(1), Me(1)		Amik(1), Cotri(1), Cipro(1), Cef(1), PT(1), Amo(1), Ampi(1), Ge(1)
Aeromonas Sp	Amik(2), Chlor(2), Cotri(2), Cipro(1), Me(1), Ge(2)	PT(2)	Cipro(1), Cef(1), Me(1), Amo(2), Ampi(2)
Acinetobacter Sp	Co(6), Amik(3), Chlor(3), Cotri(2), Cipro(4), Cef(2), PT(3), Azi(1), Me(7), Amo(2), Ampi(1), Ge(3)	Amik(2), Clor(2), PT(1), Me(1)	Amik(6), Chlor(9), Cotri(10), Cipro(10), Cef(8), PT(8), Azi(6), Me(5), Amo(9), Ampi(8), Ge(9)
Enterobacter Sp	Amik(1), Chlor(3), Cotri(2), Me(2), Ampi(1), Ge(1),Doxy(2), Vanco(2)	Cipro(1)	Cotri(1), Cipro(1), Cef(1), PT(1), Amo(2), Ampi(2), Ge(2), Peni(1), Clin(1)

Table 3: Sensitivity pattern of Gram-negative isolates from various biological fluids.

Co: Colistin; Amik: Amikacin; Chlor: Chloramphenicol; Cotri: Cotrimoxazole; Cipro: Ciprofloxacin; Cef: Ceftriaxone; PT: Piperacilline/Tazobactum; Azi: Azithromycin; Me: Meropenem; Amo: Amoxicillin/Clavunate; Ampi: Ampicillin; Ge: Gentamicin
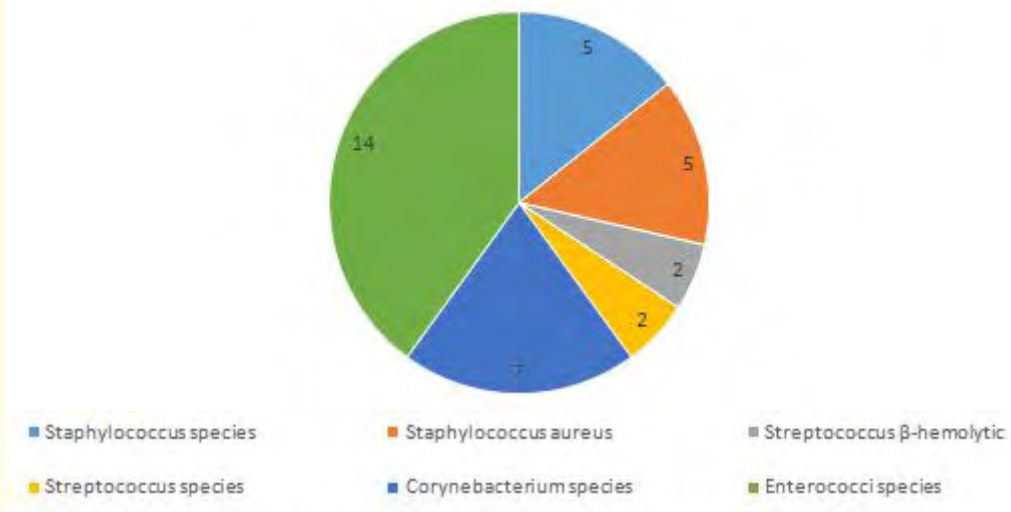
Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

286

Isolated microorganism	Sensitivity	Intermittent	Resistance
Corynebacterium Sp	Cipro(2), Cef(3), Azi(2), Me(5), Ge(1), Doxy(6), Vanco(6), Peni(2), Clin(1)	Cipro(3)	Cipro(1), Azi(4), Ge(5), Peni(4), Clin(4)
Enterococci Sp	Chlor(1), Vanco(1)		Cipro(1), Ampi(1), Peni(1)
Enterococcus Sp	Chlor(3), Cipro(1), Amo(1), Ampi(2), Doxy(3), Vanco(5), Peni(2), L(2)	Doxy(1)	Cipro(3), Ampi(3), Ge(5), Doxy(1), Vanco(1), Peni(3), Clin(3), Clo(1), S(3)
Enterococcus Faecalis	Chlor(4), Cipro(1), Amo(1), Ampi(2), Ge(2), Doxy(4), Vanco(5), S(2), L(2)		Chlor(1), Cipro(4), Ampi(3), Peni(5)

Table 4: *Sensitivity pattern of Gram-positive isolates from various biological fluids.*
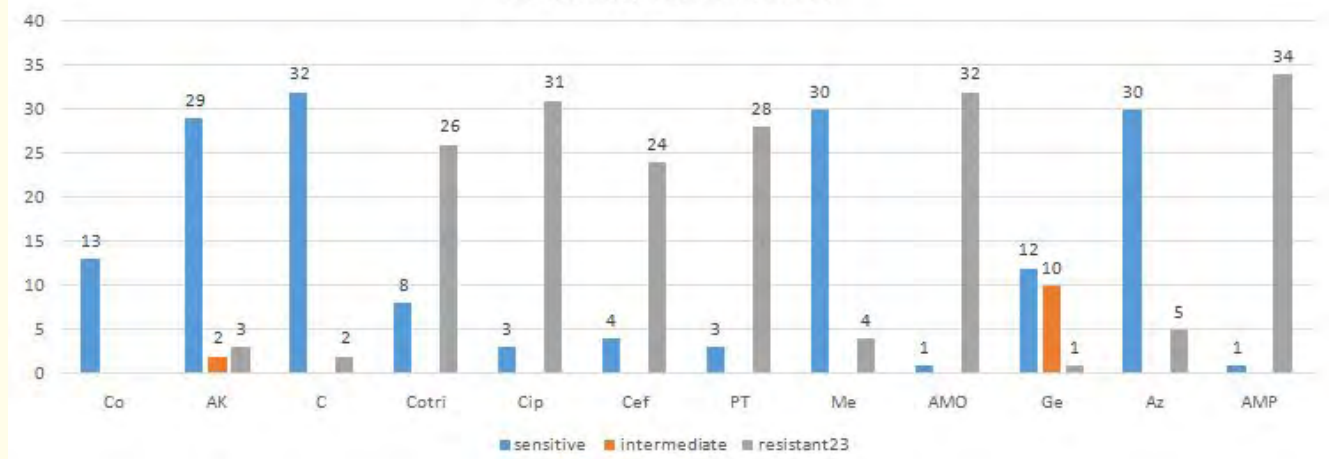
Amik: Amikacin; Chlor: Chloramphenicol; Cotri: Cotrimoxazole; Cipro: Ciprofloxacin; Cef: Ceftriaxone; Azi: Azithromycin; Me: Meropenem; Amo: Amoxicillin/Clavunate; Ampi: Ampicillin; Ge: Gentamicin; Doxy: Doxycycline; Vanco: Vancomycin; Peni: Penicillin-G; Clin: Clindamcin; Clo: Cloxacillin; S: Streptomycin; L: Linezolid
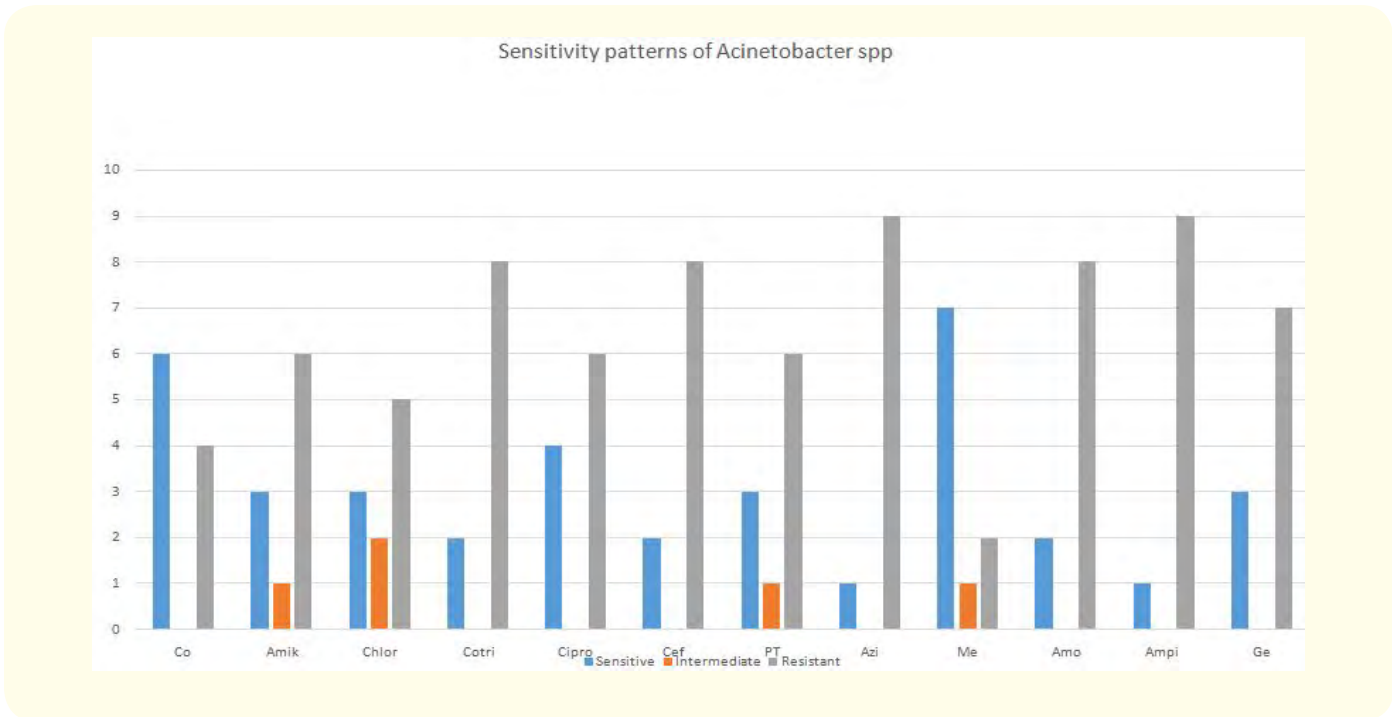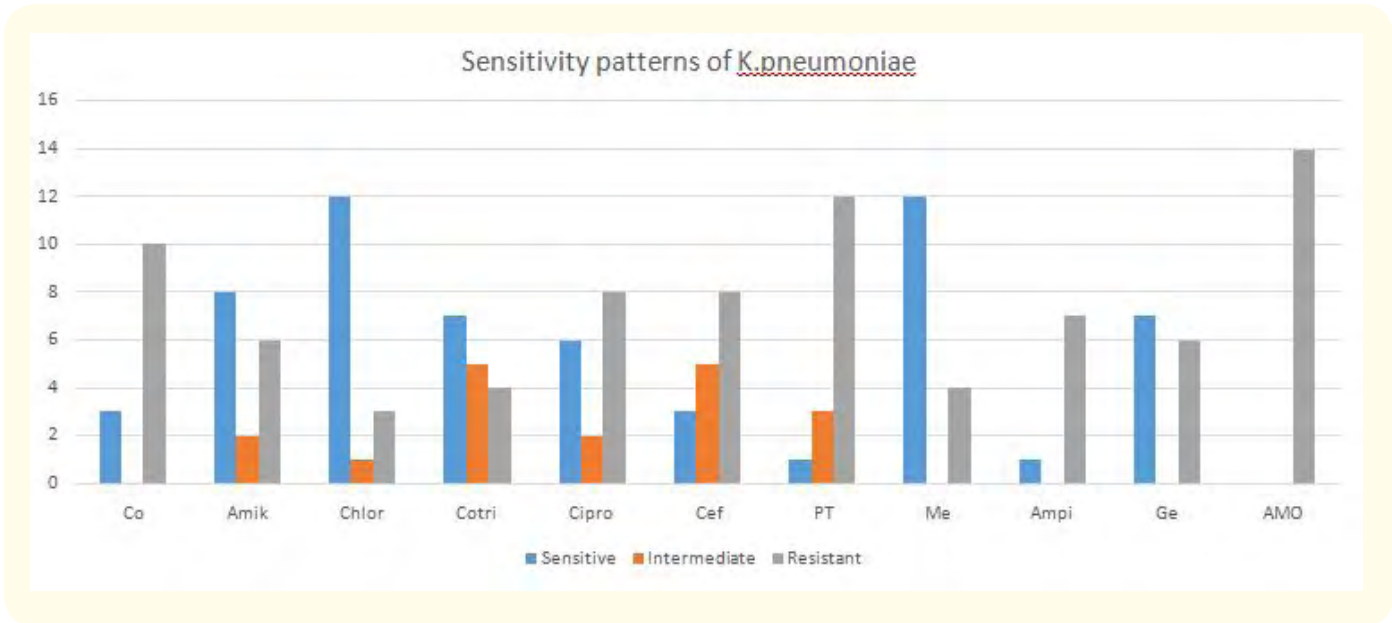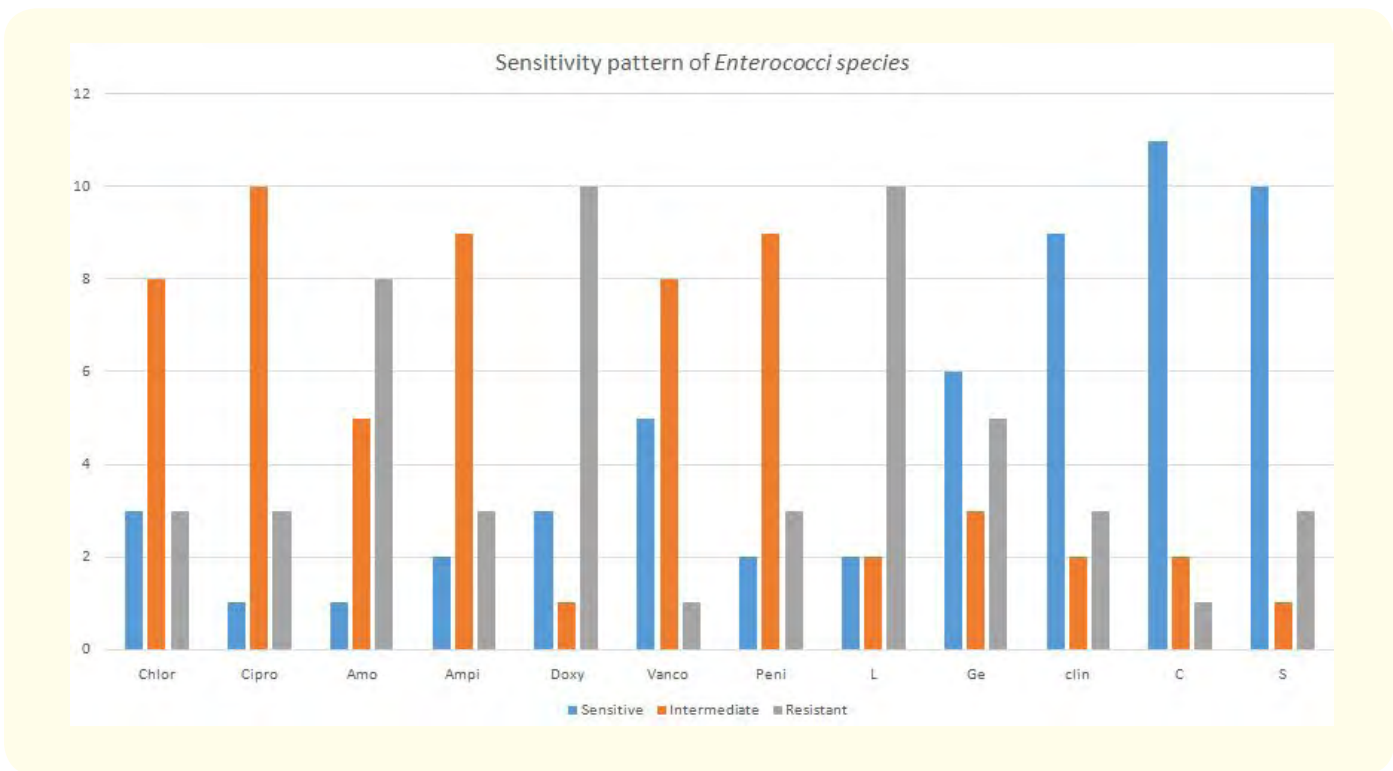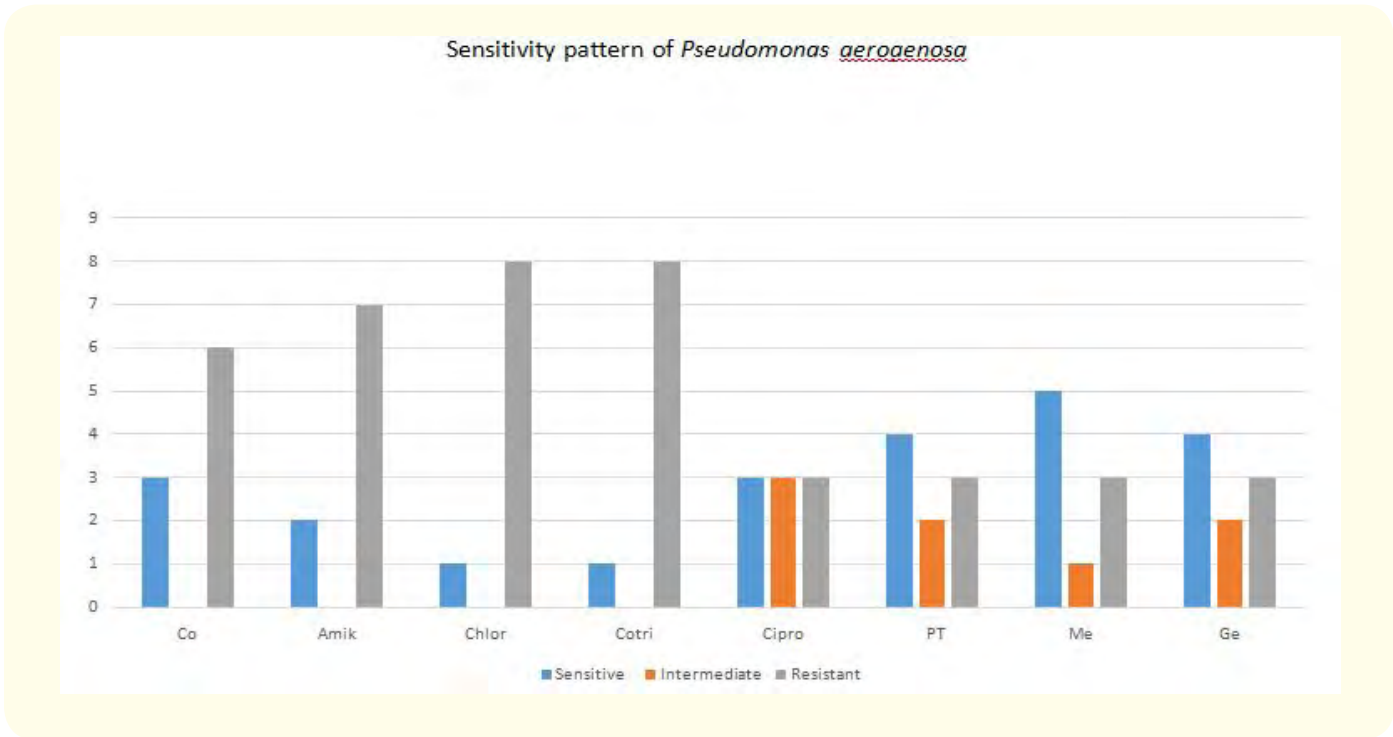

Gram negative etiological agents isolated from clinical samples

- E.Coli
- Acinetobacter speciesQtr
- Aeromonas species
- Klebsiella pneumonia
- Moraxella species
- Proteus pinneri
- Klebsiella oxytoca
- Pseudomonas aeruginosa

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

287

Gram positive etiological agents isolated from clinical samples

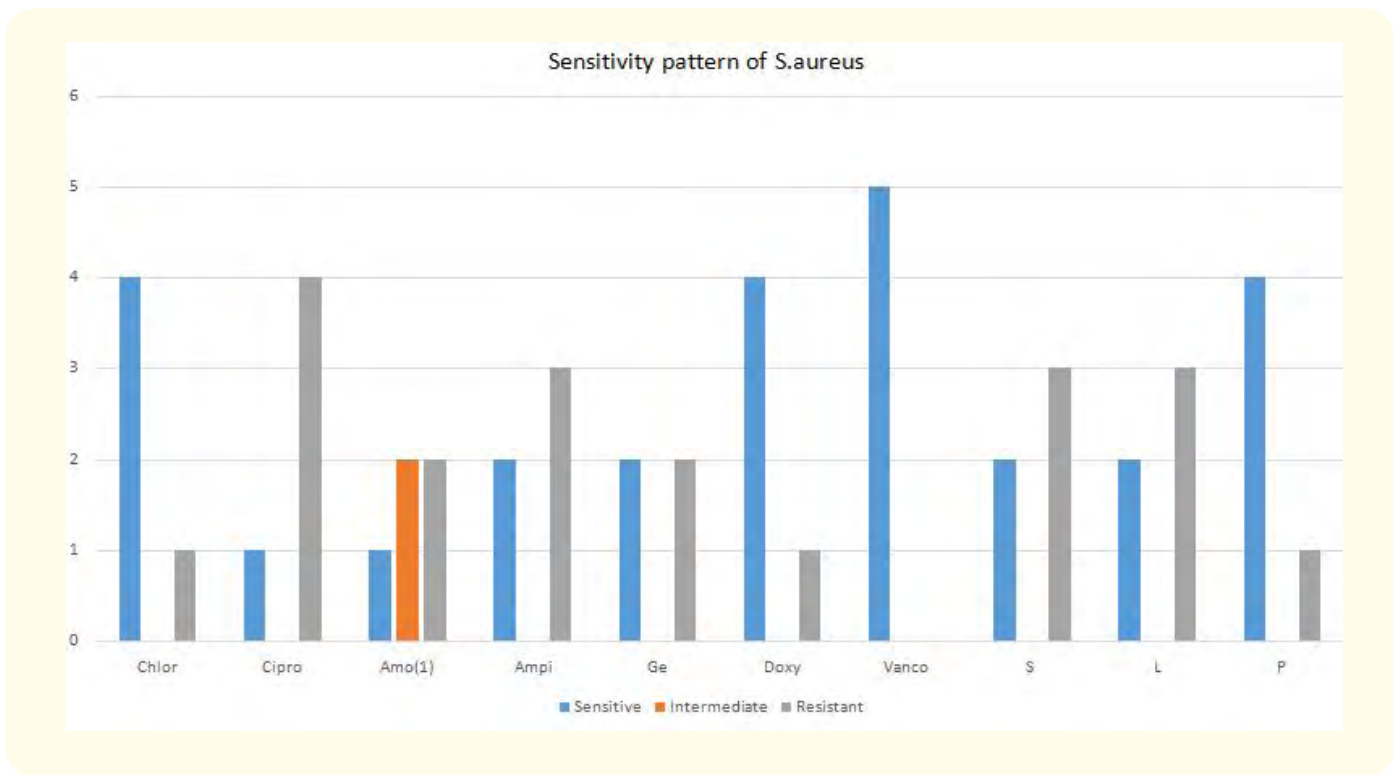
- Staphylococcus species
- Staphylococcus aureus
- Streptococcus β-hemolytic
- Streptococcus species
- Corynebacterium species
- Enterococci species

Sensitivity patterns of *E.Coli*

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

288

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

289

Sensitivity pattern of *Pseudomonas aerogenosa*

Sensitivity pattern of *Enterococci species*

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

290

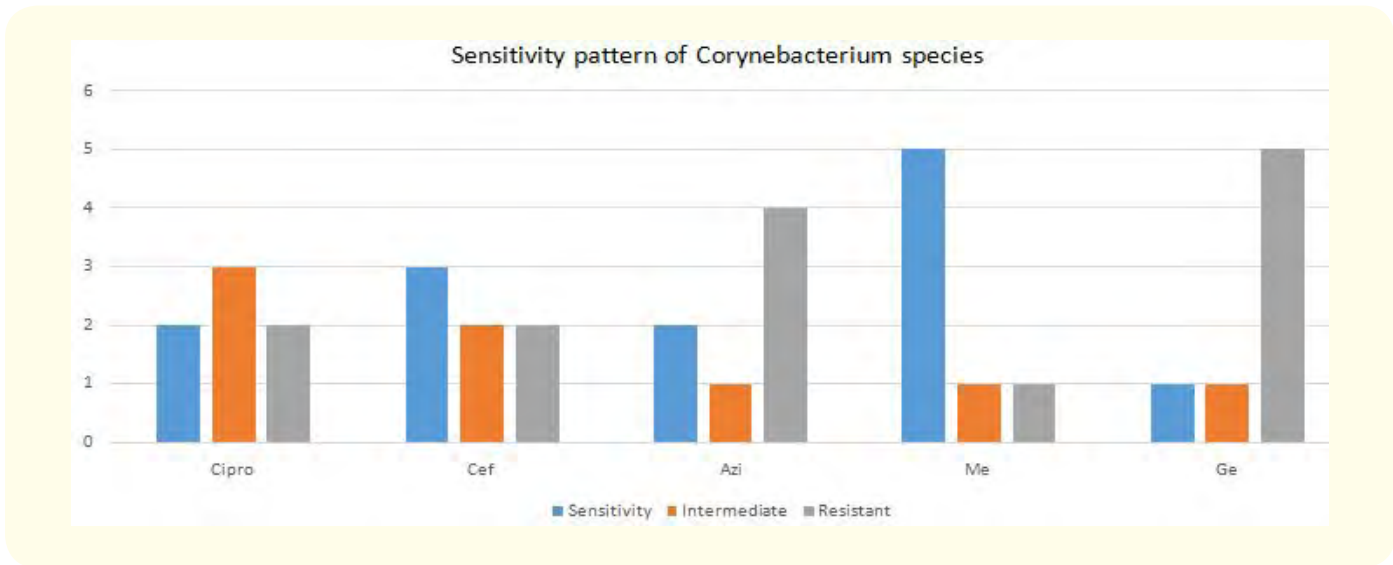Sensitivity pattern of Corynebacterium species

Sensitivity pattern of S.aureus

Discussion

Over a period of 12 months, 500 patients were admitted in the ICU with 295 clinical samples for culture and sensitivity were evaluated from 111 patients (68 males and 43 females). Out of these 116 (39.3%) showed spectrum of pathogens (38 Gram-positive isolates and 78 Gram-negative isolates) from various biological fluids.

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

291

Antimicrobial agents (AMs) are among the most commonly used drugs in ICU. Antimicrobial resistance in ICUs is of great concern as it increases the drug interactions/side effects and cost of therapy which can be a reason for prolonged hospital stay or readmission. The problem of resistance in a hospital is difficult to understand without the knowledge and understanding of antimicrobial sensitivity pattern, therefore continuous surveillance studies and review of sensitivity pattern are important [3].

With lower respiratory [3] tract being the part of infection which slightly contradict with one study as most of the infections are related to upper respiratory tract, surgical site infections and peritoneal cavity. Drugs belonging to the following classes of penicillin's, quinolones and antifungal [3], were used for the treatment of infections, whereas, our study states that the infections were treated by employing Cephalosporin's, anti-bacterial empirically.

Infectious organisms has shown high resistance to β –lactum antibiotics and susceptibility to Meropenem (100%), Fluroquinolones (100%) and gentamicin (83.3%) [3]. In the present study, Gram-negative were resistant to fluroquinlones like ciprofloxacin, cephalosporines like ceftriaxone, penicillines like amoxicilline/clavulanate, ampicillin, piperacilline/tazobactum and susceptible to colistin, chloramphenicol, amikacin, co-trimoxazole, meropenem and gentamicin. Gram-positive were resistance to ciprofloxacin, azithromycin, gentamicin, penicillin-G, ampicillin and clindamycin and susceptible to doxycycline, meropenem, streptomycin and linezolid.

In a study, presented by Arunpatel*., et al*. it is explained that the culture growth of microorganism has shown the presence of 10 different organisms like *E. coli, Klebsiella* species, *Proteus* species, *Pseudomonas* species, *Enterobacter* species, *Salmonella* species, *Acinetobacter* species, *Streptococcus* species, *Staphylococcus aureus* and *Candida* species [5] and in the current study totally 107 organisms were isolated belonging to 12 different classes like *E. coli, Klebsiella* species, *Acinetobacter* species, *Pseudomonas* species, *Aeromonas* species, *Moraxella* species, *Proteus* species, *Corynebacterium* species, *Enterococcus* species, *Staphylococcus* species, *Streptococcus* species which resembles the entire pattern, with only *Aeromonas* being identified in our study as exceptional pathogens as reported in above study.

According to Sachinejain., *et al*. their work successfully identified the increased pattern of Gram-negative infection with resistance in ICU during the study period of two years. It also explains that the high use of broad spectrum beta-lactamases has led to multi drug resistance in *E. coli, Klebsiella* species, *Acinetobacter* species*, Pseudomonas* species etc making therapy extremely difficult [1]. In the present study 94% organisms were identified to be resistance to penicillin, out of which 100% *E. coli* were resistance to ampicillin, 91.15% organisms were resistance to fluoroquinolones (ciprofloxacin), 82.3% organisms were resistance to piperacillin/tazobactam, 76.47% organisms were resistant to Co-trimoxazole, 70.58% organism were resistant to ceftriaxone and 35.29% organisms were resistant to gentamicin. High antibiotic resistant strains from clinical isolates are alarming and warrant investigation

A better outcome in the management of the ICU admitted patients with microorganism infections can be achieved by following the WHO core drug use indicators which have proved better in the clinical applications of the antimicrobial agents meant for the better outcomes [12]. such applications have proven better in the management of disorders and improving the quality of life among patients suffering with the complicated but yet manageable challenges i.e. management of diabetic retinopathy [13,14], epilepsy [15], reducing the diarrheal impacts among the paediatric patients [16]. Even following the guidelines has beneficial outcomes even in the case of development of newer chemotherapeutic agents necessary for the management of the chronic diseases [17].

Hence, a streamlined approach with research support may help in improving the quality of life by reducing the pain and suffering of the diseased population through reducing the hospital stay by resulting in improving the economical, sociological and psychological status of the patients.

Conclusion

Because of the variations in the microbial species no single chemotherapeutic has proven best for the management of all the infections. Hence, every microorganisms was needed a separate agent to be treated basing upon the results obtained after the culture sensitivity test for each organism.

Recognising the Resistance Pattern of Micro-Organisms in the Subjects Admitted in the ICU – A Prospective, Observational Study

292

Conflict of Interest

None.

Bibliography

1. Sachin Jain ZK. "Changing Antimicrobial Resistance Pattern of Isolates from an ICU Over a 2 Year Period". *Journal of the Association of Physicians of India* 60 (2012): 27-33.

2. Alberto Sandiumenge ED., *et al.* "Impact of diversity of antibiotic use on the development of antimicrobial resistance". *Journal of Antimicrobial Chemotherapy* 57.6 (2006): 1197-1204.

3. Kaushal V., *et al.* "Antibiotic Sensitivity Pattern of Bacterial Isolates from the Intensive Care Unit of a Tertiary Care Hospital in India". *Tropical Journal of Pharmaceutical Research* 11.6 (2012): 991-999.

4. Vishal Anand., *et al.* "Incidence and Outcome of Ventilator Associated Pneumonia". *Journal of the Association of Physicians of India* 61.8 (2013): 554-557.

5. Arun Patil KP., *et al.* "Isolation and Survey of Antibiotic Sensitivity in Nosocomial Infections in North Maharashtra Region". *Journal of the Association of Physicians of India* 61.7 (2013): 454-458.

6. Cummins CS. "Identification of Propionibacterium acnes and Related Organisms by Precipitin Tests with Trichloroacetic Acid Extracts". *Journal of Clinical Microbiology* 2.2 (1975): 104-110.

7. Standards Unit MS, PHE. "ID 19-Identification of Vibrio and Aeromonas species" (2014): 1-30.

8. Nadheema Hammood., *et al.* "Serological relatedness among clinical and environmental Acinetobacter baumannii isolates isolated from hospitals in Baghdad". *Iraqi Journal of Science* 54.3 (2013): 553-559.

9. Sherman JM. "The Enterococci and Related Streptococci". *Journal of Bacteriology* 35.2 (1937): 81-93.

10. Standards Unit MS, PHE. "ID 4-Identification of Streptococcus species, Enterococcus species and Morphologically Similar Organisms" (2014): 2-36.

11. Kishore J. "Isolation, identification and characterization of Proteus penneri-a missed rare pathogen". *Indian Journal of Medical Research* 135.3 (2012): 341-345.

12. Prasad PS., *et al.* "Assessment of drug use pattern using World Health Organization core drug use indicators at Secondary Care Referral Hospital of South India". *CHRISMED Journal of Health and Research* 2.3 (2015): 223-228.

13. Sadiq MJ., *et al.* "A study on evaluation of bevacizumab in the management of diabetic retinopathy". *Egyptian Retina Journal* 4 (2017): 46-48.

14. Sajida S., *et al.* "A possible case of complete loss of vision after intra ocular administration of bevacizumab: Case report". *Indian Journal of Pharmacy Practice* 6.1 (2013): 82-83.

15. Srujana MP., *et al.* "Assessment of quality of life in children with epilepsy in rural settings of South India: A cross sectional study". *CHRISMED Journal of Health and Research* 4.2 (2017): 110-116.

16. Sunanda G., *et al.* "Impact of structured educational program on maternal knowledge, attitude, and practice toward diarrhea management in children <5 years in Anantapur district". *CHRISMED Journal of Health and Research* 4.3 (2017): 186-193.

17. Reddy YP., *et al.* "A study of Nigella sativa induced growth inhibition of MCF and HepG2 cell lines: An anti-neoplastic study along with its mechanism of action". *Pharmacognosy Research* 7.2 (2015): 193-197.