



Prevalence and Control of Multi Drug Resistant (MDR) Nosocomial Pathogens Isolated from Hospital Wards (Surgical, Medical, Paediatric and Labor Unit)

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Nosocomial infection have increased and gained attention because of high isolation rates of multi drug resistant (MDR) organism in admitted and out patients in hospitals with complicated infectious ailments. The spread of multi drug resistant organisms among critically ill, hospitalized patients and subsequent epidemics, have become an increasing cause of concern. A recent manifestation of multi drug resistant organisms that has attracted public attention due to high mortality and morbidity rate is alarming.

Aims: To access the prevalence of multidrug resistant nosocomial pathogens in hospitalized patients.

Materials & Methods: This was a hospital based cross sectional study from January 2013 to December 2017. Almost 700 hospitalized and out patients who acquired nosocomial infections (NI) were enrolled, with the permission of ethical and research review committee and with the informed

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consent to the patient and attendant. Clinical samples were analysed for antibiotic sensitivity pattern by Kirby Baur method according to CLSI guidelines [1].

Results: Data analysis showed that 63% were female patients and 37% were male patients included. Almost 37% prevalence of etiological agents was found. Predominant were *E.coli*, followed by *Klebsiella pneumoniae*, *Acinetobacter* spp, and *Staphylococcus aureus*. Antibiotic resistance rate was found very high i.e up to 55 - 90% against commonly prescribed antibiotics in hospitalized and out patients having nosocomial infection resulting complicated infections.

Conclusion: Emergence of MDR strains in nosocomial infection (NI) is a matter of great concern and warrant investigation. There is need to adopt infection control strategies in public and private secondary tertiary care hospitals.

Keywords: Multi drug resistant (MDR); nosocomial infection (NI); pathogens.

ABREVIATIONS

- *MDR: Multi-drug resistant*
- *NI: Nosocomial infection*
- *ESBL: Extended-spectrum betalactamase*
- *E.coli: Escherichia coli*
- *S.aureus: Staphylococcus aureus*
- *UTI: Urinary tract infections*
- *U.S: United state*
- *CLSI: Clinical & Laboratory Standards Institute*
- *AMC: Augmentin*
- *CRO: Ceftriaxone*
- *ATM: Aztreonam*
- *IPM: Imipenem*
- *AK: Amikacin*
- *CIP: Ciprofloxacin*
- *FOS: Fosfomycin*
- *SCF: Sulzone*
- *DOX: Doxycycline*
- *TZP: Tazobactam*
- *C: Chloramphenicol*
- *CT: Colistin*
- *SXT: Sulphamethoxazole Trimethoprim*
- *F: Nitrofurantoin*
- *OX: Oxacillin*
- *LZD: Linezolid*
- *VA: Vancomycin*
- *E: Erythromycin*
- *CLED: Cystine-Lactose-Electrolyte Deficient Agar*

1. INTRODUCTION

More than 2 million people, or approximately 5 to 10% of hospitalized patients, are affected by nosocomial infections (NI) with a death rate of estimated 90,000 deaths per year in United States. As well as to modify the disease burden regarding significant morbidity and mortality of nosocomial infections, high healthcare costs are incurred in managing nosocomial infections [2].

Nosocomial infection develops within or after 48 hours of hospital admission or being discharged. [3]. Patients admitted to the ward have been shown to be at particular risk of acquiring nosocomial infection (NI) with high prevalence rate [4]. Hospital environment plays a significant role in the occurrence of nosocomial infection since it harbors a diverse population of microorganisms [5].

Multiple drug resistant (MDR) organisms are bacteria and other microorganisms that have developed resistance to antibiotics [6]. The misuse and overuse of antibiotics is worldwide both in poor and developing countries it has also increased the rate of antimicrobial resistance around [7].

Infections caused by multi-drug resistant microorganisms (MDR), often do not respond to conventional therapy and can result in prolonged illness and hospital stay as well as higher morbidity and mortality rates. Hospital acquired infections mainly occurred in surgical site infections (SSI), ventilator associated pneumonia (VAP), blood stream and urinary tract infection (UTI), and are commonly known as nosocomial infections (NI), mostly caused by extended spectrum of beta lactamases (ESBL) producing enteric pathogens and non-fermenting gram-negative organisms etc. [8].

Antimicrobial resistance among gram negative bacilli represents a major problem in nosocomial infection [9]. According to recent report, more than 30% of hospital acquired infections are due to gram negative bacteria in U.S, the majority of ventilator-associated pneumonia (47%) and UTI (45%) cases are associated with these bacteria [10].

While antimicrobial agents are considered as a solution for infectious disease, resistance of

microorganisms to various drugs has raised new problems, especially for hospital acquired infections therefore research should be conducted on risk factors related to the transmission of such infections. However, emergences of multi-drug resistance strains have left limited treatment options, so monitoring multi drug resistant organisms (MDROs) and the infections they cause in a healthcare setting warrant investigation for the wellbeing of vulnerable patient populations, and effectiveness of interventions [2].

Several studies have identified general characteristics of patients that place them at high risk for acquisition of multidrug resistant (MDR) outbreak strains [11]. However, the diversity of risk factors suggests that separate investigations should be performed in each hospital setting [2].

Therefore, identification of a microbe and determining susceptibility pattern are beneficial to the patient and assist in selection of therapy to avoid emergence of multidrug resistance organisms in hospital [12]. There are numerous reports describing the successful control of nosocomial outbreaks, but there is little data regarding control of the endemic setting. Hospital staff education was emphasized to improve their perception of and adherence to hand hygiene protocols, as well as to improve their understanding regarding the importance of controlling multidrug resistant (MDR) nosocomial infection [13]. Monthly education of new staff will perform by infection control staffs. Importance of personal protective equipment (PPE) sterilization of equipment for patients and caregivers wellbeing should be taken as of prime importance and exclusive to prevent cross-transmission between these patients in the hospital wards. The importance of clean environment for infected patients at least 3 times per day should be highlighted with the availability of alcohol-based hand rub sanitizer at all bed sides [14]. Campaigns and awareness sessions for hand hygiene should be conducted as hand colonization contributes significantly transmission and can be controlled by follow biosafety and biosecurity methods and use of antiseptic- or alcohol-based soaps [15].

2. MATERIALS AND METHODS

2.1 Study Design

This study was a hospital based observational retrospective cross sectional study to

determine the MDR nosocomial infection and its control.

2.2 Study Setting

Karachi is a metropolitan city of Pakistan, with more than 12 million population and hub of commercial activities. Large number of people from other parts of country lives and worked in Karachi due to employment opportunities. This study was conducted in "Chiniot general hospital" catering the health-care facilities, for indoor and outdoor patients including, Medicine, Pediatric, surgical, Gynecology and labor unit specialties.

2.3 Study Population

This is cross sectional study including in patients and out patients in surgical, medical, general unit with some serious infectious disease. All patients reporting some infectious condition were included; Patients with other morbid conditions were excluded. Study was also carried out in private secondary and tertiary care hospitals of Karachi city.

2.4 Sample Size

A total number of samples 700 patients were investigated.

2.5 Sampling Method

For demographic analysis of contributing risk factors and data analysis surveillance form was distributed to patients or their attendant's. For any ethical issues informed consent was taken after face to face interview. Clinical specimens obtain from patients with nosocomial infections included urine, blood, pus, sputum, ET-secretion, tracheal aspirates, urine catheter tips and body fluids were collected and were processed at microbiology laboratory of the native hospital Karachi. The specimens were cultured onto suitable culture media like MacConkey agar, sheep blood agar, chocolate agar CLED media and Sabouraud's agar. Plates were incubated aerobically for 24-48 hours. The isolates were identified by colonial morphology, gram-staining, biochemical tests like catalase, coagulase, oxidase, bile solubility. Antimicrobial susceptibility testing was performed on Mueller Hinton agar using disc diffusion method in accordance with CLSI [16]. Zone sizes of each antimicrobial agent were recorded and interpreted as resistant, intermediate or

susceptible. Intermediately susceptible isolates were considered resistant. Susceptibility was tested against following antimicrobials according to their spectrum of activity against Gram-positive or Gram-negative bacteria. Antimicrobials tested against Gram-positive bacteria were: AMC, CRO, ATM, IPM, AK, CIP, FOS, SCF, Dox, TZP, C, CT, SXT, LZD, VA and F. Methicillin resistance in MRSA was tested using OX discs. Antimicrobials tested against Gram-negative bacteria were AMC, CRO, ATM, IPM, AK, CIP, FOS, SCF, DOX, TZP, C, CT, SXT and F.

Microsoft Excel spread sheet was used to analyze the data in the form of percentages.

2.6 Ethical Concern

Prior permission and informed consent from hospital's central ethical research committee was taken.

3. RESULTS

Pathogenic bacteria have increasingly been shows resistant to antimicrobial therapy. Recently, resistance problem has been relatively much worsened in gram-negative bacilli causing infections and high mortality, almost exclusively in compromised hospital patients. It is known to be difficult to prevent emergence of multidrug resistant (MDR) infectious agents in hospitalized patients, because the organisms are ubiquitous in hospital environment, efforts to control resistant pathogens been not successful worldwide. We need concerted multidisciplinary efforts to preserve the efficacy of currently available antimicrobial agents, by following the principles of antimicrobial stewardship.

700 patients admitted at private hospital catering the needs of tertiary care setting were recruited and 285 clinical isolates were recovered during the study period of four years (January 2013-December 2017). Details of these isolates are mentioned in [Table 4].

Analysis of demographic data showed out of 700 samples 62% were females and 38% were males who presented with complications of infectious diseases [Table 1, Fig. 1].

Data analyzed showed that age group 46- 60 was the most prominent among hospitalized patients with different ailments followed by 31-45 age groups.

Table 1. Basic information of studied sample gender

Gender	N	%
Female	440	63
Male	260	37

Table 2. Basic information of studied sample – age group

Age	N	%
1 – 15	86	12.3
16 – 30	97	13.85
31 – 45	115	16.4
46 – 60	194	27.18
61 – 75	110	15.71
76 – 100	98	14.0

Out of total 700 samples, 285 were found positive for the presence of Spectrum of MDR pathogenic isolates. [Table 3, Fig. 2]. Almost 41.9% recruited patients were diagnosed with the presence of different pathogens.

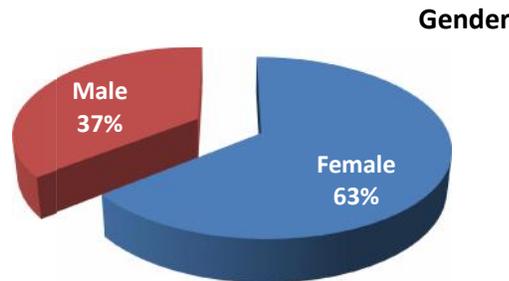


Fig. 1. Basic information of studied sample gender

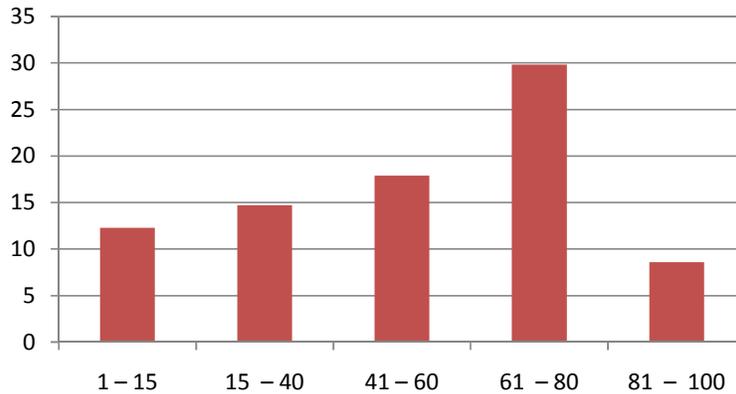


Fig. 2. % age distribution of Pathogenic isolates

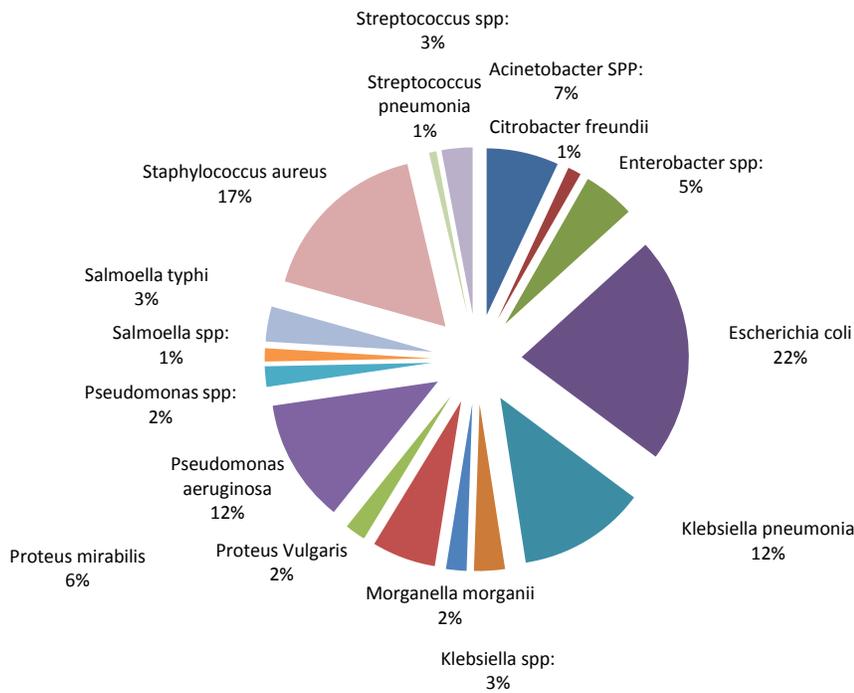


Fig. 3. Spectrum of MDR isolate

Table 3. % age distribution of isolated pathogens

Growth	n	%
No growth	442	63
Pathogen diagnosed	285	37

It was found that 41.9% samples were found with the presence of multidrug resistant (MDR) pathogens. However 19.3% *Escherichia coli* strains were found predominant, followed by 17.54% *Staphylococcus aureus*,

10.53% *Salmoella typhi*, 9.47% *Pseudomonas aeruginosa*, 7.02% *Acinetobacter spp* others as shown in [Table 4, Fig. 3].

Table 4. Spectrum of MDR isolates

S. no.	Pathogenic isolates	n	%
1	<i>Acinetobacter SPP:</i>	20	7.02
2	<i>Citrobacter freundii</i>	10	3.51
3	<i>Enterobacter spp:</i>	8	2.81
4	<i>Escherichia coli</i>	55	19.30
5	<i>Klebsiella pneumonia</i>	49	17.19
6	<i>Morganella morganii</i>	3	1.05
7	<i>Proteus mirabilis</i>	19	6.67
8	<i>Proteus Vulgaris</i>	3	1.05
9	<i>Pseudomonas aeruginosa</i>	27	9.47
10	<i>Pseudomonas spp:</i>	3	1.05
11	<i>Salmoella typhi</i>	30	10.53
12	<i>Staphylococcus aureus</i>	50	17.54
13	<i>Streptococcus pneumonia</i>	8	2.81

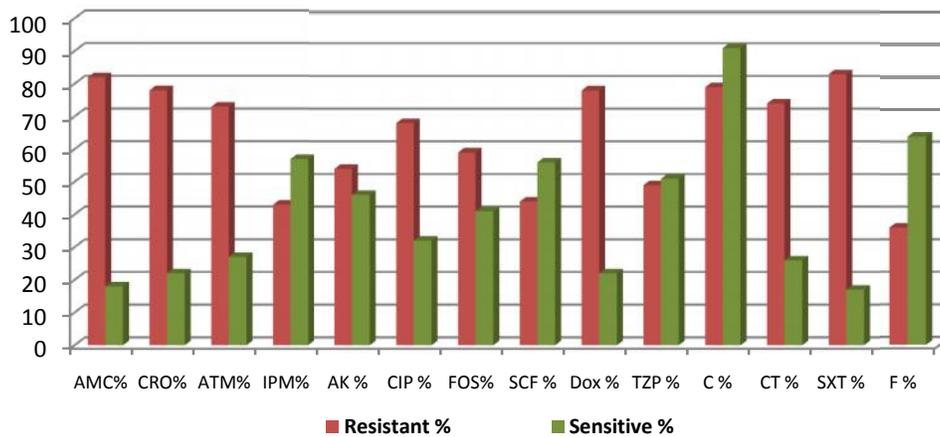


Fig. 4. Spectrum of Gram negative MDR susceptibility patterns of isolates

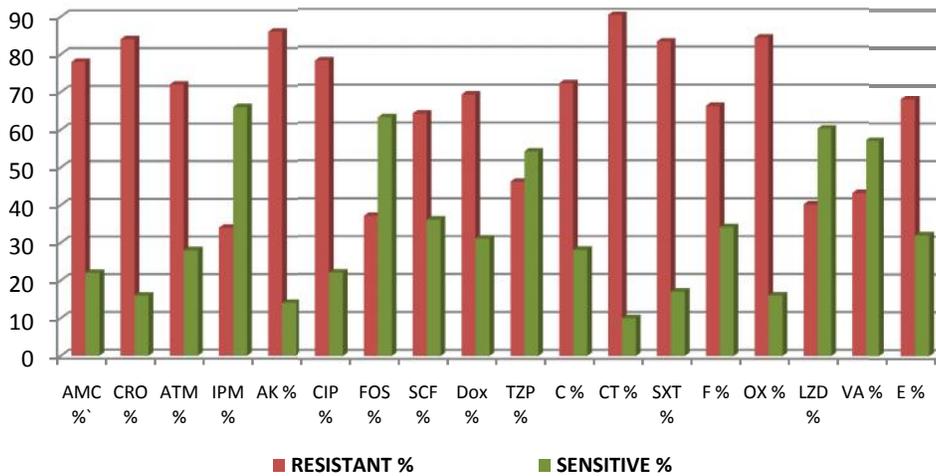


Fig. 5. Spectrum of Gram positive MDR susceptibility pattern of isolates

Table 5. Spectrum of Gram negative MDR susceptibility patterns of isolates

S no.	Isolated pathogens	AMC%	CRO%	ATM%	IPM%	AK%	CIP%	FOS%	SCF%	Dox%	TZP%	C%	CT%	SXT%	F%
1	<i>Acinetobacter SPP:</i>	93	93	93	65	93	93	93	93	80	52	93	83	98.	45
2	<i>Citrobacter freundii</i>	80	10	40	60	30	30	20	30	70	50	80	60	80	10
3	<i>Enterobacter spp:</i>	75	75	62.	37	62	50	25	50	50	50	62	50	62	37
4	<i>Escherichia coli</i>	81	87	81	32	40	63	45	43	72	58	81	65	81	36
5	<i>Klebsiella pneumonia</i>	73	94	82	26	49	79	77	31	84	57	71	92	92	59
6	<i>Morganella morganii</i>	66	66	66	0	33	66	66	33	66	66	66	66	66	0
7	<i>Proteus mirabilis</i>	68	79	68	31	58	84	53	47	63	42	58	68	84	37
8	<i>Proteus Vulgaris</i>	100	100	100	33	66	100	33	33	100	0	100	100	100	0
9	<i>Pseudomonas aeruginosa</i>	81	74	85	87	63	70	70	59	85	74	92	78	96	52
10	<i>Pseudomonas spp:</i>	100	100	33	66	33	33	100	0	100	33	66	66	66	33
11	<i>Salmoella typhi</i>	83	80	90	40	63	80	63	70	87	57	93	90	93	53
	RESISTANT	82	78	73	43	54	68	59	44	78	49	79	74	83	36
	SENSITIVE	18	22	27	57	46	32	41	56	22	51	21	26	17	64

Table 6. Spectrum of gram positive MDR susceptibility pattern of isolates

Isolated pathogens	AMC%	CRO%	ATM%	IPM%	AK%	CIP%	FOS%	SCF%	Dox%	TZP%	C%	CT%	SXT%	F%	OX%	LZD%	VA%	E%
<i>Staphylococcus aureus</i>	92	80	94	30	96	70	50	78	64	56	82	94	92	82	68	56	50	86
<i>Streptococcus pneumoniae</i>	63	87	50	50	75	87	25	50	75	37	62	87	75	50	100	25	37	50
RESISTANT	78	84	72	72	86	78	37	64	69	46	72	90	83	66	84	40	43	68
SENSITIVE	22	16	28	28	14	22	63	36	31	54	28	10	17	34	16	60	57	32

1. Sensitivity Pattern of *E. coli*:

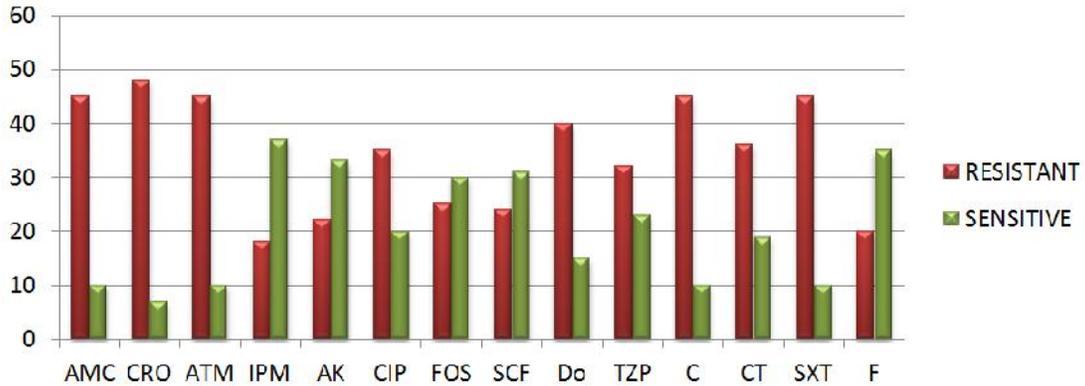


Fig. 6. Sensitivity Pattern of MDR *E. coli* susceptible pattern of isolates

2. Sensitivity Pattern of *Klebsiella pneumonia*:

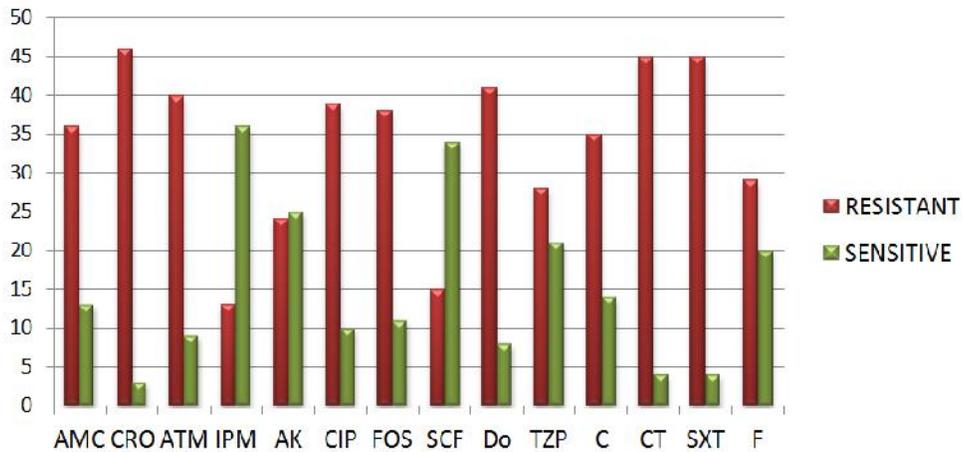


Fig. 7. Sensitivity Pattern of MDR *Klebsiella pneumonia* susceptible pattern of isolates.

3. Sensitivity Pattern of *S.aureus*

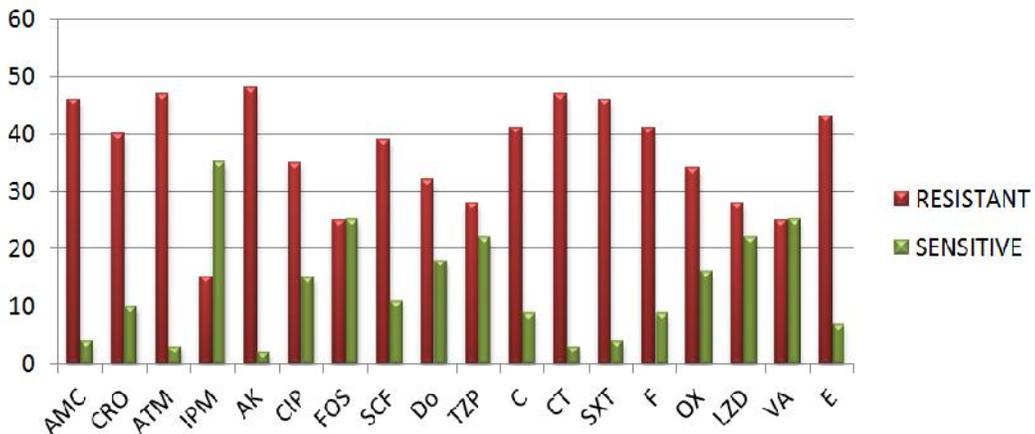


Fig. 8. Sensitivity Pattern of MDR *S.aureus* susceptible pattern of isolates.

4. Sensitivity Pattern of *Pseudomonas aeruginosa*

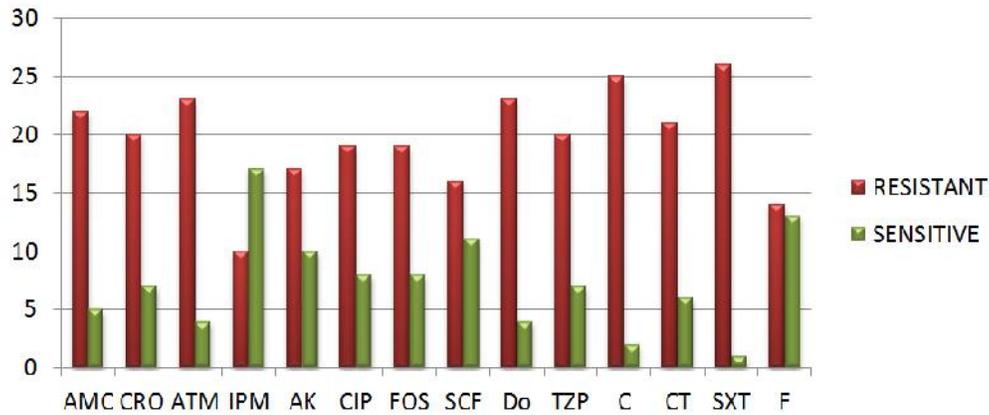


Fig. 9. Sensitivity Pattern of MDR *Pseudomonas aeruginosa* susceptible pattern of isolates.

5. Sensitivity Pattern of *Acinetobacter SPP*

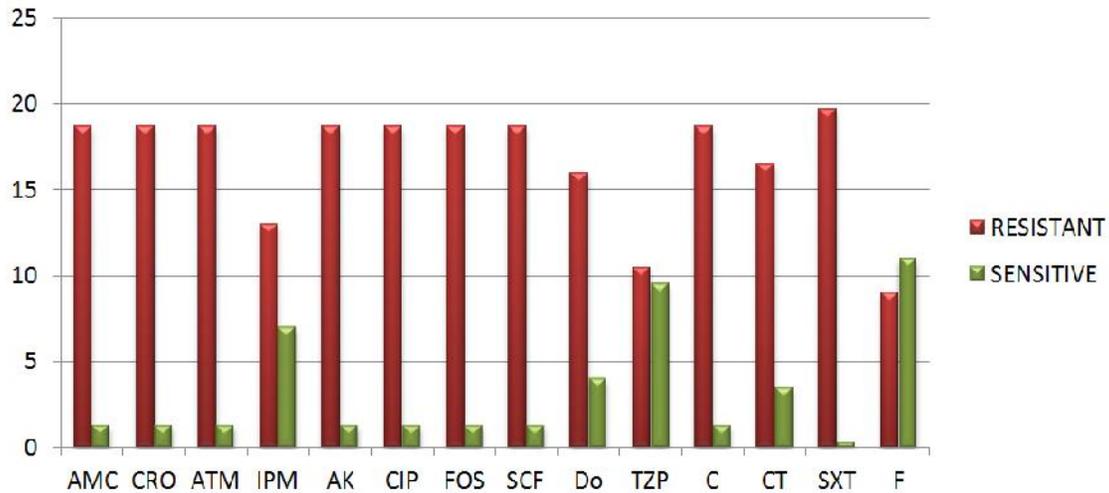


Fig. 10. Sensitivity Pattern of MDR *Acinetobacter SPP*: susceptible pattern of isolates.

4. DISCUSSION

More than 2 million people, or approximately 5% to 10% of hospitalized patients, are affected by nosocomial infections with an estimated 90,000 deaths every year [2,3]. In the United States alone the disease burden regarding significant morbidity and mortality is responsible for 8 million physician visits and more than 100 thousand admissions to the hospital per year [3].

Antibiotics play vital role in the treatment of microbes in infectious diseases and eradication of infections. However, emergence and dissemination of multi-drug resistant strains as a

result of overuse of antibiotics is a major concern among different groups of enterobacteriaceae like (ESBL) β -lactamase producing *E. coli*, *K. pneumoniae*, and many others. Multi-drug resistant strains of *E. coli* and *K. pneumoniae* are widely distributed in hospitals and are increasingly being isolated from community acquired infections. This alarming situation has increased frequently in last few years resulting in severe consequences i.e increased cost of medicines and mortality of patients.

According to demographic data analysis showed that male to female ratio (62%-38%) is very significant as more number of females patients

were enrolled in this study may be due to frequent UTI infections and gynecological problems among female population .it was much lower in other reported studies from developed countries where almost 30% registered patients were female, where as in developing countries ratio is high probably due to low socioeconomic and low personal hygienic profile [Table 1, Fig. 1]. The predominant age group suffering from nosocomial infection in this study is 46-60 [Table 2, Fig. 2].

The results does not correlate with the reported studies from developed countries where mostly sick persons acquiring nosocomial infections are more than 60 years of age [16,17].

Almost in 75% to 90% of the cases *E.coli* remains the leading cause in those patients who were hospitalized with a complicated urinary tract infection (UTI) and other ailments and is causing difficulties in treatment due to drug resistance towards commonly used drugs like ampicillin/ amoxicillin and Co-trimoxazole. In this study 19% *E. coli* [Table 4, Fig. 3] were reported after data analysis, and showed high level of resistance rate (35 - 87%) against Augmentin, Ceftriaxone, Azethroneam, Ciprofloxacin, Doxycillin, Chloromfenicol, CT and Co-trimexazole. The most probable reason might be the overuse of antibiotics in other ailments where it is not recommended as in viral and parasitic infections.

One of the major gram-negative bacteria responsible for nosocomial infections is *Acinetobacter*. *Acinetobacter* may cause severe pneumonia and infections of the urinary tract, bloodstream, and other parts of the body. In this study 7.02% *Acinetobacter* [Table 4, Fig. 3] cases were reported with (45 - 98%) resistance rate for first second and third generation antibiotics. A study carried out in Spain showed that more than 90% of *A. baumannii* infections were of nosocomial origin. [18] In this study 17% *K. pneumoniae* [Table 4, Fig. 3] considered to be responsible for (94 - 26%) of all hospital acquired urinary tract infections blood stream infections globally increasing resistance trends reported to multi Studies from both developed and developing countries [19]. The epidemiology of ESBL producing *K. pneumoniae* in the community had not changed over the last 20 years with the emergence of virulent capsular serotypes. Our findings are consistent with other studies reporting interestingly when age as a risk factor [20].

Staphylococcus aureus was the most prominent etiological agent among gram positive organisms 17.5 % [Table 4, Fig. 3] reported in this study after data analysis. Almost all isolates were resistant (30 – 96%) to Augmentin, Ceftriaxone, Amakicin, Ciprofloxacin, Doxycillin, CT, Oxacillin and Erythromycin. Our study is in line with the report issued by U.S. National Healthcare Safety Network, where more than 30% of hospital-acquired infections were reported due to gram-negative bacteria and the majority of ventilator-associated pneumonia (47%) and urinary tract infection (45%) cases are associated with these bacteria [21].

5. CONCLUSION

Time for life saving antibiotics is running out due to resistance acquiring mechanisms. Despite the clear medical need for novel antibiotics without cross-resistance issues, antibacterial research and development pipelines are nearly dry, thus failing to provide the flow of novel antibiotics required to match the fast emergence and spread of MDR bacteria. In order to tackle this serious situation, there is also a need to refrain from such activities which are the main cause of nosocomial infection, and strategies should be planned to over count this situation.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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