

A retrospective Study of Patients for Antibiotic Resistance to Organisms in Intensive Care Unit (ICU)

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Abstract: Appropriate and timely treatment is of utmost importance especially for patients in intensive care unit (ICU). Hence knowledge of antibiotic resistance pattern of common organisms that cause infection amongst the patients in ICU, can guide the medical practitioners/intensivist in administration of the antibiotic treatment accordingly and help to reduce the emergence of antibiotic resistant pathogens. The study was conducted from June 2012-to June 2013, in order to examine the prevalence and antibiotic resistance patterns among the patients in ICU at King Abdul Aziz university hospital, Jeddah (tertiary centre in the western province of Saudi Arabia). A retrospective study design, where isolates are obtained from a wide range of clinical samples including blood, Sputum and Tracheal samples from 1235 patients in the ICU, blood culture, routine sputum culture and bronchoalveolar lavage methods were used to observe the growth of organisms in the samples. The clinical samples were collected over the studied period. The results indicated that, common pathogens found in this study are *Acinetobacter Baumannii* and *Klebsiella* were found to be the most common organism amongst the ICU patients. As well as, the susceptibility to antibiotics was more or less equal in both men and women, however, the level of resistance increase with the length of the stay in ICU. *The study concluded that*, Preventing the emergence and propagation of these antibiotic resistant pathogens would substantially reduce the detrimental events and also associated expenses.

[Maimoona Mushtaq Ahmed. **A retrospective Study of Patients for Antibiotic Resistance to Organisms in Intensive Care Unit (ICU)**. *Life Sci J* 2014;11(5):24-31]. (ISSN:1097-8135). <http://www.lifesciencesite.com>. 4

Keywords: antibiotic resistance, antimicrobial-resistant, ICU, Jeddah, Saudi Arabia

1. Introduction

Nosocomial infections (NI) due to Antibiotic resistant are a leading problem globally (Weinstein, 1998) while the risk is two to twenty times higher in hospital settings especially with limited resources in comparison to developed countries (Zaidi, et al. 2005). The prevalence rate was much higher in intensive care units (32-77%) (Lahsaeizadeh, et al., 2008 and Faria, et al., 2007). Increasing number of mortality and morbidity as well as increased hospital has been associated with infection due to overuse and misuse of antimicrobial agents. Furthermore, the exclusive environment of ICU makes it even more sensitive towards the emergence and spread of various antibiotic resistant organisms/pathogens. Various sources contribute to the emergence of antibiotic resistant pathogens such as wrong diagnosis, abuse of certain drug, reuse of suction tubes, contaminated enteral feeds, duration of stay in ICU and improper disposal of suction tubes, One of the most susceptible mediums that are favorable for exponential growth of pathogens is enteral feeds (White, et al., 1979). Contamination of enteral feeding increases the risk of nosocomial infections like septicemia, pneumonia and diarrhea (Anderton, 1993). Over the last decade several studies have shown that infections caused due to multi-drug resistant organisms (MRDO) is on the rise that includes both negative and gram positive

pathogens (NNIS, 2004; Flournoy, et al., 2000; Jones, 2001; Fridkin, et al., 2002 and Streit, et al., 2004). It has been observed that the prevalence of MRDO within the hospital especially in the patients in ICU is higher than it is in non-ICU patients (Archibald, et al., 1997; Fridkin, 2001 and Gourang, 2005). The risk of hospital-acquired infections amongst the ICU patients is higher due to several reasons such as severity of the existent disease, frequency of surgical procedures and interventions, old age, overall health condition, lower immunity and other prevalent morbidities. Beside higher consumption of antibiotics and improper infection control measures the exponential growth of antibiotic resistant organisms amongst the ICU patients; significantly increase the risk of sudden outbreaks amongst the critically ill patient (Archibald, et al., 1997 and Grundmann, et al., 2006). The emergence of resistance pattern within microorganisms is directly proportionate to the volume of antibiotics administered in patients, thus in order to reduce the growth of antibiotic resistance, dosage of antibiotics needs to be regulated/controlled

(Sharma and Barman, 2010). Hence monitoring the pattern of sensitivity and usage of antibiotics is imperative. In order to provide effective treatment and reduce the antibiotic resistance in organisms it is important to evaluate and analyze the antibiotic sensitivity patterns amongst various common

organisms in critical care units (CCU) and ICUs. Given this background, the present study aimed to determine the prevalence and pattern of antibiotic resistance in common organisms amongst patients in the ICU of King Abdul Aziz university hospital, Jeddah.

2. Materials and Methods

This is a retrospective cohort study which was carried out on ICU patients of King Abdul Aziz University Hospital, Jeddah, a tertiary centre in the western province of Saudi Arabia over a period of one year from June 2012 to June 2013. Data of 1235 ICU patient was collected from the hospital between June 2012 to June 2013, this data included the demographic details of the patient, admission unit, length of stay in the hospital, red blood cells (RBS) count, white blood cell (WBC) count, specimen collected, pattern of bacterial sensitivity and pattern of antibiotic administered following the assessment of pattern of sensitivity.

Blood culture was performed with blood culture bottles from the BacT-ALERT 3D Microbial Detection System (bioMérieux, North Carolina, USA). About 5 ml of patient blood was aseptically collected and inoculated into each of two bottles containing 40 ml of broth culture media, one for aerobic and the other for anaerobic growth. Culture bottles were loaded into the instrument and remained there for up to 5 days or until designated positive. All blood culture bottles designated positive were

smear and sub-cultured. Microbial identification and antimicrobial susceptibility testing were performed using standard diagnostic microbiological techniques and Vitek 2 system (bioMérieux) in the Clinical Microbiology Laboratory at King Abdulaziz University Hospital. A number of antibiotics were assessed to determine the antibiotic susceptibility pattern in common organisms in ICU settings, antibiotics evaluated are Meropenam, Imipenam, Pip/Tazobactam, Gentamycin, Amikacin, Vancomycin, Ciprofloxacin, Cefuroxime, Ceftriaxone, Cefatoxime, Cefepime, Ceftazidime, Cefazoline, Teicoplanin, ofloxacin, Oxacillin, Levofloxacin, Clindamycin, Benzyl Penicillin, Erythromycin, Septrin, Ampicillin, Augmentin, Pipracillin, Colistin, Tegacycline, Nitrofurantoin and Linezolid. Statistical analysis was carried out using SPSS 19.0 Armonk, NY: IBM Corp. $p < 0.05$ was considered significant.

3. Result

3.1 Demographic details of the Patients

Out of 1235 ICU patients, 476 were women (38.5%) and 759 were men (61.5%) as shown in table 1. The average age for women and men was ± 56.64 and ± 58.55 , respectively. Tracheal samples were collected from 433 patients, blood samples were collected from 185 patients, and urine sample was collected from 193 patients and sputum sample from 92 patients.

Table 1: Demographic details of the Patient

Variables	Male	Female	Total
Sex	759 (61.5 %)	476 (38.5 %)	1235(100%)
Age	58.5 \pm 18.8	56.6 \pm 18.6	57.8 \pm 18.8
Days hospitalized			28.6 \pm 34.7
Age-Group			
<= 46	171(22.5 %)	140(29.4%)	311(51.9%)
47 - 60	213(28.1 %)	99(20.8%)	312(48.9%)
61 - 72	160(21.1%)	153(32.1%)	313(53.2%)
>=73	215(28.3%)	84(17.6%)	299(45.9%)
RBS	14.8 \pm 9.4(2.5-108)	15.35 \pm 7.8(4.3-78.3)	
WBC	14.5 \pm 10.3(0.6-61.8)	12.93 \pm 8.8(1.1-63.7)	

Values are presented as \pm SD or n (%)

The frequency of occurrence of the common microorganisms were observed as Pseudomonas (18%), Acinetobacter Baumannii (16.2%), Klebsiella (11.6%), Enterococcus Faecalis (10%), MRSA (7.9%), ESBL-E.Coli (7.8), ESBL-Klebsiella (6.6%), E.Coli (6.4), Staph.Aureus (5.7%), Proteus (4.8%), Morganella Morgani (1.9%), Serratia Marcescens (1.5%), Haemophilus Influenza (1.1%) and VER Enterococcus Faecalis (.7%).

According to the results shown in Table 2 and figure 1 Pseudomonas was most resistant to Pipracillin (35.6%), followed by PipTazobactam

(34.7%), Meropenam (32.9%), Cefepime (32.4%), and Imipenam (26.6%). Sensitivity recorded as per results was maximum towards Gentamycin (70.7%) and Ciprofloxacin (65.3%). Acinetobacter Baumannii was found to be resistant to most of the antibiotics most resistance recorded was towards Meropenam (79.5%) followed by Ciprofloxacin 76.5%, Ceftazidine 73.5%, Cefepime 71.5%, Imipenam 67%, PipTazobactam 63%, Septrin 59% and Gentamycin 57.5%. Sensitivity recorded as per results was maximum towards Colistin (54%). Klebsiella is less resistant than the other organisms to antibiotic;

maximum resistance recorded was against Ampicillin (37.1%). Most effective antibiotics for Klebsiella are PipTazobactam (76.9%), Gentamycin (75.5%) and

Septin (73.4%). Enterococcus Feacalis is mostly sensitive to antibiotics, the only significant resistance noted was against Ampicillin (28.5%).

Table 2: Type of organisms by isolates (%)

Type of organisms		Organisms			
		Acinetobacter Baumani	Enterococcus Feacalis	Klebsiella	Pseudomonas
Meropenam	Resistant	79.5	2.4	2.1	32.9
	Sensitive	3.0	7.3	16.8	14.4
Imipenam	Resistant	67.0	7.3	1.4	26.6
	Sensitive	3.0	21.1	3.5	5.4
PipTazobactam	Resistant	63.0	8.1	5.6	34.7
	Sensitive	8.0	3.3	76.9	13.1
Gentamycin	Resistant	57.5	16.3	9.1	22.1
	Sensitive	31.0	37.4	75.5	70.7
Amikacin	Resistant	33.5	0.8	2.1	10.8
	Sensitive	16.0	3.3	14.0	10.8
Vancomycin	Resistant	0.5	5.7	0.0	0.5
	Sensitive	2.0	41.5	3.5	2.3
Ciprofloxacin	Resistant	76.5	4.9	10.5	27.5
	Sensitive	12.0	13.0	74.8	65.3
Cefuroxime	Resistant	0.5	0.0	5.6	0.5
	Sensitive	1.0	0.8	50.3	2.3
Ceftriaxone	Resistant	0.0	0.0	1.4	0.0
	Sensitive	0.0	0.0	14.0	0.0
Cefatoxime	Resistant	1.5	0.0	0.7	0.5
	Sensitive	0.5	0.0	2.1	0.0
Cefepime	Resistant	71.5	3.3	0.7	32.4
	Sensitive	3.0	9.8	2.8	4.1
Ceftazidime	Resistant	73.5	2.4	0.7	37.8
	Sensitive	8.0	0.0	13.3	52.7
Cefazoline	Resistant	3.5	0.0	0.7	0.9
	Sensitive	1.5	0.0	7.7	2.3
Teicoplanin	Resistant	0.0	4.1	0.0	0.9
	Sensitive	0.0	21.1	1.4	0.0
Norfloxacin	Resistant	0.0	0.8	0.7	0.0
	Sensitive	0.0	0.0	1.4	0.5
Oxacillin	Resistant	1.5	2.4	0.0	0.5
	Sensitive	0.5	0.8	1.4	1.8
Levofloxacin	Resistant	0.0	4.1	0.0	0.0
	Sensitive	0.0	7.3	0.0	0.5
Clindamycin	Resistant	2.0	3.3	0.0	0.0
	Sensitive	0.0	1.6	0.0	1.4
BenzylPenicillin	Resistant	0.0	0.8	0.0	0.0
	Sensitive	0.0	0.0	0.0	0.0
Erythromycin	Resistant	2.0	3.3	0.7	0.0
	Sensitive	1.0	0.0	0.0	0.9
Septin	Resistant	59.0	6.5	18.9	5.4
	Sensitive	24.5	16.3	73.4	5.4
Ampicillin	Resistant	1.0	28.5	37.1	2.7
	Sensitive	1.0	39.8	4.2	1.4
Augmentin	Resistant	3.0	4.9	7.7	1.8
	Sensitive	2.5	4.9	49.0	0.9
Pipracillin	Resistant	6.0	3.3	48.3	35.6
	Sensitive	3.0	0.0	8.4	51.4
Colistin	Resistant	3.5	0.8	1.4	0.5
	Sensitive	54.0	4.9	4.2	21.2
Tegacycline	Resistant	24.5	2.4	1.4	0.0
	Sensitive	28.0	4.1	1.4	3.2
Nitrofurantoin	Resistant	2.5	1.6	11.9	0.9
	Sensitive	1.5	17.9	2.8	0.5
Linezolid	Resistant	0.0	0.0	0.0	0.0
	Sensitive	0.0	4.9	0.0	0.9

Table 3: Type of organisms by isolates and antibiotics by Sex

Type of organisms by isolates and antibiotics by Sex		Organisms							
		Acinetobacter Baumannii		Enterococcus Faecalis		Klebsiella		Pseudomonas	
		Male	Female	Male	Female	Male	Female	Male	Female
Meropenam	Resistant	80.2	78.3	1.5**	3.5**	0.0	4.8**	35.0**	29.1**
	Sensitive	3.8	1.4	12.1	1.8	18.8	14.3	11.2	20.3
Imipenam	Resistant	65.6**	69.6**	9.1**	5.3**	0.0	3.2**	25.2**	29.1**
	Sensitive	3.1	2.9	24.2	17.5	3.8	3.2	5.6	5.1
PipTazobactam	Resistant	60.3**	68.1**	7.6**	8.8**	3.8	7.9**	35.0**	34.2**
	Sensitive	6.1	11.6	1.5	5.3	78.8	74.6	12.6	13.9
Gentamycin	Resistant	59.5**	53.6**	19.7**	12.3**	5.0	14.3**	23.8**	19.0**
	Sensitive	31.3	30.4	36.4	38.6	75.0	76.2	67.8	75.9
Amikacin	Resistant	34.4**	31.9**	0.0**	1.8**	1.3	3.2**	11.2**	10.1**
	Sensitive	18.3	11.6	3.0	3.5	16.3	11.1	13.3	6.3
Vancomycin	Resistant	0.0**	1.4**	0.0**	12.3	0.0**	0.0**	0.7**	0.0**
	Sensitive	3.1	0.0	48.5	33.3	3.8	3.2	1.4	3.8
Ciprofloxacin	Resistant	77.1**	75.4**	3.0**	7.0	5.0**	17.5**	25.2**	31.6**
	Sensitive	11.5	13.0	13.6	12.3	75.0	74.6	65.7	64.6
Cefuroxime	Resistant	0.8**	0.0**	0.0**	0.0**	3.8	7.9**	0.7**	0.0**
	Sensitive	1.5	0.0	0.0	1.8	46.3	55.6	2.8	1.3
Ceftriaxone	Resistant	0.0**	0.0**	0.0**	0.0**	0.0	3.2**	0.0	0.0**
	Sensitive	0.0	0.0	0.0	0.0	16.3	11.1	0.0	0.0
Cefatoxime	Resistant	2.3	0.0	0.0	0.0**	0.0	1.6	0.0	1.3
	Sensitive	0.8	0.0	0.0	0.0	2.5	1.6	0.0	0.0
Cefepime	Resistant	69.5**	75.4	3.0**	3.5**	0.0	1.6**	30.8**	35.4
	Sensitive	3.1	2.9	9.1	10.5	5.0	0.0	4.2	3.8
Ceftazidime	Resistant	74.0	72.5**	1.5	3.5	1.3	0.0	37.8	38.0**
	Sensitive	6.1	11.6	0.0	0.0	16.3	9.5	53.1	51.9
Cefazoline	Resistant	4.6**	1.4**	0.0**	0.0**	0.0	1.6**	1.4**	0.0**
	Sensitive	2.3	0.0	0.0	0.0	11.3	3.2	2.8	1.3
Teicoplanin	Resistant	0.0**	0.0**	3.0**	5.3**	0.0	0.0**	0.0**	2.5**
	Sensitive	0.0	0.0	21.2	21.1	1.3	1.6	0.0	0.0
Norfloxacin	Resistant	0.0**	0.0	0.0	1.8**	0.0	1.6**	0.0**	0.0
	Sensitive	0.0	0.0	0.0	0.0	2.5	0.0	0.7	0.0
Oxacillin	Resistant	2.3**	0.0**	1.5**	3.5**	0.0	0.0**	0.7**	0.0**
	Sensitive	0.8	0.0	1.5	0.0	2.5	0.0	2.1	1.3
Levofloxacin	Resistant	0.0**	0.0**	4.5**	3.5**	0.0	0.0**	0.0**	0.0**
	Sensitive	0.0	0.0	7.6	7.0	0.0	0.0	0.0	1.3
Clindamycin	Resistant	3.1**	0.0**	1.5**	5.3**	0.0	0.0**	0.0**	0.0**
	Sensitive	0.0	0.0	3.0	0.0	0.0	0.0	1.4	1.3
BenzylPenicillin	Resistant	0.0**	0.0**	1.5**	0.0**	0.0	0.0**	0.0**	0.0**
	Sensitive	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Erythromycin	Resistant	3.1**	0.0**	0.0**	7.0	0.0	1.6	0.0**	0.0**
	Sensitive	1.5	0.0	0.0	0.0	0.0	0.0	0.7	1.3
Septrin	Resistant	60.3**	56.5**	4.5**	8.8**	17.5	20.6**	4.9**	6.3**
	Sensitive	21.4	30.4	18.2	14.0	73.8	73.0	5.6	5.1
Ampicillin	Resistant	0.8**	1.4**	28.8**	28.1	32.5	42.9	1.4**	5.1**
	Sensitive	0.0	2.9	39.4	40.4	3.8	4.8	1.4	1.3
Augmentin	Resistant	3.1**	2.9**	4.5**	5.3**	3.8	12.7**	2.8**	0.0**
	Sensitive	1.5	4.3	3.0	7.0	48.8	49.2	0.7	1.3
Pipracillin	Resistant	6.9**	4.3**	3.0**	3.5**	40.0	58.7**	32.9**	40.5**
	Sensitive	3.1	2.9	0.0	0.0	8.8	7.9	53.8	46.8
Colistin	Resistant	5.3**	0.0**	1.5**	0.0**	1.3	1.6**	0.0**	1.3****
	Sensitive	58.0	46.4	6.1	3.5	3.8	4.8	22.4	19.0
Tegacycline	Resistant	25.2**	23.2**	0.0**	5.3**	0.0	3.2**	0.0**	0.0**
	Sensitive	29.0	26.1	6.1	1.8	1.3	1.6	1.4	6.3
Nitrofurantoin	Resistant	3.1**	1.4**	1.5	1.8**	10.0	14.3**	0.0**	2.5**
	Sensitive	1.5	1.4	12.1	24.6	2.5	3.2	0.7	0.0
Linezolid	Resistant	0.0**	0.0**	0.0	0.0**	0.0	0.0**	0.0**	0.0**
	Sensitive	0.0	0.0	1.5	8.8	0.0	0.0	0.0	2.5

** denotes P < 0.001; *denotes P<0.05;

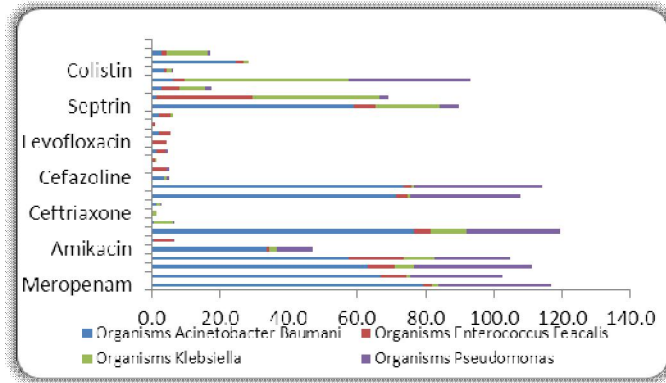


Figure (1) Type of organisms

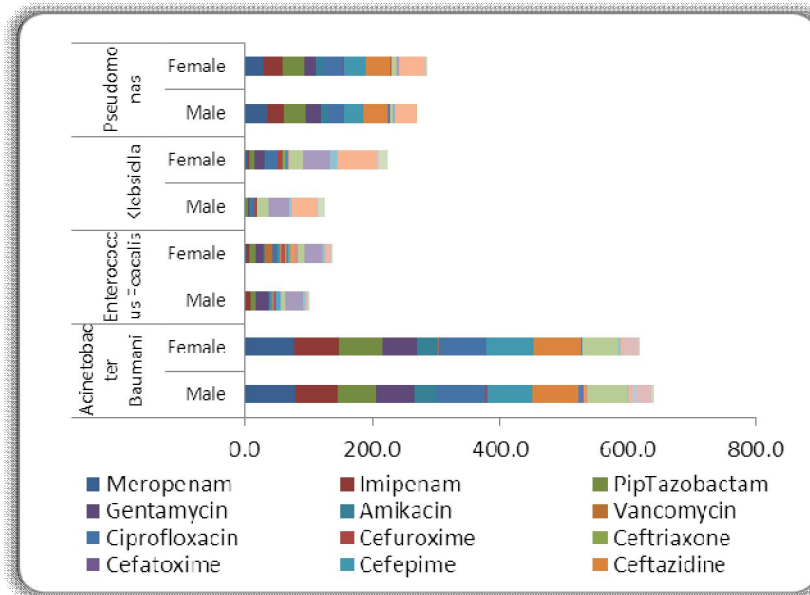


Figure (2) Type of organisms by isolates and antibiotics by Sex

Acinetobacter Baumannii is the most resistant to antibiotics in both male (80.2%) and female (78.3%) (Table 3 and figure, 2). Acinetobacter Baumannii is most resistant to Meropenam and Imipenam in both the gender and the most effective antibiotic is Colistin. The next resistant organism observed was Pseudomonas in both male and female and is resistant to number of antibiotics namely Meropenam, PipTazobactam and Cefepime, while effective antibiotics for Pseudomonas are Ciprofloxacin, Ceftazidine and Pipracillin in both the genders. However, for the other organisms Klebsiella and Enterococcus Faecalis the percentage of resistance is not significant.

Table 4 and figure 3 represents the percentage of antibiotic resistance based on length of stay in the ICU in hospital which has been divided into four duration (in day) slots as ≤ 5 , 6 – 17, 18 – 37 and ≥ 38 . As per the results it was noticed that

Acinetobacter Baumannii resistance to antibiotics Meropenam, Imipenam, PipTazobactam, Ciprofloxacin, Cefepime and Ceftazidine was observed to be increasing with the length of stay. Sensitivity towards Gentamycin and Septrin was observed to be reducing with the increase in length of the stay, only sensitivity towards Colistin was more or less consistent and was not impacted with the increase in duration of the stay. For Enterococcus Faecalis resistance towards Gentamycin was more in ≥ 38 day of stay, it was less sensitive with the increased duration of stay. Klebsiella shows a reducing sensitivity towards PipTazobactam and Gentamycin with increasing length of stay. Pseudomonas shows increased resistance towards Meropenam, Imipenam, PipTazobactam and Ceftazidine. Sensitivity towards Gentamycin has been more or less consistent throughout except in ≥ 38 days slot where it has reduced.

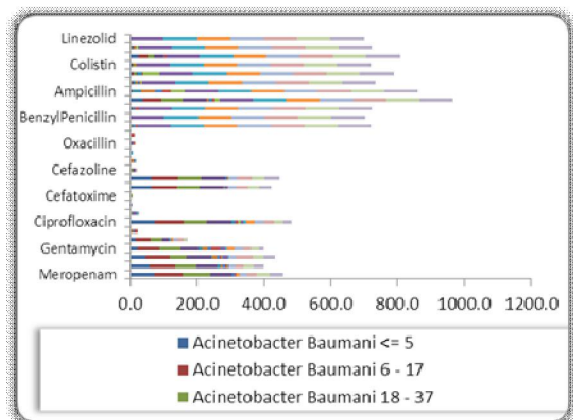


Figure (3) Type of organisms by isolates and antibiotics by No. of days hospitalized

Overall these results suggest that *Acinetobacter Baumannii* is the most antibiotic resistant organism whose resistance pattern is more or less the same in both the genders. However the only antibiotic against which its sensitivity was recorded is Colistin which was consistent throughout the length of the stay.

4. Discussion and conclusion

The common pathogens found in this study corroborates with other studies where *Acinetobacter Baumannii* and *Klebsiella* were found to be the most common organism amongst the ICU patients

(Vessal, et al., 2006 and Panahi, et al., 2008). Organisms resistance to antibiotics in ICU patients is concerning. In a study conducted in Turkey in 2007 *Acinetobacter baumannii* resistance to imipenam was observed in 53.7% patients (Gulseren, et al., 2008). However in the present study it was found *Acinetobacter Baumannii* was the most resistant organism to most of the antibiotics namely Meropenam, Imipenam, Ciprofloxacin, Ceftazidime, Cefepime, Imipenam, PipTazobactam, Septrin and Gentamycin. In fact another research established the fact that other antibiotics such as ceftazidim, piperacillin and tazobactam, demonstrated no difference in the resistance level of *Acinetobacter* (Jukemur, et al., 2000).

In this study it was found that susceptibility to antibiotics was more or less equal in both men and women. It was also noticed that the level of resistance increase with the length of the stay in ICU. Positive cultures of blood, sputum and trachea were found in the ICU patients mainly for *Acinetobacter Baumannii*, *Klebsiella*, *Pseudomonas* and *Enterococcus*, beside these *Feacalis*, *E.Coli*, *Proteus*, *Morganella Morgani*, *Haemophilis Influenza*, *Serratia Marcescenc* and *VER Enterococcus Feacalis* was also found, however the frequency of occurrence was low. Result also indicate that organisms are

mostly resistant to antibiotics such as Meropenam, Imipenam, PipTazobactam, Gentamycin, Cefepime and Ceftazidime especially *Acinetobacter Baumannii*. However sensitivity to Colistin has been consistent. Findings also indicate that in most of the cases with regular administration the level of resistance increases and sensitivity towards antibiotics reduce. Knowledge of antibiotic resistance pattern is important for the intensivist for prevention, treatment and management. Preventing the emergence and propagation of these antibiotic resistant pathogens would substantially reduce the detrimental events and also associated expenses. Further, to prevent increasing antibiotic resistance in the organisms, administration of antibiotics should be done appropriately; proper care should be taken in terms of length of the treatment, optimal selection, dosage and control of excessive use of antimicrobials (AM) and/or antibiotics (Shlaes, et al. 1997). One of the main limitations of this study is that the patients were already undergoing a treatment and were administered antibiotics even before the sample were collected, the overall antibiotic usage would have influenced the results. Hence utility of this result in other institutions could be limited.

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