Acinetobacter Spp: Resistance and therapeutic decisions at the turn of the novel millennium

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Abstract: This study was planned to evaluate sample wise isolation and antimicrobial resistant trends of *Acinetobacter* spp in different departments of a tertiary care hospital. This was a transversal descriptive study, carried out in the clinical microbiology laboratory of the Allama Iqbal Medical College/ Jinnah Hospital, Lahore, Pakistan, during the period of January 2015 to December 2016. Every clinical specimen was processed for bacterial culture and antimicrobial susceptibly testing. A total of 3590 (2015=1780, 2016=1810) clinical specimens were processed. Of the total, only 54.7% were gram-negative, among these *Acinetobacter* spp were isolated from 10.1% and 16.5% samples respectively in 2015-16 with an overall rate of 24.3%. The highest occurrence of *Acinetobacter* spp isolates was reported from Intensive care units (ICU) (54%) followed by surgical units (25%) and medical units (16%). It is noteworthy that ICU and internal medicine showed the highest resistance rates, whereas, lower resistance rate was observed for the outdoor patients (OPD). Although collistin showed 0% resistant while ceftriaxone, ciprofloxacin, gentamicin, and tigecycline showed 90%, 68%, 66%, 66% and 62% resistance against *Acinetobacter* spp. respectively. An alarming increase in the resistance rate of meropenem, cefoperazone/sulbactam, piperacillin/ tazobactam, ciprofloxacin, and imipenem was observed from the year 2015 to 2016. This startling resistance acquired by *Acinetobacter* spp. within a period of one year, represent very limited therapeutic options left for the infections caused by *Acinetobacter* spp. Unavailability of effective drugs and limited therapeutic options enforce the health care practitioners to prescribe expensive and broad range antibiotics, which may cause harm to the patient. Therefore, it is need of an hour to better understand the antimicrobial patterns and optimize antimicrobial prescription policies for the control of multidrug-resistant *Acinetobacter* spp.

Keywords: *Acinetobacter*, drug resistance, susceptibility testing.

INTRODUCTION

The terminology of "nightmare bacteria" is quoted by health professionals to describe the issue of antibiotic resistance that "leads to a catastrophic threat'' to the world. (Rao, Susanti *et al*. 2016). Among gram-negative pathogens, multi-drug resistance *Acinetobacter* spp are posing a potential threat to the globe due to their ability to survive on dry and harsh environments. Researchers showed that there are wide ranges of intrinsic and acquired mechanisms attributed to the higher resistance rate in *Acinetobacter* spp. which are directly and indirectly associated with increased morbidity and mortality (Pajand *et al*., 2013; Bojkovic *et al*., 2016; Poirel *et al*., 2017). This causative infectious agent leads to a wide spectrum of infections such as pneumonia, bacteremia, post-surgery infections, secondary meningitis, and urinary tract infections, mostly victimizing patients with impaired host defenses systems (Dexter *et al*., 2015). Different proportions of multi-drug resistant strains (MDR) of *Acinetobacter* spp. were isolated and reported from different regions of the world. The variability of occurrence in the frequency of the *Acinetobacter* spp. is found to be different from place to place, community to community and ward to ward. However, the trend towards increasing resistance in this species is undisputed (Hasan *et al*., 2014).

The world is going to enter a post-antibiotic era, where various common infections will remain incurable and results in the destruction of human health. Therefore to combat this nightmare, global antibiotic resistance partnership (GARP) was established to address the issue and develop effective policies and their implementation in low and middle-income countries. Unfortunately at least 50% of all the antibiotics prescribed are not required or are not optimally effective as prescribed. This is one of the major reasons behind the emergence of drug resistance against different pathogens. The spread of the resistant pathogenic strains via person to person and from the environment including food is another contributor

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major for the development of growth of antibiotic resistance.

In recent years, resistance rate in *Acinetobacter* spp. is growing against a wide spectrum of therapeutic regimes due to the transmission of mobile genetic elements, which poses the threat of many nosocomial infections. In mechanisms of drug resistance, production of beta-lactamases enzyme has played a major role against carbapenems is identified as the major cause. Genetic mutation is another dominating factor which confers the quinolones by blocking antibiotic binding sites. Hence, these resistant strains are serious therapeutic and clinical challenge for the world and are responsible for the loss of many lives. It's very crucial to make best empirical antibiotic choices to overcome this dilemma of resistance in bacteria; therefore, the microbiological surveillance offers the best possible way to doctors for dealing with this mystery by obtaining valuable information about these bugs. This 2 years based study was conducted to investigate the variation in susceptibility pattern of *Acinetobacter* spp. against various classes of antimicrobial agents and their association with samples type, patient demographical data and wards.

The aim of this study was to collect the data about the previous and current susceptibility pattern of antibiotic for the *Acinetobacter* spp and to determine the epidemiology of *Acinetobacter* spp in the population of the Punjab, Lahore. The outcome of our study will help the health advisors to make strategies to limit the cost of treatment, establish valuable antibiotics for treatment and implement appropriate preventive measures..

MATERIALS AND METHODS

This was a transversal descriptive study, carried out in the clinical microbiology laboratory of Allama Iqbal Medical College/ Jinnah Hospital, Lahore (AIMC&JHL), Pakistan.

Clinical specimens

A total of 3590 samples (Pus 1073, blood 206, pleural fluid 301, sputum 819, tracheal aspirates 603, BAL, 588) were received and all the concerning strains of *Acinetobacter* spp were collected in the time span of 2 years, from January 2015 to December 2016. All isolated strains of *Acinetobacter* spp were collected from outdoor patient (OPD) and indoor patients department of Jinnah Hospital, Lahore, which is a 1600 bedded tertiary care hospital situated in the middle of the Punjab province, Pakistan. Study protocols were approved from the ethical review board of AIMC.

Inclusion & exclusion

The strains of *Acinetobacter* spp with incomplete susceptibility data and as well as strains proved to be contaminant were excluded from the study. The inclusion criteria of the study included all the strains of *Acinetobacter* spp isolated from diagnostic referred specimens of pus, blood, pleural fluids, sputum, and tracheal aspirate and bronchoalveolar lavage.

Bacterial identification

A total of 479 isolates of *Acinetobacter* spp. were identified. Identification of *Acinetobacter* spp. was done by routine lab procedure of culturing and microscopic morphology (size, shape, and color) was noted.

Antimicrobial sensitivity

Clinical and Laboratory Standards Institute guidelines (CLSI) recommended standard method of Kirby Bauer disc diffusion agar method was performed to determine the antibiotic susceptibility. Standard discs of amikacin (30ug), cefoperazone (75ug), ceftriaxone (35ug), ciprofloxacin (5ug), colistin (10ug), imipenem (10ug), polymyxin b (300 units) were selected in the panel of antibiotics for *Acinetobacter* spp. *Escherichia coli* ATCC 25922 were used as a control strain.

Extraction of data and statistical analysis

For the descriptive analysis of the data, the statistical software of SPSS version 21 was used. The extraction of data included, type of specimen, isolated infectious agent, as well as antibiotics tested with their susceptibility profile ("S" for sensitive, "I" for intermediate, "R" for resistant). In the calculation of the percentages of resistance, the "intermediary" results were included in the category "resistant".

STATISTICAL ANALYSIS

Specimen types, ward and year. Chi-square test was used as a test of significance; p-value of <0.05 was considered statistically significant. Win Pepi software was used for statistical analysis of the data.

RESULTS

In this microbiological surveillance, total 3590 samples (2015=1780, 2016=1810) were received, of total only 54.7% were gram-negative, among these *Acinetobacter* spp. were isolated from 10.1% and 16.5% samples respectively in 2015-16 with an overall rate of 24.3% (table 1).

In order to find out any association with the nature of ward and prevalence of *Acinetobacter* spp. the distribution of *Acinetobacter* spp. in different wards and hospital locality was also studied. In 2015, most of the *Acinetobacter* spp isolated were from ICU which was 54% of total *Acinetobacter* spp isolated followed by surgical units and medical units which were 25% and 16 % respectively. A similar trend was observed in 2016. The overall isolation frequency was depicted in (table 1).

Table 1: Distribution of *Acinetobacter* spp according to their referral ward in 2015-16

Location	Total Samples	*Acinetobacter* spp	Total Samples	*Acinetobacter* spp	Total Samples	*Acinetobacter* spp	Statistics Pc & Pv
ICU	413/23%	98/54%	476/26%	187/62%	889/25%	285/59%	24.571 P= 0.000
Surgical unit	460/26%	46/25%	599/33%	76/25%	1059/29%	122/25%	625.559 P= 0.000
Medical unit	645/36%	29/16%	436/24%	23/8%	1081/30%	52/11%	0.345 P= 0.557
OPD	262/15%	7/4%	299/16%	13/4%	561/16%	20/4%	1.141 P= 0.285
Total	1780/100%	180/100%	1810/100%	299/100%	3590/100%	479/100%	
P- value	0.0001		0.0001		0.0001		
Pc=Pearson's chi-squar, Pv= P value							

Table 2: Sample based frequency distribution of *Acinetobacter* spp 2015-2016

Sample Type	Total Samples	*Acinetobacter* spp	Total Samples	*Acinetobacter* spp	Total Samples	*Acinetobacter* spp	Statistics Pc & Pv
Pus	523/29%	79/43%	550/30%	143/48%	1073/30%	222/46%	10.450 P = 0.001
Blood	32/2%	18/10%	174/10%	29/10%	206/6%	47/10%	24.049 P = 0.000
Pleural fluid	185/10%	4/2%	116/6%	8/3%	301/8%	12/2%	4.175 P = 0.041
Sputum	450/25%	11/6%	369/20%	14/5%	819/23%	25/5%	1.248 P = 0.264
Tracheal aspirate	381/21%	63/35%	222/12%	96/32%	603/17%	159/33%	51.534 P = 0.000
BAL	209/12%	5/3%	379/21%	9/3%	588/16%	14/3%	0.000 P = 0.989
Total	1780/100%	180/100%	1810/100%	299/100%	3590/100%	479/100%	
P- value	0.000		0.000		0.000		
Pc=Pearson's chi-squar, Pv= P value							

Table 3: Department wise Antimicrobial resistance pattern of *Acinetobacter* spp 2015-16

Antibiotics	ICU (n=285)		Surgical unit (n=122)		Medical unit (n=52)		OPD (n=24)		Statistics Pc & Pv
	Proportion	%	Proportion	%	Proportion	%	Proportion	%	
Gentamicin	202	72.0	83	68.6	23	46.3	10	42.0	20.507 P = 0.000
Meropenem	157	55.0	53	47.5	18	36.5	8	32.8	12.395 P = 0.006
Cefoperazone-sulbactam	100	35.3	64	59.8	22	45.1	9	32.8	12.836 P = 0.005
Piperacillin/ tazobactam	149	56.2	60	53.0	19	39.0	10	45.3	4.961 P = 0.175
Ciprofloxacin	183	64.0	83	71.6	36	70.7	13	67.1	2.215 P = 0.529
Ceftriaxone	203	73.6	72	62.0	37	70.7	14	50.0	7.043 P = 0.071
Colistin	0	0	0	0	0	0	0	0	===
Imipenem	162	59.2	54	48.7	19	37.8	9	34.3	12.162 P = 0.007
Amikacin	134	46.7	46	36.1	24	46.3	10	45.3	3.143 P = 0.370
Ceftazidime	150	46.7	41	34.3	28	42.4	14	50.0	15.192 P = 0.002
Cefoperazone	109	37.7	65	56.6	20	57.3	14	50.0	10.622 P = 0.014
Tigecycline	139	59.1	110	90.9	41	80.4	8	34.3	76.625 P = 0.000
Co-trimoxazole	48	16.7	20	16.8	8	15.8	3	28.1	0.346 P = 0.951
Pc=Pearson's chi-squar, Pv= P value									

The *Acinetobacter* spp. isolates were obtained from different specimens (table 2), pus specimens being the most frequently associated with infection (46%), followed by tracheal aspirate (33%) (table 2). The resistance rate of all applied antibiotic panel and their changing trend were studied form different wards. Worth noting that ICU and internal medicine showed the highest resistance rate, however lower resistance rate was observed in OPD (table 3).

In our study, the most active antibiotic was collistin (table 4), which showed 0% resistance against *Acinetobacter* spp. Moreover, cefoperazone-sulbactam and cotrimoxazole were used as the best therapeutic choices against *Acinetobacter* spp (table 4), ceftriaxone, ciprofloxacin, gentamicin, and tigecycline showed 90%, 68%, 66%, 66% and 62% resistance against *Acinetobacter* spp respectively.

An alarming increasing trend in the resistance rate of meropenem, cefoperazone -sulbactam, piperacillin/ tazobactam, ciprofloxacin, and imipenem was observed from 2015 to 2016. In 2015, these drugs were sensitive but within one year these *Acinetobacter* spp develop resistance for this therapeutic choice (table 4)

DISCUSSION

Acinetobacter spp. are opportunistic nosocomial pathogens which offer a great challenge to the therapeutic support of many associated infections such as urinary tract infections (UTI), septicemia and pneumonia by subsequent hospitalization, particularly in fragile patients (Arsalane *et al*., 2010; Decré 2012). The changing trend of *Acinetobacter* spp. against available therapeutic choices and their emergence was the target of this study. From this study, we observed a dramatic increase in the proportion of *Acinetobacter* spp. from 10.1% in 2015 to 16.5% in 2016, therefore, it demands the significant attention to control this increasing trend (table 1). In this current study period, the frequency of 46% *Acinetobacter* spp was recovered from the pus samples. Moreover, only 4% isolated *Acinetobacter* spp. were of bronchioalveolar lavage (BAL) origins (table 1). Whereas, other studies reported *Acinetobacter* spp. as a second most common bacterial pathogen associated with pneumonia infection (Xia *et al*., 2012; Xu *et al*., 2013). Furthermore, the low detection rate of *Acinetobacter* spp. in different body fluid reported in another study is relatable to our findings (Xia *et al*., 2012). This low positivity rate can partly be suspected of false negativity and hence put forth the necessity of paying more attention to the proper examination of sterile body fluids for *Acinetobacter* spp. so that more cases can be detected from blood, BAL, and serous effusions.

From the data collected in this 2 years' time period, 54% *Acinetobacter* spp. were recovered from the ICU department of Jinnah hospital, Lahore, which is an alarming sign for the clinicians. This is due to the critical condition of patients, prolong hospitalization, weak immune defense system, and frequent invasive procedure such as tracheotomy and other server underlying diseases, (Mireya *et al*., 2007). Therefore, patients in ICU are considered high-risk patients for hospital-acquired infections (HAI). A similar higher proportion of *Acinetobacter* spp. was reported from other regions of the world. A study from Italy and Slovakia showed 97.5% and 56% saturation of *Acinetobacter* spp. in their ICUs of Hospital (Krcmery and Kalavsky 2007; Sunenshine *et al*., 2007; Dent *et al*., 2010; Wadl *et al*., 2010). Another study from Pakistan reported that *A. baumannii* showed the uppermost resistance (91, 100%) against carbapenems, fluoroquinolones, cephalosporins, and a β-lactam group of drugs. Among aminoglycosides, tobramycin showed better activity than amikacin. Tetracycline also showed the highest resistance (60, 65.93%) while tigecycline and minocycline showed zero resistance (91, 0.00%). Among all antibiotics used in this study, tigecycline and minocycline were found to be most effective against *A. baumannii*). All the clinical isolates of *A. baumannii* were found resistant to most of the antibiotics and were considered as multi-drug resistant. Among the 91 samples, the highest prevalence of *A. baumannii* was observed in the endotracheal tubes secretions (23, 25.27%) followed by tracheal secretions (18, 19.78%) and the least in pus (15, 16.48%). The highest prevalence of *A. baumannii* was found in neonatal intensive care unit NICU (37, 42.85%), followed by Medical (ICU) (18, 19.78%) and the least was found in the out-patient department (9, 9.89%) (Begum *et al*., 2013). The variation in this rate has been observed, but the overall data showed that more than 50% incidence rate has been witnessed for the rapid spread of *Acinetobacter* spp. which showed the severity of the infection due to this pathogen (Capone *et al*., 2008).

The data of the current study showed the higher activity of amikacin, ceftazidime, and cefoperazone in the duration of two years as compared other applied antibiotics. These antibiotics retained their activity above 50% in two years. Among the group of aminoglycosides, amikacin were the most effective antibiotics (table 4). Nearly equal sensitivity patterns were reported by a study conducted at General Hospital of Douala, Cameron, which shows 24.43% of resistance strains for *Acinetobacter* spp (Ebongue *et al*., 2015). The reason behind this may be the less subscription of this antibiotic in our hospital. However, the date of previously published work showed the increasing resistance over the years and loss of the effectiveness of this drug against *Acinetobacter* spp. (Memish *et al*., 2012; Patel *et al*., 2013; Xu *et al*., 2013).

In Asian countries, the cephalosporins and fluoroquinolones were the most commonly prescribed antibiotics. In the present study, we have observed a significant increase in the resistance rate of nine different antibiotics. Overall two-fold increases in resistance were noticed in meropenem, piperacillin/ tazobactam, ceftriaxone, and imipenem. The current rate of resistance for meropenem is 64% which has been previously reported as 22% in 2015. Similarly, the considerable increasing trend in resistance rate of piperacillin/ tazobactam, ceftriaxone and imipenem from 14% to 71%, 48% to 80% and 26% to 66% respectively has been observed from the year 2015-2016. This is an indication of the alarming situation in Pakistan (table 4). The low activity of these antibiotic groups serve to prove the general behavioral tendency of the cephalosporin's and fluoroquinolones to face multi-resistant strains (Andriamanantena *et al*., 2010; Ahmed *et al*., 2012; Shahla *et al*., 2012).

Table 4: Year wise Antimicrobial resistance pattern of *Acinetobacter* spp

Antibiotics	2015 (n=180)		2016 (n=299)		2015-2016 (n=479)		Statistics Pc & Pv	
	Proportion	%	Proportion	%	Total	%		
Gentamicin	106	59	213	71	319	66	7.70	P = 0.006
Meropenem	40	22	193	64	233	49	80.57	P = 0.000
Cefoperazone/sulbactam	53	29	142	47	195	41	15.16	P = 0.000
Piperacillin/ tazobactam	25	14	213	71	238	50	147.81	P = 0.000
Ciprofloxacin	104	58	211	70	315	66	8.16	P = 0.004
Ceftriaxone	86	48	240	80	326	68	54.55	P = 0.000
Imipenem	47	26	199	66	246	51	73.57	P = 0.000
Amikacin	85	47	129	43	214	45	0.75	P = 0.385
Ceftazidime	87	48	146	49	233	49	0.01	P = 0.916
Cefoperazone	85	47	133	44	218	45	0.34	P = 0.560
Tigecycline	108	60	190	63	298	62	0.60	P = 0.438
Co-trimoxazole	37	20	42	14	79	16	3.45	P = 0.063
Colistin	0	0	0	0	0	0	---	
Pc=Pearson's chi-squar, Pv=P value								

In our study, the susceptibility rate to all the antibiotics is below the average. Only colistin showed well in vitro activity against *Acinetobacter* spp with only 100% susceptibility which is amazing. This effectiveness of colistin was also reported elsewhere (Ahmed *et al*., 2012; Morfin-Otero *et al*., 2012; Baadani *et al*., 2013). Particularly, colistin is frequently the final resort in many Asian, African, American and European health institutions (Andriamanantena *et al*., 2010; Ahmed *et al*., 2012; Cai *et al*., 2012; Cheah *et al*., 2015; Cheah *et al*., 2016).

The trend of rapid increase in multi-resistant strains is a genuine therapeutic problem. Indeed it is essential to implement swiftly the preventative measures for the effectiveness of therapeutic regime which are expensive and generally establish the last therapeutic lines. High antibiotic resistance demonstrates the demand of bi-ant biotherapy to deal with these infectious strains, this affects the community and nosocomial both isolates without substantial transformation and its variability depending on the specimens and services.

Limitations

It should be admitted that finding of this study was retrieved from the only single hospital of Pakistan, hence uninterrupted multi-center surveillance programmers to evaluate the actual picture of antimicrobial resistance/susceptibility pattern of *Acinetobacter* spp in Pakistan population is still compulsory to generate adequate descriptive data. Furthermore, more advanced molecular tools, such as pulsed-field gel electrophoresis (PFGE), drug-resistance gene typing (DRGT), and multi-locus sequence typing (MLST) should be performed to analyze the issue on the molecular basis. Thus, existing outbreaks caused by the epidemic clonal spread of a single resistant strain could be monitored.

CONCLUSION

It is important to better understand the antimicrobial patterns and optimize antimicrobial prescription policies to control the occurrence of drug-resistant *Acinetobacter* spp. When effective treatment choices are limited or unavailable, healthcare providers are enforced to advise the more expensive and less effective antibiotics which might be more toxic to the patient. Furthermore, researchers showed even when alternative treatments exist, patients with infectious strains are often showed more mortality rate, and survivors have meaningfully prolonged hospital stays, long-term disability and delayed recuperation. Struggles to avert such threats build on the establishment of confirmed public health strategies: infection control, antibiotic stewardship, immunization, protecting the food supply and reducing spread via person-to-person by screening, treatment, and awareness.

REFERENCES

Ahmed NH and K Baba *et al*. (2012). *In vitro* activity of tigecycline against clinical isolates of carbapenem-resistant *Acinetobacter baumannii* complex in Pretoria, South Africa. *BMC Research Notes*, **5**(1): 215.

Andriamanantena TS and E Ratsima *et al*. (2010). "Dissemination of multidrug-resistant Acinetobacter baumannii in various hospitals of Antananarivo Madagascar. *Ann. Clin. Microbiol. Antimicrob.,* **9**(1): 17.

Arsalane L and Y Qamouss *et al*. (2010). Epidémiologie des bactéries multi résistantes dans un service de réanimation polyvalente d'un hôpital universitaire de Marrakech entre octobre 2006 et septembre 2009. Les technologies de laboratoire **5**: 21.

Baadani AM and SI Thawadi *et al*. (2013). Prevalence of colistin and tigecycline resistance in Acinetobacter baumannii clinical isolates from 2 hospitals in Riyadh

Region over a 2-year period. *Saudi Medical Journal,* **34**(3): 248-253.

Begum S and F Hasan *et al*. (2013). Prevalence of multi drug resistant Acinetobacter baumannii in the clinical samples from Tertiary Care Hospital in Islamabad, Pakistan. *Pak. J. Med. Sci***.,** **29**(5): 1253.

Bojkovic J and DL Richie *et al*. (2016). Characterization of an Acinetobacter baumannii lptD deletion strain: permeability defects and response to inhibition of lipopolysaccharide and fatty acid biosynthesis. *J. Bacteriol.,* **198**(4): 731-741.

Cai Y and D Chai *et al*. (2012). Colistin resistance of Acinetobacter baumannii: Clinical reports, mechanisms and antimicrobial strategies. *J. Antimicrob. Chemother.,* dks084.

Capone A and SD'arezzo *et al*. (2008). *In vitro* activity of tigecycline against multidrug-resistant *Acinetobacter baumannii*. *J. Antimicrob. Chemother.,* **62**(2): 422-423.

Cheah SE and J Li *et al*. (2016). Colistin and polymyxin B dosage regimens against *Acinetobacter baumannii:* Differences in activity and the emergence of resistance. *Antimicrob. Agents Chemother.,* **60**(7): 3921-3933.

Cheah SE and J Wang *et al*. (2015). New pharmacokinetic/pharmacodynamic studies of systemically administered colistin against *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in mouse thigh and lung infection models: Smaller response in lung infection. *J. Antimicrob. Chemother.,* **70**(12): 3291-3297.

Decre D (2012). *Acinetobacter baumannii* et resistance aux antibiotiques: Un modèle d'adaptation. *Revue Francophone des Laboratoires,* **441**: 43-52.

Dent LL and DR Marshall *et al*. (2010). Multidrug resistant *Acinetobacter baumannii*: A descriptive study in a city hospital. *BMC Infectious Diseases* **10**(1): 196.

Dexter C and GL Murray *et al*. (2015). Community-acquired *Acinetobacter baumannii*: Clinical characteristics, epidemiology and pathogenesis. *Expert Rev. Anti Infect. Ther.,* **13**(5): 567-573.

Ebongue CO and ER Mengue *et al*. (2015). Antimicrobial Multi-Resistance of *Acinetobacter baumanii* isolated from clinical specimens in Douala (Cameroon). *Journal of Diseases and Medicinal Plants,* **1**(2): 31-36.

Hasan B and K Perveen *et al*. (2014). Emergence of carbapenem-resistant *Acinetobacter baumannii* in hospitals in Pakistan. *J. Med. Microbiol***.,** **63**(1): 50-55.

Krcmery V and E Kalavsky (2007). Multidrug-resistant *Acinetobacter baumannii*. *Emerging Infect. Dis.* **13**(6): 943.

Memish ZA and AM Shibl *et al*. (2012). Antimicrobial resistance among non-fermenting Gram-negative bacteria in Saudi Arabia. *J. Antimicrob. Chemother.,* **67**(7): 1701-1705.

Mireya UA, PO Martí *et al*. (2007). Nosocomial infections in paediatric and neonatal intensive care units. *Journal of infection,* **54**(3): 212-220.

Morfin-Otero R and JC Tinoco-Favila *et al*. (2012). Resistance trends in gram-negative bacteria: Surveillance results from two Mexican hospitals, 2005-2010. *BMC Research Notes,* **5**(1): 277.

Pajand O and MA Rezaee *et al*. (2013). Study of the carbapenem resistance mechanisms in clinical isolates of *Acinetobacter baumannii*: Comparison of burn and non-burn strains. *Burns,* **39**(7): 1414-1419.

Park YK and SI Jung *et al*. (2012). Changes in antimicrobial susceptibility and major clones of Acinetobacter calcoaceticus-baumannii complex isolates from a single hospital in Korea over 7 years. *J. Med. Microbiol.,* **61**(1): 71-79.

Patel PH and JD Pethani *et al*. (2013). Prevalence of nonfermenting Gram negative bacilli infection in tertiary care Hospital in Ahmedabad, Gujarat. *Indian Journal of Basic & Applied Medical Research,* **6**(2): 608-613.

Peleg AY and H Seifert *et al*. (2008). *Acinetobacter baumannii:* Emergence of a successful pathogen. *Clin. Microbiol. Rev.,* **21**(3): 538-582.

Poirel L and A Jayol *et al*. (2017). Polymyxins: antibacterial activity, susceptibility testing, and resistance mechanisms encoded by plasmids or chromosomes. *Clin. Microbiol. Rev.,* **30**(2): 557-596.

Rao J, D Susanti *et al*. (2016). Multidrug-resistant acinetobacter baumannii-plasmid-borne carbapenem and aminoglycoside co-resistance causing outbreak in Southwest Virginia. *Int. J. Infect. Dis.,* **45**: 112-113.

Shahla M and R Mozhdeh *et al*. (2012). Prevalence of β-Lactamase production and antimicrobial susceptibility of multidrug resistant clinical isolates of non-fermenting Gram negative bacteria from hospitalized patients in Kerman/Iran. *Jundishapur Journal of Microbiology,* 2(Spring): 405-410.

Sunenshine RH and MO Wright *et al*. (2007). "Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization. *Emerging Infect. Dis.,* **13**(1): 97.

Totsika M (2016). Benefits and challenges of antivirulence antimicrobials at the dawn of the post-antibiotic era. *Drug Deliv. Lett.* **6**(1): 30-37.

Wadl M and K Heckenbach *et al*. (2010). "Increasing occurrence of multidrug-resistance in Acinetobacter baumannii isolates from four German University Hospitals, 2002-2006. *Infection,* **38**(1): 47-51.

Xia W and Y Chen *et al*. (2012). Changing trend of antimicrobial resistance among pathogens isolated from lower respiratory tract at a university-affiliated hospital of China, 2006-2010. *J. Thorac. Dis***.,** **4**(3): 284-291.

Xu T and W Xia *et al*. (2013). A 4-year surveillance of antimicrobial resistance patterns of Acinetobacter baumanni in a university-affiliated hospital in China. *J. Thorac. Dis.,* **5**(4): 506.