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ORIGINAL RESEARCH

Prevalance and antibiogram of *Acinetobacter baumannii* from various clinical samples in a tertiary care hospital

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Abstract
Acinetobacter baumannii, an opportunistic pathogen in humans, is one of the major causes of nosocomial infections in the healthcare settings. It has been recognized as an agent of pneumonia, septicemia, meningitis, urinary tract and wound infections and is associated with high mortality especially in critically ill patients. The increased antimicrobial resistance in *Acinetobacter baumannii* and the occurrence of strains resistant to virtually all available drugs is quite alarming**.** The present study aimed to determine the prevalence and antibiogram of *Acinetobacter baumannii* from various clinical specimens which was undertaken for a period of one year from September 2019 to September 2020 during which total number of 490 samples were received in the microbiology department of Heritage institute of medical sciences amongst which 116 samples were of *Acinetobacter baumannii*. Bacterial identification was done by direct microscopy, culture, biochemical tests and Antibiotic susceptibility testing was performed for the isolates. Out of 116 isolates 92 (79%) were Multidrug resistant (MDR) and 24 (21%) were Extensively drug resistant (XDR). Maximum resistance was seen against cephalosporins, carbapenems, aminoglycosides, fluoroquinolones, tetracyclines and sulfa drugs. Ampicillin -sulbactum (69%) showed highest sensitivity than piperacillin-tazobactam (3.5%) and ticarcillin-clavulanate (3.5%) amongst beta-lactam drugs. The present study suggests that combination therapy with sulbactam or doxycycline can be a better option for MDR/XDR *Acinetobacter baumannii.*

Keywords: *Acinetobacter baumannii*; Multi-drug resistance; Extensively drug resistance; antibiotics; beta-lactam drugs; ampicillin-sulbactam

Introduction

*Acinetobacter baumannii (A. baumannii)*was isolated for the first time from soil by a Dutch bacteriologist Beijerinck in 1911 and was described as *Micrococcus calcoaceticus*.[1]It is a non-fermenter Gram-negative coccobacillus, was considered a low-category pathogen in the past, but has now emerged as a leading cause of hospital- and community-acquired infections.[2]Commonly associated with aquatic environment[3] it has been shown to colonize the skin as well as being isolated in high numbers from the respiratory and oropharynx secretions of infected individuals.[4] In recent years, it has been designated as a "red alert" human pathogen, generating alarm among the medical fraternity, arising largely from its extensive antibiotic resistance spectrum.[5]

Acinetobacter baumannii and its close relatives, Genomic species 3 and 13TU, form what is called the "A. baumannii complex." These are the 3 species of the most clinical importance,

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causing a vast majority of Acinetobacter infections, but they cannot be differentiated by routine diagnostic tests. They are often just referred to as *A. baumannii* in most literature unless stated otherwise. Acinetobacter baumannii is just 1 of many Acinetobacter species that can cause disease in humans, but in 2004, the Centers for Disease Control (CDC) reported that *A. baumannii* accounts for approximately 80% of all reported Acinetobacter infections.[6]

A. baumannii is considered as a low-virulence pathogen, unless it is isolated from patients having comorbidities such as neonates with low birth weights and elderly patients with chronic illnesses such as malignancy. Major predisposing factors important in the acquisition of *A. baumannii* infection include prolonged hospital stay, mechanical ventilation, intravascular device, advanced age, immunosuppression, previous broad-spectrum antimicrobial therapy, previous sepsis, ICU stay, and enteral feedings.[7]

The most frequent clinical manifestations are pneumonia associated with mechanical ventilation, bloodstream infections, urinary tract infections, and bacteremia associated with long periods of device use, meningitis, eye infections, intra-abdominal infections, surgical sites, the respiratory tract, and the gastrointestinal tract.[8-9]

The exacerbated and undue use of antibiotics associated with ineffective hospital interventions are related to the spread of MDR and consequently reduce treatment options. The World Health Organization (WHO) published in early 2017 a list of priorities for research into the development of active antibiotics against MDR and extensively resistant bacteria, which put *A. baumannii* first in the list of critical situations around the world.[10]

The rapid emergence of multi- and pandrug-resistant strains of Acinetobacter highlights the organism's ability to quickly acclimatize to selective changes in environmental pressures. The upregulation of the organism's innate resistance mechanisms coupled with the acquisition of foreign determinants have played a crucial role in the express route the organism has taken to becoming a multidrug-resistant pathogen.[11]

Acinetobacter baumannii strains can develop multiple antibiotic resistance mechanisms, which cause a major health problem in immuno-compromised patients. These strains showed resistance to broad-spectrum β-lactams antibiotics involved carboxy-pencillins, the third generation of cephalosporins, and most recent carbapenems resistance. Furthermore, these strains can produce various aminoglycoside-modifying enzymes and most of these enzymes are related to fluoroquinolones resistance.[12]

Objectives

- To determine the prevalence of *Acinetobacter baumannii* from various clinical specimens.
- To analyse the antibiotic susceptibility pattern of the isolated *Acinetobacter baumannii.*

Methods

The present study was undertaken for a period of one year from September 2019 to September 2020 during which total number of 490 samples from various clinical departments were received in the microbiology department of Heritage institute of medical sciences. Direct microscopy from the specimen was done by Gram staining technique for presumptive identification. Further processing was done by plating the specimen into various culture media like blood agar, MacConkey's agar, chocolate agar, CLED agar and Brain heart infusion broth depending upon the specimen and the plates where then incubated at 37 degree Celsius for 18-24hours. The organisms isolated were identified using an array of biochemical tests like oxidase test, indole test, citrate test, urease test, triple sugar iron agar and oxidation - fermentation media. Antibiotic susceptibility testing for all the isolates where done on Mueller-hinton agar by kirby-bauer disc diffusion following CLSI guidelines 2019.

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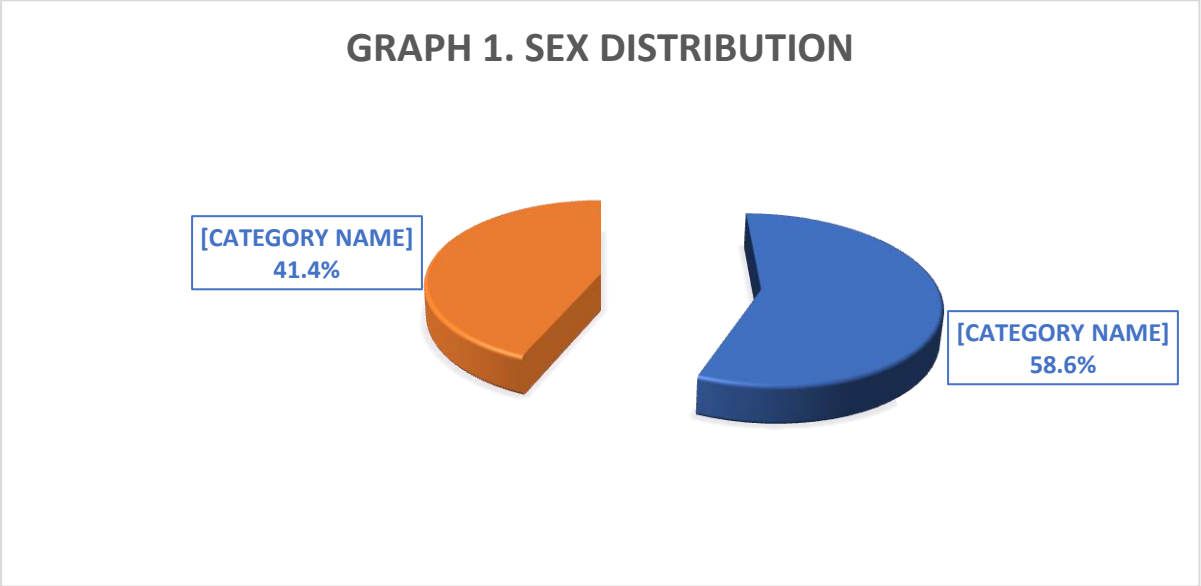
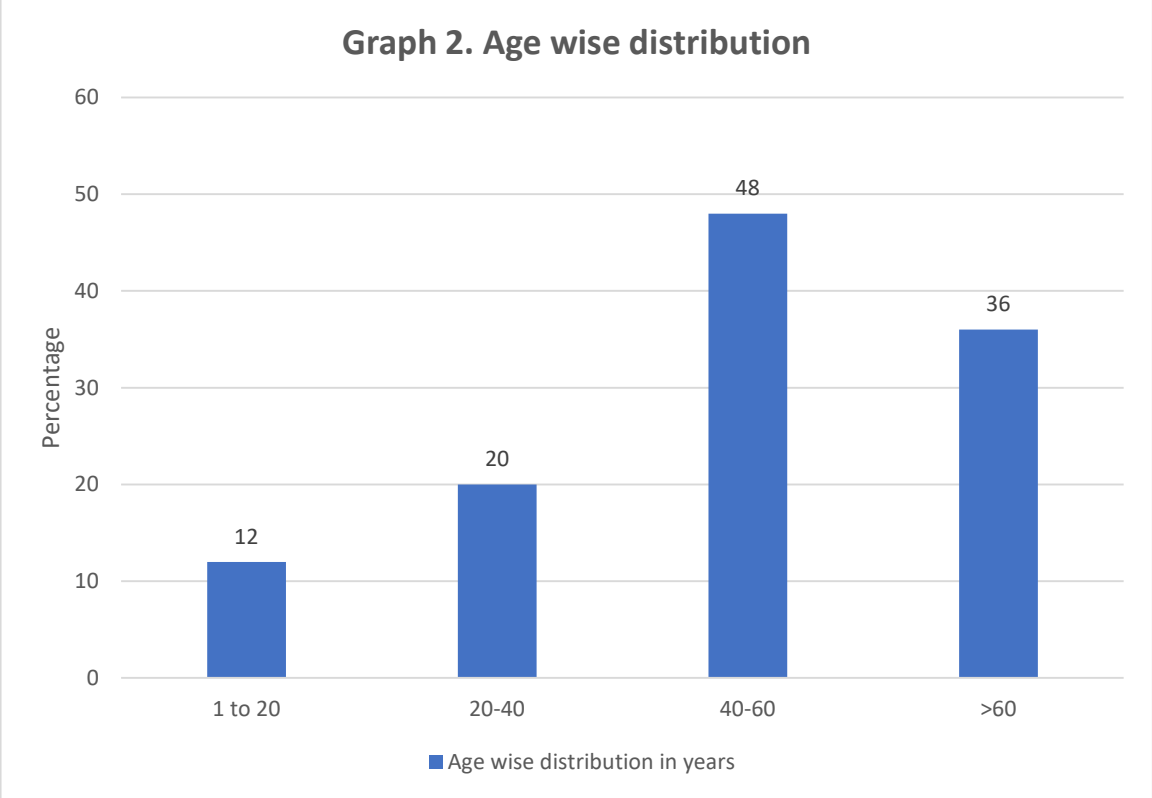
Results

Out of total 490 samples 116 samples were of Acinetobacter baumannii (23.6%). Male preponderance was seen in sex distribution. 58.6% (68/116) of the patients were male and 41.4% (48/116) were female in this study (Graph 1).



In Age distributionwide range from 1day to 72 years of age was seenand the maximum cases (48/116) were seen in the age group of 40 to 60 years (41.4%) followed by 36 (31.0%) cases in age group of above 60 years and 20 (17.2%) cases in age group of 20-40 years. Least number of cases (12/116) 10.3% were seen in age group of 1 day to 20 years.(Graph 2)



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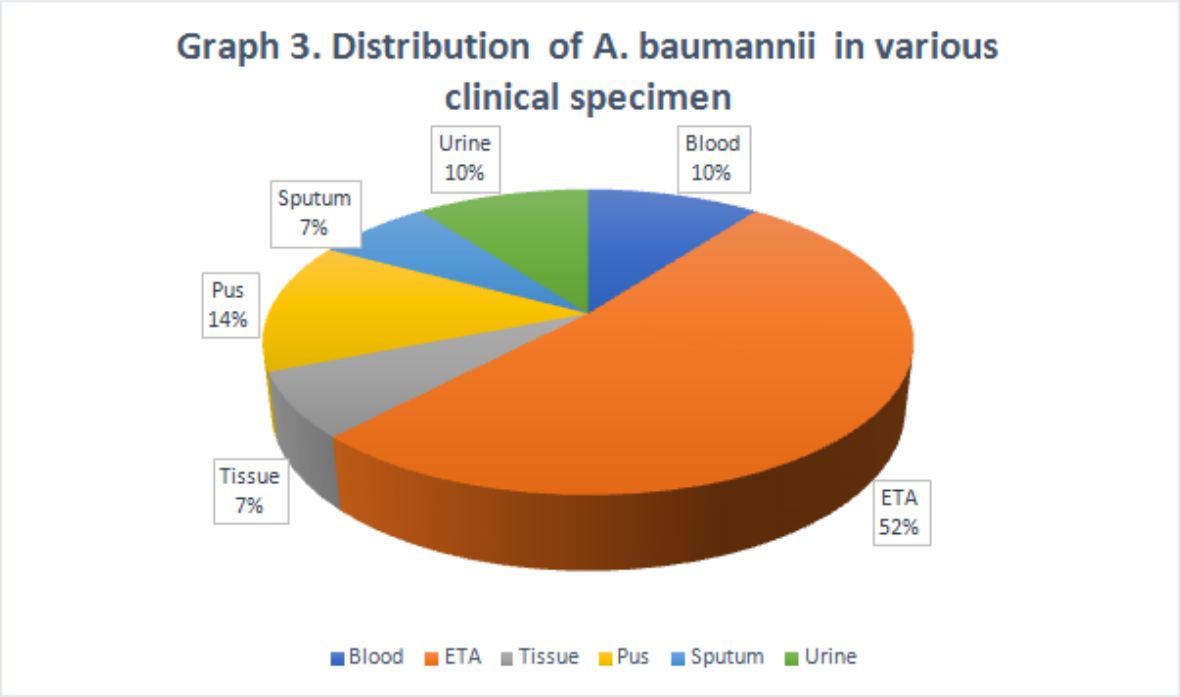
Endotracheal aspirates were the most common specimen from which *A. baumannii* (52.0%; 60/116) were isolated; the next highest source was pus (14.0%; 16/116) followed by urine (10.0%; 12/116), blood (10.0%; 12/116), tissue (7.0%; 08/116) and sputum (7.0%; 08/116). (Graph 3)



Out of 116 isolates 92 (79.3%) were Multidrug resistant (MDR) and24 (20.7%) were Extensively drug resistant (XDR). The antibiotic susceptibility pattern showed that 96% of the isolates were resistant to ceftriaxone, ceftazidime, imipenem and ticarcillin-clavulanate followed by piperacillin-tazobactam (93.0%), piperacillin (90%), ofloxacin (90%), ciprofloxacin (83%), meropenem (82%), levofloxacin (76%),sulfamethoxazole-trimethoprim (76%).69% of the isolates were susceptible to Ampicillin-sulbactam followed by doxycycline (31%), tetracycline (28%), tobramycin (23%) and gentamicin (12%).

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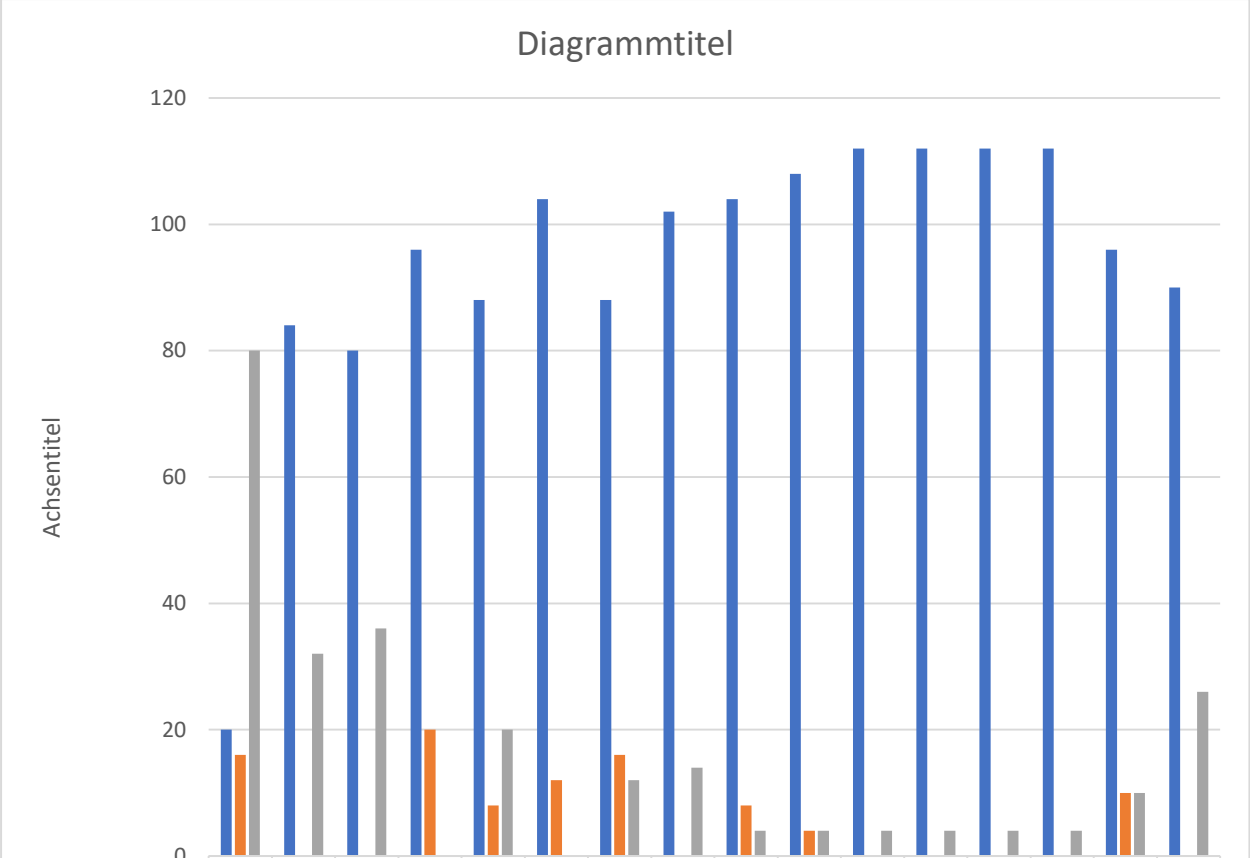

	Ampicillin-sulbactam	Tetracycline	Doxycycline	Ciprofloxacin	levofloxacin	Oflox acin	Sulfamethoxazole-trimethoprim	Gentamicin	Piperacillin	Piperacillin-tazobactam	Ticarcillin-clavulanate	Imipenem	Ceftriaxone	Ceftazidime	Meropenem	Tobramycin
Resistant	20	84	80	96	88	104	88	102	104	108	112	112	112	112	96	90
Intermediate	16	0	0	20	8	12	16	0	8	4	0	0	0	0	10	0
Susceptible	80	32	36	0	20	0	12	14	4	4	4	4	4	4	10	26

Discussion

Acinetobacter baumannii has become a major concern for scientific attention due to extensive antimicrobial resistance. This resistance causes an increase in mortality rate because strains resistant to antimicrobial agents are a major challenge for physicians and healthcare workers regarding the eradication of either hospital or community-based infections. These strains with emerging resistance are a serious issue for patients in the intensive care unit (ICU). Antibiotic resistance has increased because of the acquirement of mobile genetic elements such as transposons, plasmids, and integrons and causes the prevalence of multidrug resistance strains (MDR). In addition, an increase in carbapenem resistance, which is used as last line antibiotic treatment to eliminate infections with multidrug-resistant Gram-negative bacteria, is a major concern. Carbapenems resistant A. baumannii (CR-Ab) is a worldwide problem. Because these strains are often resistant to all other commonly used antibiotics. Therefore, pathogenic multi-drug resistance A. baumannii (MDR-Ab) associated infections become hard to eradicate. Plasmid-mediated resistance causes outbreaks of extensive drug-resistant. A. baumannii (XDR-Ab).[13]

The present study was undertaken at Heritage institute of medical sciences, Varanasi in the department of microbiology to determine the prevalence of *Acinetobacter baumannii* from

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various clinical specimens and to analyse the antibiotic susceptibility pattern of the isolated *Acinetobacter baumannii.*The age of the patient varied from I day to 72 years of age in which most of the patients (48/116) were seen in the age group of 40 to 60 years (41.4%) followed by 36/116 (31.0%) cases in age group of above 60 years and 20/116 (17.2%) cases in age group of 20-40 years. Least number of cases (12/116) 10.3% were seen in age group of 1 day to 20 years.

In the present study 58.6% of the patients were male and 41.4% were female. Predominant number of Acinetobacter baumannii were isolated from pulmonary samples (endotracheal aspirates 51.8%, sputum 6.9%). This observation was consistent with the results reported by Ben Haj Khalifa and Khedher[14] who stated the airway as the main isolation site for this species. Furthermore, Delbos[15] reported that hospital-acquired pneumonia is still the most common infection caused by *A. baumannii*. Our results also showed that *A. baumannii* was present in 13.8% of pus samples which was lower than (32.5%) study done by Falagas et al.[16] and higher than (3.8%) study carried out by Sileem et al.[17]*A. baumannii* were also isolated from 10.3% of blood samples which was in concordance to study done by Uwingabiye et al.[18] which indicated the presence of *A. baumannii* in 14.51% of blood samples. 10.3% 0f the *A.baumanni* isolates were from urine specimen which is in contrast to study done by Rachana et al[19] who have shown predominance of*A.baumanni* isolates (38.8%) from urine samples. Least number of isolates (6.9%) were found from tissue specimens.

Multidrug resistant Acinetobacter baumannii (MDRAB) is defined as resistance to more than three classes of antibiotics. 79% (92/116) isolates were MDRAB in our study which was consistent with a study done by Dent et al[20] were 72% of the isolates were MDRAB. More recently, the term "extensively drug-resistant" A. baumannii (XDRAB) has been used to characterize bacterial isolates resistant to all authorized antibiotics except two categories of antibiotic such as tigecycline and polymyxins.[21]21% (24/116) isolates in our study were extensively drug resistant acinetobater baumannii (XDRAB) which is almost similar to study done by Lakshmi et al.[22]

The antibiotic susceptibility pattern showed high resistance rate for cephalosporins (96%) which is comparable and is similar to studies done byOmer MI et al[23](95%)and Chakraverti et al[24] (96%) in which high resistance was seen to cephalosporins.In our study, we observed significantly high resistance to piperacillin (90%) which is more than studies done by Tewari et al (68.9%)[19] and Nazmul et al. (77.5%)[25] but is lower than study done by Shakibaie et al.[26]which reported 100% resistance to piperacillin.

In the β-lactam and β-lactamase inhibitor our study showed high resistance rate to piperacillin–tazobactam(93%) and ticarcillin-clavulanate (96%) in comparision to ampicillin-sulbactam which showed high sensitivity rate of 69% which is in concordance to study done by Jingyi Shi et al[27]in which they stated that when it came to the in vitro activities of beta-lactamase inhibitors, sulbactam was superior to clavulanic acid and tazobactam. Sulbactam has good intrinsic antimicrobial activity against multidrug-resistant acinetobacter strains at concentrations readily achievable in human serum.[28]Several studies have highlighted the importance of using Sulbactamcontaining regimens which appeared to be comparable to regimen of other agents when the infecting organisms were susceptible to sulbactam in patients with A. baumannii pneumonia and blood stream infections.[29-31] Mixed results have been reported for use of sulbactam to treat A. baumannii meningitis, and this likely relates to impaired drug penetration. Whether higher dosages are more efficacious or reduce the risk of resistance, or even whether ampicillin-sulbactam should be used in combination with other agents is yet to be determined.

Carbapenems have been the mainstay of antimicrobial therapy against A. baumannii infections since 1990. Alarmingly, a recent review mentioned 50%, 85%, and 62%–100% as the frequency of carbapenem-resistant Acinetobacter in Singapore, India, and Pakistan,

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respectively. Likewise, the frequency of carbapenem-resistant A. baumannii was reported to be 70%, 92%, and 100% in Chile, Korea, and Portugal, respectively. The resistance to carbapenems also renders other beta-lactam drugs ineffective.[32]In the present studyresistance rate of imipenem and meropenem was 96% and 82% respectively which was similar to study done by Shi et al[27] in which imipenem and meropenem showed resistance rate of 93% and 92% respectively. Similar other studies by Jaggi et al. (90%)[33] and Nazmul et al. (92.5%)[25] have reported high resistance rate of the A. baumannii towards carbapenems.

Aminoglycosides appear to retain activity against many A. baumannii isolates but as with all antimicrobial agents and multidrug-resistant pathogens, resistance is increasing. In the present study tobramycin (23%) has shown high susceptibility rate than gentamicin (12%). Similar findings have been seen in an analysis done by Akers et al[34] in which Tobramycin maintained the highest overall susceptibility rates amongst aminoglycosides. In a trend analysis of 5 years done by Ayenew et al[35] the resistance to aminoglycoside was found to vary among the different agents in which resistance to gentamycin was shown to increase (48% to 58%) whereas a decreasing trend of resistance was observed for tobramycin (56.5% to 42.8%) and resistance to tobramycin was below 50%.

In our study, high resistance rate was seen amongst fluoroquinolones in which ofloxacin (90%) has shown maximum resistance followed by ciprofloxacin (83%) and levofloxacin (76%). Our study results were in concordance to various studies showing resistance rate of ciprofloxacin between 70-90%.[23,35,36]

Tetracyclines are not commonly prescribed to treat the infections caused by *A. baumannii*, however, doxycycline and minocycline have been recently administered in combination with other antibiotics to improve clinical effectiveness in eradicating *A. baumannii* infections.[16] The findings in the present study also shows good susceptibility rate of tetracycline (28%) and doxycycline (31%) in comparison to other antibiotic group.Beheshti Maryam et al.[37] have shown high susceptibility rate of 96.93% to doxycycline and 43.87% to tetracycline. This study showed adequate *in vitro* activity of doxycycline and minocycline in burned patients and only of doxycycline in VAP, showing promising clinical and microbiological effectiveness of tetracyclines either as monotherapy or in combination with other agents for the treatment of *A. baumannii* infections. Maleki *et al*.[38] in their study have also found a resistance rate of 18% to doxycycline while 80% of isolates showed resistant to tetracycline.

Conclusion

Acinetobacter baumannii has emerged as an important nosocomial pathogen exhibiting high level of resistance to many antibiotics. This may be partly due to ability of this bacterium to acquire resistance gene by horizontal gene transfer and its ability to adapt to the nosocomial environment resisting adverse environmental challenges. Multi drug resistant (MDR) and extensive drug resistant (XDR) isolates are routinely being reported along with upsurge into pan-drug resistant isolates. Although newer drugs like tigecycline and colistin arebeing frequently used for these drug resistant isolates, but their use should be restricted due to disadvantage of toxicity produced and emerging resistance against these drug reported from all over the world.Revival of old antibiotic groups with newer approaches is much needed.When it comes to the in vitro activities of beta-lactamase inhibitors, sulbactam was superior to clavulanic acid and tazobactam. Tetracycline and doxycycline have shown promising results. Studies of combination therapy with these antibiotics can be an area of further research.

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