

Determination of antibiotic resistance characteristics of *A. baumannii* isolated from hospitalized patients

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Abstract : Patients who are immuno-compromised or hospitalized for longer duration are more prone to nosocomial infection. *A. baumannii* is one of the most common causes of such infection. Multidrug resistance (MDR) properties of such species make it difficult to treat the disease. This MDR properties varies from species to species. It is highly depend in the environmental conditions and antibiotic exposures. Here a study was designed to evaluated the antibiotic resistance of *A. baumannii* in the patients of Surat city. For this study, samples from 198 patients in form of blood, urine and pus were collected and studied. Initial isolation and screening were done by using blood agar, MacConkey's agar and Nutrient agar. Identification was carried out by Vitek GN2 ID card and antibiotic sensitivity was determined by Vitek2 automated system AST with N262. Results of the study have shown that many strains of *A. baumannii* are resistance against 3rd and 4th generation of antibiotics as well as against certain beta lactamase drugs. The only drugs which are found effective are colistin and tigecycline which can be used better alternates for the treatment.

Keywords: *A. baumannii*, Multidrug Resistance, ICU patients, Surat

I. Introduction

Acinetobacter baumannii is one of the most opportunistic pathogen which infects immuno-suppressed patients. (Nocera, Attili, & De Martino, 2021; Sarshar, Behzadi, Scribano, Palamara, & Ambrosi, 2021) In the hospitalized patients, it causes a variety of nosocomial infections which includes infections of blood stream and urinary tract, meningitis, wound and many others. (Pimentel et al., 2021; Rafa, Walaszek, Walaszek, Domanski, & Rozanska, 2021; Repizo et al., 2017) In a report World Health Organization (WHO) has categorize the multidrug resistance (MDR) *A. baumannii* as top most priority pathogen for which quick antibiotic development is sought. (Singh et al., 2020; Vazquez-Lopez et al., 2020; Zhen, Stalsby Lundborg, Sun, Gu, & Dong, 2020) Studies have shown that there are various antibiotics which may be effective against many drug-resistant microorganisms. Most of these antibiotics belong to either 3rd or 4th generation of drug. Still there are certain species of *A. baumannii* which has gained resistance against these drugs and able to survive. This rapid transformation in multidrug-resistant strains is now became a global concern. (Bhamidimarri et al., 2019; Fodor et al., 2020; Gellings, Wilkins, & Morici, 2020; Kousovista et al., 2021) The current scenario leads researchers to think about the need for regular monitoring of the sensitivity of nosocomial strains of *Acinetobacter* spp. It was seen that the antibiotic resistance property of *A. baumannii* varies from strain to strain. This variation is result of exposure of various environmental conditions and drugs use for treatment. (Bedenić & Meštrović, 2021; Cheng et al., 2020; Cifuentes et al., 2020) Studies have also revealed that *A. baumannii* can acquire genes from other resistance bacteria especially *Pseudomonas* and *Escherichia*. (Nguyen et al., 2021; Zhen et al., 2020) Genetic modification or mutation many also enhance the antibiotic resistance of the strains. Study of antibiotic resistance can provide significant information about the strain stability against antibiotics and may also suggest possible treatment. (Agard, Ozer, Morris, Piseaux, & Hauser, 2019; Chen, Shu, & Lin, 2021; Cheng et al., 2020) Here a similar study was carried out to determine the antibiotic resistance of *A. baumannii* strains isolated from the intensive care unit patients of a hospital in Surat, India. Objective of the study was to prepare an antibiogram for *A. baumannii* for aid better treatment.

II. Material and Methods

2.1 Collection of Samples

For isolation of *A. baumannii* blood/urine/pus samples of 198 patients admitted in intensive care unit of the hospital of Surat were selected. These patients are either suffering from severe pneumonitis or urinary tract infraction. A few patients having post surgical patients were also considered for the study. For collection of blood, venipuncture method was performs and blood was collected in sterile BHI media containing vial with proper labeling. Urine samples were collected from catheters in sterile containers. Pus samples were collected by swab stick method. All the collected samples were immediately processed for isolation of microorganisms.

2.2 Isolation of *A. baumannii*

Blood agar, MacConkey's Agar and Nutrient agar were used cultivation media for isolation of microorganisms from collected samples. Spread plate method was performed for each sample. Serial dilution was with sterile distilled water for required samples. 100 µl of sample were speared on each plate and plates were incubated at 37 °C until the visible colonies are observed in the plates. (Ejaz et al., 2021; Tiwari, Vashist, Kapil, & Moganty, 2012)

2.3 Primary screening of *A. baumannii*

A. baumannii is a gram negative microorganism. For primary screening, colonies of all the plates were observed carefully for colony characteristics. Colonies having different morphology were subjected to gram staining. Among them, colonies having gram negative character and round/coccobacillus shape were further purified on nutrient agar and preserved for future applications. (Alamri, Alsultan, Ansari, & Alnimr, 2020)

2.4 Identification of *A. baumannii*

All the purified microbes were processed for identification using Vitek2 system using Vitek2 GN ID card (bioMerieux Vitek, USA). Results of the analysis were interpreted based on the current clinical and laboratory standard institute guidelines. (El-Kazzaz et al., 2020; Tyumentseva et al., 2021)

2.5 Antibiotic Sensitivity Test

Vitek2 automated system AST with N262 card was used for antibiotic sensitivity test. This card can perform the sensitivity test for Piperacillin/Tazobactam (PTF 128 µg/L), Ceftazidime (CAZ 64 µg/L), Cefoperazone/sublactam (CFS 64 µg/L), Cefepime (FE 32 µg/L), Imipenem (IMP 16 µg/L), Meropenem (MEM 16 µg/L), Amikacin (AK 64 µg/L), Gentamicin (GM 16 µg/L), Netilmicin (NET 2 µg/L), Ciprofloxacin (CIP 4 µg/L), Levofloxacin (LEV 8 µg/L), Minocycline (MN 1 µg/L), Tigecycline (TG 1 µg/L), Colistin (CS 0.5 µg/L), Trimethoprim/sulfamethoxazole (TX 160 µg/L). All the microbes to grow at mentioned concentration were considered as resistance whereas those which are not able to grow were considered as sensitive microorganisms. Species which have shown less growth in presence of antibiotic were considered as intermediate resistance. (El-Kazzaz et al., 2020; Kirtikliene, Mierauskaite, Razmiene, & Kuisiene, 2021; Tyumentseva et al., 2021)

III. Results and Discussion

From 198 samples, 50 different isolates were obtained which were gram negative in nature and identified as *A. baumannii* in Vitek2 GN ID card. Results obtained for antibiotic sensitivity test in mentioned in the table 1.

Table 1 Antibiotic sensitivity of various *A. baumannii* strains

Isolate Name	Antibiotic (Resistance/Intermediate resistance/Sensitive)														
	PTZ	CAZ	CFS	FE	IMP	MEM	AK	GM	NET	CIP	LEV	MN	TG	CS	TSX
SS01	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS02	R	R	S	I	R	R	R	I	S	R	R	S	S	S	S
SS03	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS04	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS05	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS06	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS07	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS08	R	R	S	I	R	R	S	I	S	R	R	S	S	S	S
SS09	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS10	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS11	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS12	R	R	I	I	R	R	R	I	S	R	R	S	S	S	R
SS13	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS14	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS15	R	R	S	R	R	R	S	I	S	R	R	S	S	S	S
SS16	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS17	R	R	I	I	R	R	R	I	S	R	R	S	S	S	R
SS18	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS19	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS20	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS21	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS22	R	R	S	R	R	R	S	R	S	R	R	S	S	S	S
SS23	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS24	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS25	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R

SS26	R	R	I	I	R	R	R	I	I	R	R	S	S	S	R
SS27	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS28	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS29	R	R	I	I	R	R	R	R	I	R	R	S	S	S	R
SS30	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS31	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS32	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS33	R	R	I	I	R	R	R	I	S	R	R	S	S	S	R
SS34	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS35	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS36	R	R	R	R	R	R	R	R	R	R	R	S	S	S	R
SS37	R	R	I	I	R	R	R	I	I	R	R	S	S	S	R
SS38	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS39	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS40	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS41	R	R	S	I	R	R	S	R	S	R	R	S	S	S	S
SS42	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS43	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS44	R	R	I	I	R	R	R	I	I	R	R	S	S	S	R
SS45	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS46	R	R	R	R	R	R	R	R	I	R	R	I	S	S	R
SS47	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R
SS48	R	R	I	I	R	R	R	I	I	R	R	S	S	S	R
SS49	R	R	R	R	R	R	R	R	R	R	R	I	S	S	R
SS50	R	R	R	R	R	R	R	R	I	R	R	S	S	S	R

Based on the results of antibiotic sensitivity assay, it was observed that, all the isolates strains were completely resistance against PTZ, CAS, IMP, MEM, CIP and LEV. More than 90% of isolated strains were resistance to AK and TSX. 80% strains were found resistance against FE and GM. In case of NET, only 30% strains have shown pure resistance whereas 54% were considered as intermediate resistance. Another important observation was all the strains were completely sensitive to TG and CS. MN also proved to be good antibiotic as it has killed around 74% of total strains. (Figure 1). Results have indicated that all the isolated species are highly resistance against certain third/fourth generation molecules (e.g. CAS), quinolones (e.g. CIP and LEV), combination of amonipenicillins with beta lactamase inhibitors (e.g. PTZ), certain monobactam (e.g. IMP and MEM). This reflects that these strains have gain resistance against various class and generation of antibiotics. Treatment with these antibiotics will be useless and sick more alternatives for better treatment. (Nwabor, Terbtothakun, Voravuthikunchai, & Chusri, 2021; Singh et al., 2020; Vazquez-Lopez et al., 2020; Vrancianu, Gheorghe, Czobor, & Chifiriuc, 2020) But two drugs namely colistin and tigecycline hav shown excellent results against isolated *A. baumannii* species. Colistin which is a polymyxin class drug is found to be one of the most effective molecules against isolated strains. It breaks the cytoplasmic membrane of the cell resulted into bacterial cell death. (Katip, Uitrakul, & Oberdorfer, 2020; Sacco, Visca, Runci, Antonelli, & Raponi, 2021) Tigecycline is the very first drug belongs to glycyctcline. It is one of the most used broad spectrum antibiotic for gram negative bacteria. It is responsible for the bacteriostatic activity by controlling the protein

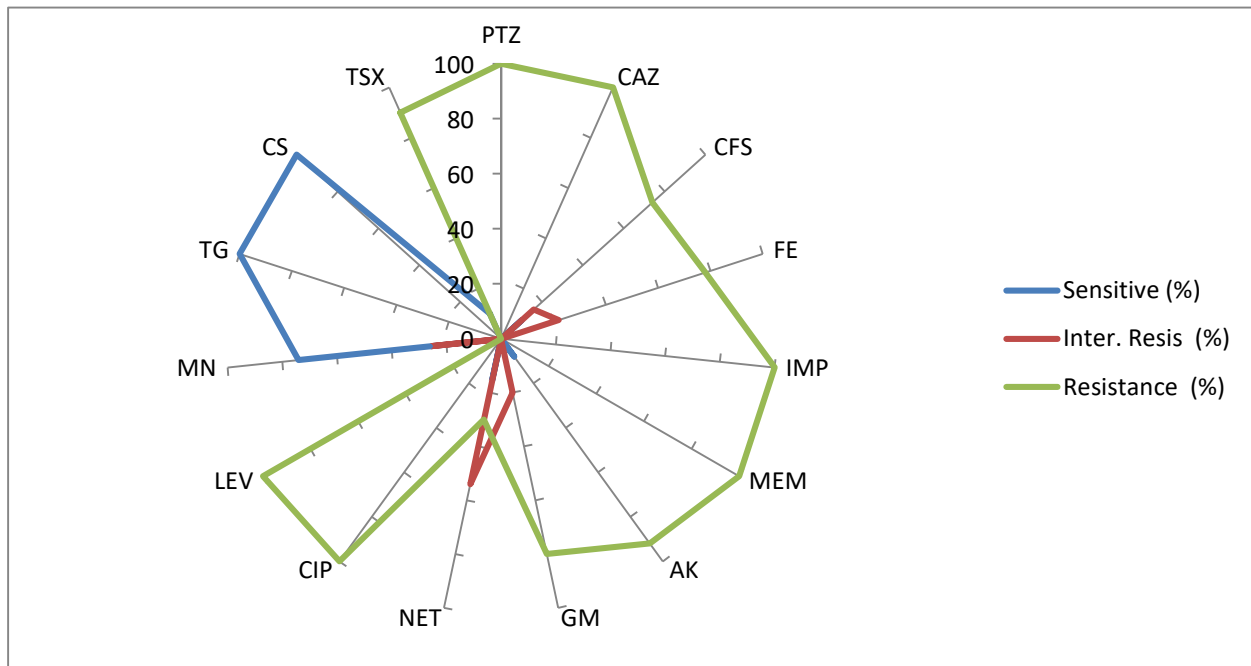


Figure 1. Antibiogram of various *A. baumannii* strains

formation through blocking interaction of amoniacyl-tRNA with A site of ribosome. (Hua et al., 2017; Huang et al., 2016; Lasarte-Monterrubio et al., 2021) Another antibiotic of tetracycline class known as minocyclin has also shown good inhibition of *A. baumannii*. Around 74% strains were found sensitive against this drug. So it can also be consider as an alternate molecules for the treatment. (Kousovista et al., 2021; Monnheimier et al., 2021; Vrancianu et al., 2020) Many previous studies have shown that the frequent exposure of antibiotics for longer duration results into resistance against these antibiotics. Many scientists have preferred to study the molecular characterization certain gene and proteins involve in the resistance. They have shown that these multidrug resistance (MDR) properties can be acquired by the microorganisms by point mutation or gene transfer from the other resistance microorganisms. (Ejaz et al., 2021; Hamidian et al., 2020; Traglia et al., 2019) Even it was found that many *A. baumannii* have highly mutated their genes and gain resistance against more the 40 antibiotics. Treatment for such resistance microorganism is becoming a challenging task which leads researchers to synthesize new molecules and novel mechanism to deal with such microorganisms. (Ramirez, Bonomo, & Tolmasky, 2020; Yakkala, Samantarrai, Gribskov, & Siddavattam, 2019; J. Zhang, Liu, & Li, 2015; L. Zhang et al., 2020; Zhao et al., 2020)

IV. Conclusion

A. baumannii, a most common nosocomial microorganism can gain resistance against broad spectrum of antibiotics. Here in this study, most of the isolated species of Surat patients were highly resistance against 3rd and 4th generation of antibiotics. Currently, the only preferable treatment is to use colistin and tigecycline drugs.

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