Research Article

COMPARISON BETWEEN EFFICACY OF TYGECYCLINE AND MINOCYCLINE IN MULTI DRUG RESISTANT ACINETOBACTER BAUMANII ISOLATED FROM RESPIRATORY TRACT INFECTIONS

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ABSTRACT

Acinetobacter baumannii is gram-negative coccobacilli, widely distributed in environment. It is one of the important infectious agents for nosocomial infections. Multidrug resistance (MDR) is a clinical dilemma in our region. This study was designed to compare efficacy of Tygecycline and Minocycline against MDR *A. baumanii* isolated from respiratory tract infections. All respiratory tract samples including sputum, tracheal aspirate and bronchial lavage were collected, isolated, identified and antimicrobial susceptibility was assessed by using standard protocols. *A. baumanii* isolated from 122 tracheal aspirates and 66 sputum samples. Bronchial lavage showed no bacterial growth. Age group 41-60 years showed 45% isolation of tracheal aspirates, whereas, sputum samples showed predominance (41%) recovered from older age group (>60 years). Sensitivity of Colistan was 10% in tracheal aspirates and 12% in sputum. These samples showed sensitivity of Cotrimoxazole in 6% and 3% in sputum and tracheal aspirates respectively while Beta lactams showed < 5% in both types of specimens. Tygecycline exhibited antibiotic sensitivity 34% from tracheal aspirates and 30% from sputum. Minocycline was found to be sensitive in 27% in tracheal aspirates and 23% from sputum. Our study concluded that Tigecycline found to be more effective as compared to Minocycline for the treatment of respiratory tract infections caused by multidrug resistant *A. baumanii*. Further studies are required to confirm these findings and large clinical trials will be required to make evidence based management guidelines in this regard

Key Words: Minocycline, Tigecycline, *Acinetobacter baumannii*, Multi Drug Resistant

INTRODUCTION

Acinetobacter baumannii is gram-negative coccobacilli, widely distributed in environment (1). It is one of the important micro-organisms causing nosocomial infections, including cardiovascular infections, superficial and deep wound infections, mening-encephalitis, urinary tract infections, sepsis and ventilator associated pneumonia particularly in intensive care units (2). The peculiar ability of nosocomial outbreaks is linked with biofilm formation (3). The antimicrobial resistance of *Acinetobacter baumannii* is on surge and becoming a clinical dilemma. It is getting resistant to almost all antibiotics, including Aminoglycosides, Fluoroquinolones, β-lactams and Carbapenems (4). Major contributing factors of the antibiotic resistance include prolonged hospital stay, urinary catheterization, and different invasive procedures (5). The World Health Organization (WHO) has marked Acinetobacter species as one of the top priority that require development of new antibiotics (6). Moreover, multidrug-resistant (MDR) *A. baumannii* with bacteremia is linked with high mortality rates (i.e. 56.2%), in comparison with non –MDR *A. baumannii* strains (4.7%) (7, 8).

Minocycline is a bacteriostatic semi-synthetic derivative among class of antibiotic Tetracycline with activity against both aerobic, anaerobic gram-positive and gram-negative bacteria. It acts by inhibiting protein synthesis in bacteria (9).

Tigecycline is a glycylcycline, derivative of Minocycline. It was established to overcome emerging antimicrobial resistance with broad spectrum activity against gram positive and gram negative bacteria (10).

Both Minocycline and Tigecyclin belong to the same group of antibiotics with encouraging clinical outcome against MDR *A. baumannii* infections (11). Therefore, this study was designed to compare the efficacy of Tygecyclin and Minocycline against MDR *A. baumanii* isolated from respiratory tract infections.

METHODS

This was a comparative cross-sectional study conducted at Dow Diagnostic Research laboratory, Dow University of Health Sciences, Karachi, Pakistan. The study was conducted during the period from 1 December 2021 till 30 May 2022. All respiratory tract samples including sputum, tracheal aspirate and bronchial lavage were collected from patients suffering from *A. baumanii* infections. Clinical samples were inoculated on Sheep blood agar plate, Chocolate agar plate (aerobic with 5% CO2) and Mac Conkeys according to standard microbiological protocols. Identification of bacterial growth, was performed by specific methods, followed by confirmation by API 20NE (bioMerieux France). Mueller Hinton agar (MHA) (oxoid Ltd, England) used for antimicrobial susceptibility testing by modified Kirby Bauer's disc diffusion.

Statistical analysis

Data was collected and analyzed on Statistical Package for Social Sciences (SPSS) version 21.0. Descriptive data was presented as frequency distribution in number and percentage.

RESULTS

A. baumanii isolated from 122 tracheal aspirates and 66 sputum samples, whereas, bronchial aspirates showed no growth. Age group 41 to 60 years showed (45%) isolation of tracheal aspirates followed by (34%) from greater than 60 years and then (13%) from 21 to 40 years. Sputum samples showed predominance (41%) recovered from age group greater than 60 years, followed by (32%) from 41 to 60 years (Figure 1). Majority of tracheal aspirates collected from high dependency units (HDU) (45%), followed by medical Intensive Care units (ICU) (37%) and surgical ICU (16%). Predominance of sputum was found in HDUs (52%), then medical ICUs (30%) and surgical ICUs (12%) (Table 1).

A. baumanii showed highest sensitivity towards Tygecycline (34%) from tracheal aspirates and (30%) from sputum. Minocycline was sensitive (27%) in tracheal aspirates and (23%) from sputum. Colistan was found to be sensitive in (10%) and (12%) in tracheal aspirates and sputum, respectively. Beta lactams including Ceftriaxone, Cefoperazone salbactum, Tazobactam, Meropenem were about to be least sensitive among all antibiotics (less than 5%) in both sputum and tracheal aspirates. Amikacin (7%) and Gentamicin (5 %) were sensitive in tracheal aspirates, whereas, (6%) and (5%) in sputum, respectively. Cotrimoxazole showed (6%) sensitivity in sputum and (3%) in tracheal aspirates (Figure 2). Tygecycline was more sensitive than Minocycline in age groups 41 to 60 years from sputum and all age groups from tracheal aspirates. Higher frequency of Minocycline was observed from 0 to 20 years and greater than 60 years in sputum (Figure 3, 4).

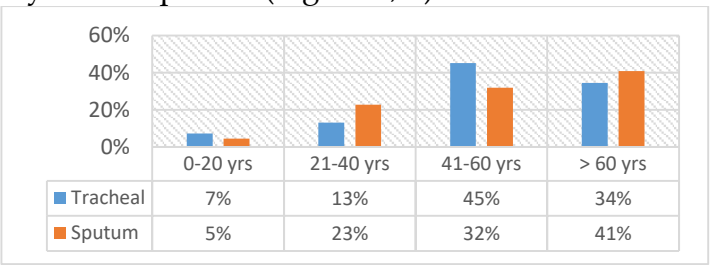
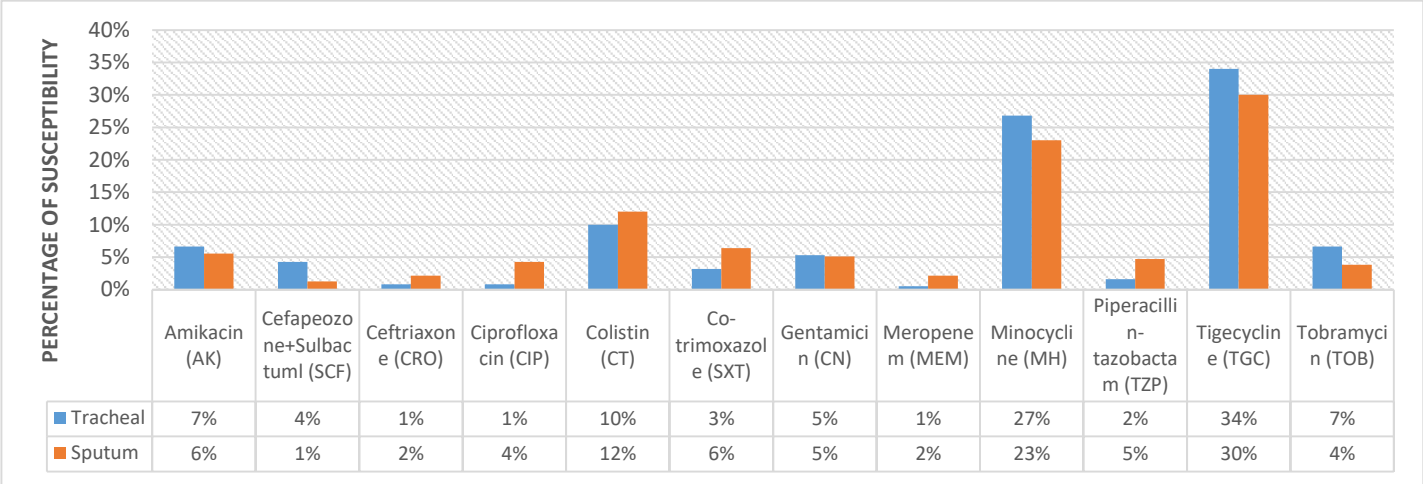


Figure 1 : Age wise Distribution of Clinical Samples

S.No	Hospital Ward	Trachea	Sputum
1	High Dependency Unit (HDU)	45%	52%
2	Medical Intensive Care (ICU)	37%	30%
3	Surgical Intensive Care (SICU)	16 %	12%
4	Private Ward	2%	6%

Table1: Frequency of Respiratory Tract Samples isolated from Different Hospital Wards



	Amikacin (AK)	Cefapeozone+Sulbactuml (SCF)	Ceftriaxone (CRO)	Ciprofloxacin (CIP)	Colistin (CT)	Co-trimoxazole (SXT)	Gentamicin (CN)	Meropenem (MEM)	Minocycline (MH)	Piperacillin-tazobactam (TZP)	Tigecycline (TGC)	Tobramycin (TOB)
Tracheal	7%	4%	1%	1%	10%	3%	5%	1%	27%	2%	34%	7%
Sputum	6%	1%	2%	4%	12%	6%	5%	2%	23%	5%	30%	4%

Figure 2 : Antibiotic Susceptibility Pattern of *Acinetobacter baumanii* isolated from Respiratory Tract Samples

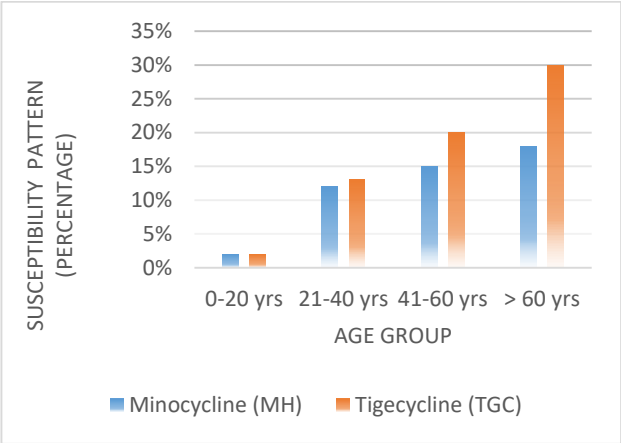


Figure 3: Comparison of Antimicrobial Susceptibility Pattern of Tygecycline and Minocycline isolated from Sputum among Different Age groups

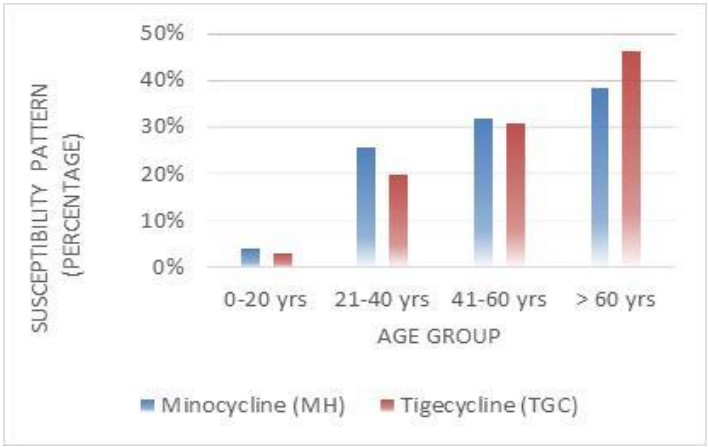


Figure 4: Comparison of Antimicrobial Susceptibility Pattern of Tygecycline and Minocycline isolated from Tracheal Aspirates among Different Age groups

DISCUSSION

Respiratory tract infections are amid most prevalent and significant concerns in Medicine. Acute respiratory tract infections are most common ground for antibiotic prescription worldwide. *Acinetobacter baumannii* is a gram-negative aerobic bacillus notorious for hospital acquired pneumonia. Its multidrug resistant strains are emerging rapidly and gaining the focus of research to find effective antibiotic against this pathogen. Current study observed high prevalence of *A. baumannii* in age group 41 to 60 and greater than 60 years from tracheal aspirates and sputum respectively, endorsed by other study (12). Present study reported that majority of patients were admitted in HDU and Medical ICU, which is consistent with the studies reported earlier (13). Medical and surgical interventions including intubation, urinary and central venous catheterization are probable risk factors associated with Acinetobacter baumannii infection in patients admitted in ICU and HDU.

Our study observed male predominance, is also in line with a previously reported studies where the number of male patients was more than females (13). Present study has found high resistance to Ceftriaxone and Carbapenems, as reported by other study (14). Acinetobacter baumanii has intrinsic resistance towards Cephalosporins and Penicillin. Carbapenems were ideal choice but their injudicial use has led to the development of resistance. The most common acquired mechanism to carbapenem

resistance in *A. baumannii* is the production of enzyme oxcillinase. A number of studies reported the emergence of Carbapenem-resistant *A. baumannii* has increased in the past two decades (15, 16).

The quick upsurge of antibiotic resistance has multiple factors, including spread of resistant clones among patients, transfer through asymptomatic colonised patients and health workers, travellers and refugees from high antimicrobial resistance prevalent areas (17). Ciprofloxacin is second highest resistant antibiotic in present study. Studies endorsed our results and discovered that mutations (gyrA/parC) could be responsible for Ciprofloxacin resistance (18, 19). Resistance of Acinetobacter baumanii is also observed against Aminoglycosides including Amikacin and Gentamicin in present study. Aminoglycosides are important substitute for the treatment for MDR *A. baumannii* infections. Resistance mechanism developed through Aminoglycoside-modifying enzymes and target modifications (20).

Our study reported resistance against Colistan, in line with other study (21). Colistin is being used as a "last-resort" treatment option after Carbapenem resistance against MDR *A. baumannii*. Colistan plays important role alone or in combination with other drugs against resistant bacteria especially *A.baumanii*. Plasmid mediated resistance due to mobile genetic elements is reported to be responsible in the distribution of Colistan resistance (22). Due to this worsening scenario of emergence of MDR, XDR and pan DR *A. baumanii* with paucity of new antibiotics, few options have been left.

Reinstituting the use of older antimicrobials has now become a choice. The role of an antibiotics like Minocycline and Tygecycline in the treatment of *A. baumannii* is still being discovered. The promising safety profile and low cost, make Minocycline an attractive therapeutic option. However, studies have encouraged the use of Tygecycline in eradicating *A. baumannii* in the ICU(23).

The current study observed the comparison between therapeutic effectiveness of Tygecycline and Minocycline. The comparison showed high susceptibility of Tygecycline in all age groups except 41 to 60 years in sputum samples, whereas, in tracheal aspirates it was found to be more sensitive than Minocycline in all age groups, studies have contrasting results(24, 25). The most important mechanism for attaining resistance in tetracycline is by efflux pumps (25). However, Tigecycline has the unique capability to overwhelmed most of the efflux pumps but other mechanisms of resistance can be seen in *A. baumanii* (26). WHO has suggested infection prevention approaches; including hand hygiene, investigation for Carbapenem resistant bugs, contact and airborne precautions, environmental hygiene and patient cohorting. These measures have to be strengthened by auditing of strategies and health care surveillance system (27).

CONCLUSION

Our study concluded that Tigecycline found to be more effective agent as compared to Minocycline for the treatment of respiratory tract infections caused by multidrug resistant *A. baumanii*. The development of resistance against Tigecycline and Minocycline is a matter of concern. The judicious use of these life-saving antibiotics with infection control measures is urgently needed.

ETHICAL CONSIDERATION: This study was approved by local Research Ethics committee.

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CONFLICT OF INTEREST: Authors declare no conflict of Interest

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