



Research Article

Assessment of Tigecycline Response Level against Extended-Spectrum Beta-Lactamases Producing Pathogens Isolated from Surgical Site Infections

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Abstract

Tigecycline is one of the sole antibiotics that can use in cases of extensive multidrug-resistant pathogens include Extended-Spectrum Beta-Lactamases (ESBL) producing pathogens. Tigecycline revealed significant efficacy and safety against Gram-positive, Gram-negative, and anaerobic microorganisms. The study aimed to reveal the antimicrobial sensitivity and resistance pattern of Tigecycline against ESBL pathogens isolated from surgical site infections. A total of 382 patients with confirmed surgical site infections included in this two-year study.

MICs for Tigecycline had determined by using the broth microdilution method with a fresh Mueller-Hinton medium. The MIC breakpoints were as follows: ≤ 2 $\mu\text{g/g/ml}$ for susceptible; >2 to <8 $\mu\text{g/g/ml}$ for intermediate; and ≥ 8 $\mu\text{g/g/ml}$ for resistance. MIC₅₀ and MIC₉₀ represent the minimal concentration of antibiotic that inhibited the growth of 50% and 90% of the isolates. All ESBL producing pathogens in both gender and age groups and those admitted in the ICU had shown the highest sensitivity level against Tigecycline (100%) when compared to the

other antimicrobial agents. Among the eight different pathogens obtained from culture results, *E.coli* was the common pathogen met in 49.2% of the samples. Among all medications, ampicillin showed the most resistant rate (100%) toward all pathogens, followed by ceftriaxone in 91.7%. About 64.6% of Fluoroquinolones, 72% against cephalosporins, and 8.2% toward Carbapenems were resistant against ESBL producing pathogens. Although ESBL cases are related to increased morbidity and mortality rates due to its nature of multidrug resistance pattern, Fortunately, Tigecycline gained the utmost sensitivity rate against all pathogens included *Acinetobacter baumannii* and *Pseudomonas aeruginosa*.

Keywords: *Acinetobacter baumannii*; Antimicrobial resistance; Surgical Site Infection; Tigecycline; Mortality

1. Introduction

Surgical Site Infections (SSI) become a tremendous and widespread obstacle that presents significant morbidity and mortality, prolonged hospital stay, and increased health-care costs [1]. Globally, SSI stated as the third most common nosocomial infection preceded just by urinary tract infections and pneumonia [1, 2]. The outcome of SSI is partly associated with an increase in antimicrobial-resistant bacterial pathogens [3]. There is an increasing number of extended-spectrum beta-lactamases (ESBL) producing pathogens isolated from the surgical site infection that generates a significant threat toward the development of rising antimicrobial resistance against ESBL cases [4]. ESBL is related to a higher rate of morbidity and mortality [5]. Bacteria that produce ESBL had founded with increasing prevalence across healthcare settings. The prevalence of ESBL producing pathogens

isolated from the surgical site infection differs in nations [6]. A lot of specific risk factors known to develop the risk of ESBL in hospitalized patients include severe comorbidities/illness, excessive or prolonged use of antimicrobial agents, surgical intervention/invasive procedures, use of catheters and central lines, long pre-infection hospital and intensive care unit stay [7, 8]. Tigecycline is one of the sole antibiotics that can use in cases of extensive multidrug-resistant pathogens include extended-spectrum beta-lactamases (ESBL) producing pathogens. Tigecycline revealed significant efficacy and safety against Gram-positive, Gram-negative, and anaerobic microorganisms. Most ESBL cases became resistant to the common antibiotics that also prolong hospitalization time and raise the health-related expenditures in the low and middle-income countries where several of the strong medications included Tigecycline, Colimycin, Vancomycin, and Teicoplanin are not accessible or at a high charge [9, 10]. Tigecycline has described as a broad-spectrum activity against pathogens frequently associated with SSI, as well as it has significant coverage of both Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*, *Enterococcus faecalis*) and Gramnegative (*E. coli*) bacteria that contribute a valuable therapeutic option in treating patients with SSI [11, 12].

In our knowledge, there is no notational surveillance of the prevalence of surgical site infection and spectrum of ESBL producing pathogens in Somalia, and there are no previous studies in this era. The current study is the first study intended to reveal the frequency and distribution of ESBL cases and to declare the antimicrobial sensitivity and resistance pattern.

2. Method

A total of 382 patients with confirmed surgical site infections included in this retrospective study from 2019 to 2020 at Mogadishu Somali Turkey Training and Research Hospital (a tertiary hospital in Somalia) whose medical files assessed retrospectively. Among 382 patients with confirmed culture-positive SSI findings that included for the study, 63 patients with extended-spectrum beta-lactamases producing pathogens were selected for the study. The specimens collected from the primary surgical site of infection were sent to our laboratory and microbiology unit for identification of the isolates and were tested for susceptibility to tigecycline by Kirby-Bauer disk diffusion tests. The isolates obtained were subcultured and tested for the susceptibility pattern at a central laboratory by using both broth microdilution tests, to determine the Minimal Inhibitory Concentration (MIC) and Kirby-Bauer disk diffusion tests by procedures published by the Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS) [13]. MICs for tigecycline were determined by a reference broth microdilution method with a fresh Mueller-Hinton medium. The provisional MIC breakpoints, based on previous preclinical investigations, were as follows: ≤ 2

$\mu\text{g/g/ml}$ for susceptible; >2 to <8 $\mu\text{g/g/ml}$ for intermediate; and ≥ 8 $\mu\text{g/g/ml}$ for resistance [14-16]. MIC50 and MIC90 represent the minimal concentration of antibiotic that inhibited the growth of 50% and 90% of the isolates, respectively. Approval form had obtained from the ethics committee of Mogadishu Somali Turkey Recep Tayyip Erdogan Training and Research Hospital, and the patients had received informed consent. The study design was a retrospective descriptive univariate study design using the IBM SPSS 23 version to analyze the data of the patients.

3. Results

A two-year retrospective study design had enrolled in a total of 382 patients with confirmed SSI. The prevalence of extended-spectrum beta-lactamases producing pathogens in our study was 16.5%. Among eight different pathogens obtained from culture results, *E.coli* was the common pathogen met in 49.2% of the samples followed Klebsiella pneumonia in 30.2%, Pseudomonas aeruginosa in 6.3%, Proteus mirabilis in 4.7%, and Acinetobacter baumannii in 3.2%. The details of the pathogens had demonstrated in (Table 1).

Type of Microorganisms	No. of Patients	Percentage
<i>E.coli</i>	31	49.20%
Klebsiella pneumonia	19	30.20%
Pseudomonas aeruginosa	4	6.30%
Proteus mirabilis	3	4.70%
Acinetobacter baumannii	2	3.20%
Enterobacter cloacae	2	3.20%
Citrobacter freundii	1	1.60%
Enterococcus faecium	1	1.60%
Total	63	100.00%

Table 1: Common Pathogens.

Among the total isolates of *E.coli*, and *Klebsiella pneumonia*, ESBL producing *E.coli* seen in 22.6%, and *Klebsiella* in 38.8%. Among individual pathogens, *Klebsiella pneumonia* had produced the most ESBL. The antimicrobial sensitivity and resistance toward all ESBL producing pathogens had weighed particularly with special attention to Tigecycline. The top 10 most sensitive medications had imitated in table 2. Tigecycline, Colimycin, Vancomycin, and Teicoplanin showed the highest sensitivity rate (100%) against all ESBL cases. Carbapenems were also recognized to have a high sensitivity rate against pathogens (91.5%). Fortunately, tigecycline had the utmost sensitivity against *Acinetobacter*

baumannii and *Pseudomonas aeruginosa* that are multidrug-resistant pathogens in nature.

Among all medications, ampicillin showed the most resistant rate (100%) toward all identified pathogens followed by ceftriaxone in 91.7%, Cefuroxime in 88.9%, and ciprofloxacin in 63.8%. About 64.6% of Fluoroquinolones, 72% against cephalosporins, and 8.2% toward Carbapenems were resistant against ESBL producing pathogens. An inclusive detail for the pattern of antimicrobial resistance against pathogens has illustrated in (Table 3).

Medications	Sensitivity level
Tigecycline	100.00%
Colimycin	100.00%
Vancomycin	100.00%
Teicoplanin	100.00%
Levofloxacin	93.80%
Meropenem	93.30%
Ertapenem	91.40%
Imipenem	89.70%
Amikacin	85.50%
Piperacillin-tazobactam	79.20%

Table 2: Top 10 most sensitive medications against pathogens.

Most ESBL cases admitted in the surgical intensive care unit (57.1%); these patients had polymicrobial and multi-resistant pathogens. Tigecycline was sensitive against all patients admitted to the Intensive Care Unit (ICU) that has various comorbidities and prolonged hospitalization time. The study included 43 males and 20 females. The mean age

was 35.2 years. According to all ESBL producing pathogens in both gender and age groups and those patients admitted in the ICU had shown the highest sensitivity level against Tigecycline activity when compared to the other antimicrobials agents.

Medications	Resistant level
Ampicillin	100.00%
Ceftriaxone	91.70%
Cefuroxime	88.90%
Cefixime	87.50%
SMX-TMP	82.50%
Ceftazidime	77.30%
Cefoperazone-sulbactam	71.40%
Ciprofloxacin	63.80%
Piperacillin	57.10%
Gentamicin	44.50%

Table 3: Antimicrobial resistant pattern.

4. Discussion

In the present study, tigecycline revealed significant efficacy and safety, and it can use as monotherapy treatment not needing additional coverage against Gram-positive, Gram-negative, and anaerobic microorganisms included Methicillin-Resistant *Staphylococcus aureus*, Vancomycin-resistant pathogens, and ESBL producing pathogens. ESBL producing pathogens isolated from surgical site infections are a serious and worrying scenario as correspondingly reported in other studies [17, 18]. The current study intended to reveal the antimicrobial sensitivity and resistance pattern of Tigecycline against ESBL pathogens isolated from surgical site infections and to demonstrate the frequency and distribution of ESBL cases and to declare the antimicrobial sensitivity and resistance pattern. The prevalence of extended-spectrum beta-lactamases producing pathogens in our study was 16.5% which is comparable to the other previous studies [19-21].

Among the total isolates of *E.coli*, and *Klebsiella pneumoniae*, ESBL producing *E.coli* was seen in 22.6% of

the total samples, and *Klebsiella* in 38.8%, which is in contrast to the previous studies [21, 22]. Fortunately, tigecycline had the utmost sensitivity against *Acinetobacter baumannii* and *Pseudomonas aeruginosa* that are multidrug-resistant pathogens in nature. Tigecycline has a broad-spectrum antimicrobial activity against pathogens frequently associated with SSI, as well as it has significant coverage of both Gram-positive (*Staphylococcus aureus*, *Streptococcus pyogenes*, *Enterococcus faecalis*) and Gramnegative (*E. coli*) bacteria that contribute a valuable therapeutic option in treating patients with SSI caused by multidrug-resistant and extensively drug-resistant pathogens [11, 12]. Cephalosporins are the furthestmost common antimicrobial class prescribed for most of the patients admitted in the hospitals; nonetheless, ESBL cases showed a higher resistance rate (72%) against cephalosporins [22-24]. About 20 to 70% of beta-lactamases inhibitors were resistant against ESBL cases. The study revealed that Carbapenems had a higher sensitivity rate against pathogens (91.5%). The ultimate and powerful antibiotics showed a higher sensitivity rate (100%) against ESBL cases included Tigecycline,

Colimycin, Vancomycin, and Teicoplanin. Another interesting finding in our study is that young patients were the leading group for the ESBL cases which is equivalent to similar studies [4, 19]. The study revealed significant increasing shifting trends of *E.coli* isolates producing ESBL (22.6%) which is corresponding in a study reported by Yoshio Takesue et al (23%) and other studies [25, 26].

5. Conclusion

Tigecycline is one of the sole antibiotics that can use in cases of extensive multidrug-resistant pathogens include Extended-Spectrum Beta-Lactamases (ESBL) producing pathogens. All ESBL producing pathogens in both gender and age groups and those patients admitted in the ICU had shown the highest sensitivity level against Tigecycline activity when compared to the other antimicrobials agents. Patients admitted to the hospital are more susceptible to develop hospital-acquired infections. Although ESBL cases are related to increased morbidity and mortality rates due to its nature of multidrug resistance pattern, Fortunately, Tigecycline gained the utmost sensitivity rate against all pathogens included *Acinetobacter baumannii*.

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