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Research Article

High Prevalence and Antibiogram Pattern of Extended Spectrum Beta Lactamases Producing Escherichia Coli and Klebsiella Pneumonia Isolated from Inpatients Units in a General Hospital in Saudi Arabia

Sabir Awad Mustafa*

Clinical Microbiologist at Wadi Aldawasir General Hospital, Wadi Aldawasir, Riyadh, Saudi Arabia

***Corresponding Author:** Sabir Awad Mustafa, Clinical Microbiologist at Wadi Aldawasir General Hospital, Wadi Aldawasir, Riyadh, Saudi Arabia.

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Abstract

Extended spectrum beta lactamases (ESBL) producing *Escherichia coli (E. coli)* and *Klebsiella pneumoniae (K. pneumoniae)* emerged as a major problem in nosocomial infection all over the world due to their resistance to the extended spectrum Cephalosporin.

Thus the aim of this study was to determine the high prevalence of ESBL producing *E. coli* and *K. pneumoniae* among hospitalized patients to put a proper antimicrobial therapy guideline to treat infections caused by these organisms at small hospital.

A total of 92 clinical isolates were isolated where ESBL-producing *E. coli* and *K. pneumoniae* were confirmed by automated system VITEK 2 (*Biomerieux*) and susceptibility test using common antibiotics.

Among 92 clinical isolates 56 (60.86%) were *E. coli* and *K. pneumoniae*. All the clinical isolates were from the inpatients units obtained from different clinical specimens of Wadi Aldawasir hospital from April to August 2016.The overall prevalence of ESBL-producing *E. coli* and *K. pneumoniae* was 84% (47/56).The prevalence of ESBL-producing *E. coli* was found to be high 68%(32/47). Antibiogram pattern of these isolates confirmed, Tigecycline to be the drug of choice for ESBL producing *E. coli* and Amikacin for ESBL producing *K. pneumoniae*. Advance drug resistance surveillance is necessary to guide appropriate use of antibiotics.

Keywords: *Extended Spectrum Beta Lactamases (ESBL); Escherichia coli; Klebsiella pneumonia; Antibiogram; Antimicrobial Susceptibility*

Introduction

Extended spectrum beta-lactamases (ESBL) [1,2] are enzymes secreted by some *Enterobacteriaceae* most commonly *Escherichia coli (E. coli)* and *Klebsiella pneumonia (K. pneumonia)* [3]. These bacteria are Gram-negative bacilli found primarily in the bowel of humans and animals as a normal flora. ESBL producing *E. coli* and *K. pneumoniae* are nosocomial infection causing organisms due to their resistivity towards most of the antimicrobial agents, ESBL producing *E. coli* and *K. pneumonia* has become a major threat in most hospitals around the world with. Highest rate of threat has been reported in India, China and Brazil where the frequency of *K. pneumoniae* was higher than *E. coli* [4].

The name of this enzyme comes from its increased spectrum of activity and can inactivate beta lactam antibiotics [5] like Penicillin, first, second, third, and fourth generation cephalosporin [6] and aztreonam and prevent them from killing bacteria, by this way bacteria developed resistance to antibiotics but are inhibited by carbapenems and clavulanic acid and tazobactam [7]. So, Carbapenems are the drug of choice for treatment of severe infection caused by ESBL producing organisms. The enzymes have several groups, derived by mutation, the largest groups are TEM, SHV and CTX-M enzyme [8] because the organisms producing these enzymes sometimes colonized gastrointestinal tract without causing any infection then it can spread by contact directly by hands of health worker or by contaminated items, equipment and environmental surfaces [9]. To prevent the transmission of these organisms, all staffs and visitors should be remind for practicing a proper hand hygiene, also contact precaution should be followed and infection control practitioner should be notify [10]. The present study shows the frequency of ESBL producing by *E. coli* and *Klebsiella pneumoniae* obtained from hospitalized patient in Wadi Aldawasir general hospital Saudi Arabia.

Objectives

To determine the frequency of ESBL producing by *E. coli* and *Klebsiella pneumoniae* and to assess the susceptibility patterns for these clinical isolates to common antibiotics that are important for treating Hospital acquired infection, in Wadi Aldawasir General Hospital Saudi Arabia.

Materials and Methods

This Cross-Sectional study was conducted from microbiology laboratory at Wadi Aldawasir Hospital, on data collected from reports of 47 gram negative *Enterobacteriaceae* that confirmed as ESBL producing *E. coli* and *K. pneumoniae*, thus these organisms were selected for this study because they are more frequent organisms producing ESBL in Wadi Aldawasir Hospital and were isolated from different clinical specimens like sputum, blood, urine and swabs from wound, high vagina, and ears, were taken from inpatients departments in Wadi Aldawasir General Hospital which is a small hospital with 150 beds distributed over 6 units, of which 9 beds in intensive care unit and the others found in medical, surgical, obstetrics and gynecology, nursery and pediatrics words, from April 2016 to August 2016, all clinical specimens were received in laboratory for culture and sensitivity, identification and susceptibility test was done according to the standard operating procedures of the hospital, urine is routinely cultured on (CLED) agar and all other clinical samples culture on MacConkey agar and blood agar, for other samples like blood, sputum, and some swabs were cultured on MacConkey agar, blood agar and chocolate agar. Then identification of organisms was done from the morphology of colonies, because *E. coli* and *K. pneumoniae* are lactose fermenter so the colonies will be pink in MacConkey agar and by doing gram stain, which appear as gram negative bacilli then the identification completed by using automated system VITEK 2 (Biomerieux) for identification by using GN card and susceptibility to antibiotics and the detection of ESBL production are performed by gram negative susceptibility card AST-N291 [11] confirmation was performed using the double disc methods, microtablets ceftazidime (30), cetazidime / clavulanic acid (30/10) were placed at a distance of 30 mm between them in Muller Hinton medium the interpretation of the results was done using the CLSI standard.

For the privacy of the patients no personal data was collected from patients, King Fahad Medical City approved the current study.

Result

A total of 92 gram negative and gram positive bacteria were isolated ,which were obtained from clinical specimens during a period of four months of study conducted to hospitalized patients to all units of hospital, of these 61% (n = 56) were found to be *E. coli* and *Klebsiella pneumoniae*. Of these 47 (84%) were ESBL producing *E. coli* and *K. pneumoniae* while the other *E. coli* and *K. pneumoniae* non-producing this ESBL enzymes were found to be 16% (n = 9) among these number ESBL producing by *E. coli* were found to be 68% (n = 32) while ESBL producing by *K. pneumoniae* were found to be 26% (n = 12). The distribution of isolates according to hospital units are shown on figure 1 Most of the *Klebsiella pneumoniae* isolates came from sputum and tracheal aspirate specimens of ICU patients 73% no *Klebsiella*

pneumoniae nor *E. coli* were isolated from pediatrics unit. About 16% of *E. coli* was isolated from neonatal ICU. Most of ESBL producing by *E. coli* were isolated from surgical units 25% and most specimens were urine 31% (n = 10 of 32) the distribution of isolates according to clinical specimens are shown in figure 2. Antibiogram profile was performed, the antimicrobial susceptibility pattern is found in table 1. Tigecycline was identified to be most effective antibiotics against ESBL producing by *E. coli* and Amikacin was found to be most effective against ESBL producing by *Klebsiella pneumoniae*. Imipenem and meropenem, and nitrofurantoin were found to be more sensitive to ESBL producing by *E. coli* than ESBL producing by *Klebsiella pneumoniae*. Zero % resistance was confirmed against amikacin in the cases of be ESBL producing by *Klebsiella pneumoniae* while 3% (n = 1) in case of ESBL producing by *E. coli* also zero % resistance was found against Tigecycline in case of ESBL producing by *E. coli*, while 7% (n = 1) in the cases of be ESBL producing by *Klebsiella pneumoniae* and imipenem was more sensitive to ESBL producing by *Klebsiella pneumoniae* than meropenem, in cases of ESBL producing by *E. coli* was found to be resistant to ampicillin, ceftazidime, ceftriaxone and cefepime which were 100% ,while in ESBL producing by *Klebsiella pneumoniae* were found to be 93% (14 of 15) except ampicillin which was found to be 100% resistant. Resistance of amoxicillin/clavulanic acid against *E. coli* was found to be 81 % while was found to be 87 % in *K. pneumoniae*, piperacillin/tazobactam, which was 96% in *E. coli* and 87 % in *K. pneumoniae*.

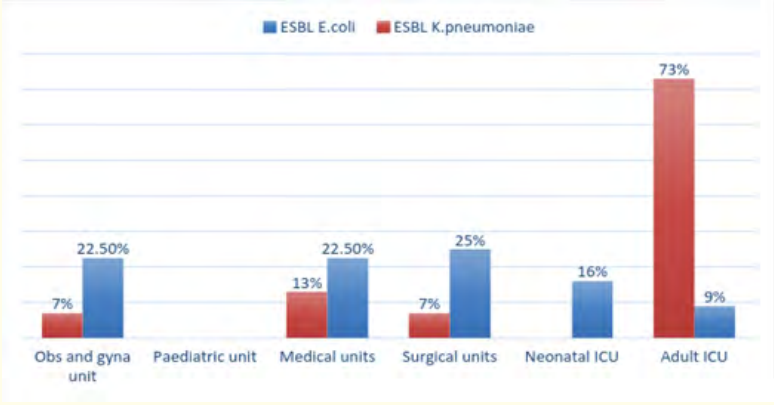

Figure 1: *Distribution of clinical isolates according to hospital units.*

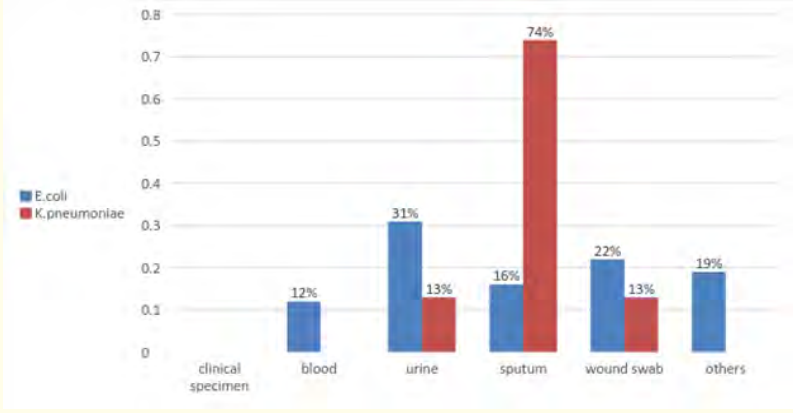

Figure 2: *Distribution of ESBL producing E. coli and K. pneumoniae according to clinical specimens.*

	ESBL *E. coli*		ESBL *K. pneumoniae*	
Antibiotic	**Resistant**	**Sensitive**	**Resistant**	**Sensitive**
Ampicillin	100%	0%	100%	0%
Amoxicillin/Clavulanic acid	81%	19%	87%	13%
Piperacillin/Tazobactam	94%	6%	73%	27%
Cephalothin	75%	25%	100%	0%
Cefoxitin	91%	9%	47%	53%
Ceftazidime	100%	0%	93%	7%
Ceftriaxone	100%	0%	93%	7%
Cefepime	97%	3%	93%	7%
Imipenem	3%	97%	47%	53%
Meropenem	3%	97%	53%	47%
Amikacin	3%	97%	0%	100%
Gentamicin	19%	81%	47%	53%
Ciprofloxacin	56%	44%	60%	40%
Tigecycline	0%	100%	7%	93%
Nitrofurantoin	6%	94%	73%	27%
Trimethoprim-Sulfamethoxazole	53%	47%	60%	40%

Table 1: *Antimicrobial resistance pattern of ESBL producing E. coli and K.pneumoniae in different clinical specimens.*

Discussion

In the present study we noticed that 79 % (n = 37) of all *E. coli* and *K. pneumoniae* isolated were ESBL producing microorganisms we observed that the prevalence of ESBL producing by organism was very high in comparison to other studies [12,13], overuse of broad spectrum antibiotics together with use antibiotics without doing culture and sensitivity most of the time may share on the cause of high prevalence. 68% of these clinical isolates were *E. coli* while 32% were *K. pneumoniae* as compared with other studies the *E. coli* found to be more common than *K. pneumoniae* but in this study the rate is higher than other studies [14].

During the study period ESBL producing by *E. coli* and *Klebsiella pneumoniae* was isolated from patients of most hospital units with ICU as commonest place which was 73%, and the second place was units surgical 25% then medial and gynecological units 22.5% for each one and 16% was isolated from neonatal ICU, zero % was isolated from pediatric unit disassociated to previous study that was done on India which shows a prevalence of ESBL producing organism was reported to be high from intensive care unit, surgery units, and neonatal ICU [15] and the sputum as the commonest source of isolates ESBL producing by *Klebsiella pneumoniae* 34% of these 69% were confirmed as ESBL producing by *Klebsiella pneumoniae*.

The result from this study showed high resistance ESBL producing E. coli and Klebsiella pneumoniae to Ceftriaxone, Ceftazidime, and Cefepime which are more antibiotics used empirically to treat most infection in Hospital [16]. Ciprofloxacin was found to be less effective in treating infection caused by ESBL producing by *E. coli* and *Klebsiella pneumoniae*, similar to previous study [17].

High resistance was observed with Piperacillin/Tazobactam 94% unlike study that done in Saudi Arabia was found to be 8% [18].

Higher resistance was seen with amoxicillin-clavulanic acid 81% to *E. coli* and 87% to *Klebsiella pneumoniae* than other studies [19].

Tigecycline was identified to be the most effective antibiotics against ESBL producing by *E. coli* and Amikacin was found to be most effective against ESBL producing by *Klebsiella pneumoniae* not going with other researches which were reported the high rate of resistance against Amikacin [12].

Nitrofurantoin was found to be more sensitive against ESBL producing by *E. coli* than ESBL producing by *K. pneumoniae* it was unsimilar to finding that reported in other studies, in those studies showed Nitrofurantoin are sensitive to all ESBL producing by *E. coli* and *Klebsiella pneumoniae* [20].

In current study the meropenem and imipenem were active against most ESBL producing *E. coli* (97 %) but were less effective against ESBL producing *K. pneumoniae* (53 %) unsimilar to early report that meropenem and imipenem were fully susceptible to ESBL producing by *E. coli* and *Klebsiella pneumoniae* (100%) [21], also there was study regarded carbapenems as drug of choice for treatment of infection caused by ESBL-producing organisms [22-24]. So, Tigecycline and Amikacin are drug of choice for the treatment of infection caused by ESBL producing by *E. coli* and *Klebsiella pneumoniae* and Nitrofurantoin is very effective in treatment of urinary tract infection.

Conclusion

ESBL producing by *E. coli* and *Klebsiella pneumoniae* is more common among hospital acquired infection. So, regular surveillance of multiple drug resistant microorganisms is needed and also implementation of hospital infection control policy to prevent the transmission of antibiotics resistance organisms. Of all of the antimicrobial agents, Tigecycline and Amikacin are the most effective treatment for infection caused by ESBL producing by *E. coli* and *Klebsiella pneumoniae*. Few studies was done on the prevalence of ESBL producing *E. coli* and *K. pneumoniae* in Saudi Arabia and their resistance still unclear so more studies are needed.

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