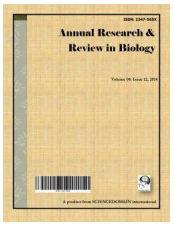

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Epidemiology of Extended-Spectrum Beta-Lactamases (ESBLs)-Producing Bacteria in Different Regions in Saudi Arabia: A Systematic Review

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Authors' contributions

This work was carried out in collaboration between all authors. Author AGAS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors AGSM and GMM managed the analyses of the study. Author GMM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Recently, a number of Saudi studies have indicated the emergence of a new genetic mutation in gram-negative bacteria (GNB) strains, particularly in extended spectrum beta-lactamase (ESBL) producing isolates, which accounts for about 8% to 38% of the total GNBs detected at Saudi hospitals. ESBLs are enzymes identified in GNB and have ability to resist beta lactam antimicrobial agents by breaking down the lactam ring. To ensure the objectiveness of this study, this paper presents most of the published studies on ESBL infection in Saudi Arabia (available online). ESBL-producing bacteria were detected using disk diffusion methods, dilution methods, double-disc synergy test, E-test strip and molecular detection methods. Risk factors contributing to the spread of

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ESBL infection include renal disease, diabetes, age, gender, hospital admission and previous exposure to antibiotics. CTX-M, TEM and SHV genotypes are the most common in the studies that have been performed in Saudi hospitals. Imipenem, meropenem, tigecycline and nitrofurantoin are still the best options to treat the ESBL infection. Appropriate infection control policies should be applied to reduce the risk factors of such infections.

Keywords: Extended-spectrum beta-lactamases (ESBLs); Enterobacteriaceae; risk factors; antimicrobial resistance.

1. INTRODUCTION

Extended-spectrum beta-lactamases (ESBLs) are enzymes that confer resistance to beta-lactam antibiotics, such as penicillins [1] and cephalosporins [2]. ESBLs also confer resistance to monobaccals. In 1983, 1985 and 1989, ESBLs were identified in Germany, France and the United States, respectively. In the early 1990s, a nosocomial outbreak of ESBLs occurred [3]. Infections by ESBL producers range from uncomplicated urinary tract infections to high mortality rates [4,5]. The two main bacteria that produce ESBLs are the *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) species [6].

The prevalence of ESBLs as a result of multidrug-resistant bacteria is a real challenge worldwide, particularly in developing countries where economic conditions and health care systems are inadequate. The lowest percentage of ESBL-producing bacteria is found in Australia, with < 5%, while the highest is found in Asia, with < 80% [3]. Furthermore, the spread of ESBL organisms worldwide differs for each region. *K. pneumoniae* is predominant in North America (1.8–25%), compared to *E. coli* (0.5–5.9%) [3]. In Asia, *K. pneumoniae* is less common than *E. coli* with rates of 66% and 80%, respectively [3]. The prevalence of ESBL genotypes also varied even within the same country. In the Al-Ahasa region of Saudi Arabia, the prevalence of *blaSHV* in *K. pneumoniae* isolates was about 78% [7], while in Makkah hospitals it was less than 14% [8]. The enormous diversity of the genetic recombination of bacteria leads to an increase in their ability to resist antibiotics and, as a result, ESBL infections are spread further [9].

The treatment options for ESBL-producing organisms are very limited; thus, controlling risk factors is an important tool in the prevention of serious diseases [3]. It is necessary to concentrate on healthcare environments and society to address this issue and prevent the emergence of multi-resistant organisms. There are several factors that play a significant role in the prevalence of ESBL infections. Many studies have concluded that the quality of the healthcare environment is the most important risk factor of an ESBL infection [10]. Other risk factors, such as household contact, should be also considered in the community. Studies show that the length of hospital stays, mechanical ventilation and previous antimicrobial exposure are other common risk factors of infections caused by ESBLs [11,12]. However, a 10-year cohort study suggests that quality control procedures may contribute to the reduction of the spread of such infections in hospitals [13].

According to Mahesh et al. [14], there are different ways to anticipate the risk factors for acquiring ESBL-positive urinary tract infections (UTI), such as male gender, a history of hospitalization, antibiotics exposure, catheterization and urogenital surgery. In addition, a case study focusing on children showed that recent antibiotic exposure was clearly the most important predisposing factor associated with the ESBL infection *K. pneumoniae* [6]. Another study indicated that female patients are more likely to be infected with the ESBL-producing *E. coli*, while non-ESBL *E. coli* was more predominant in children with UTIs [15]. Recent research has shown that one of the most important risk factors for acquiring an ESBL infection is international travel to areas where ESBLs are highly endemic [16]. Nevertheless, a new study found that old age, male gender and a recent operation were not significantly associated with ESBL-producing Enterobacteriaceae infections [10].

In Saudi Arabia, published studies examining the geographical distribution of ESBLs are limited, especially in the Northern and Southern regions. Therefore, this study sought to: (i) determine the risk factors associated with ESBL infection in different regions of Saudi Arabia; (ii) determine their genotypes; and (iii) examine recent ESBL

detection methods and effective treatments. A control policy for ESBL infection is also discussed.

2. EPIDEMOLOGY OF ESBL IN SAUDI ARABIA

The ESBL-producing bacteria are spread dramatically and alarmingly quickly around the world. In Saudi Arabia, the prevalence of ESBLs was between 8–38% (Fig. 1) [17]. There is diversity in the prevalence of these organisms, including with respect to the difference in their genetic composition. *E. coli* and *K. pneumoniae* are the most common gram-negative bacteria (GNB) that produce beta-lactamase enzymes [6]. In addition, there are a number of microbes that have the ability to secrete this enzyme, such as *Pseudomonas aeruginosa (P. aeruginosa)* and *Acinetobacter baumannii (A. baumannii),* but these are less widespread in the community and in hospital environments [18]. *Klebsiella oxytoca (K.oxytoca)*, *Enterobacter cloacae (E. cloacae)*, *Enterobacter aerogenes (E. aerogenes), Serratia marcescens (S. marcescens), Citrobacter freundii (C. freundii)* and *Proteus mirabilis (P. mirabilis)* have been detected in different regions of Saudi Arabia, but rates remain low compared to *E. coli* and *K. pneumoniae*. Generally, the CTX-M genotype is the most universally prevalent, particularly CTX-M-15 in *E. coli* [19]. Other major genotypes, such as SHV and TEM, are found in *K. pneumoniae*, while the VEP and OXA are the most common in *P. aeruginosa and A. baumannii* [18,19].

2.1 Central Region

Rates of ESBLs among Enterobacteriaceae ranging between 4.8% and 15.8% have been reported in Saudi Arabia, with the highest frequency recorded in the Central region and the lowest frequency in the Eastern region [20]. During 2011 and 2012, Al-Mously and her colleagues studied the spread of UTIs as a result of the ESBL-producing *E. coli* in Riyadh. It was observed that the rate of this infection increased by almost 7% at the end of 2012 [21]. Most of these cases, approximately 65%, were inpatients and almost 36% were outpatients. The pediatric department had more positive results for ESBL-producing *E. coli* causing UTIs and then the surgery unit. Another study indicated that pediatric, adult and elderly patients were infected with ESBL-producing *E. coli* at rates ranged from 3% to 8% [22].

According to Al-Otaibi and Bakhari [15], male patients are less likely to contract UTIs caused by ESBL *E. coli* than women, therefore gender is a risk factor for this infection. In addition to gender, hospitalization, surgical intervention, renal disease and recurrent UTI cases are the most important risk factors [15,20]. These findings are consistent with another study of 49 non-hospitalized patients in Spain; the risk factors there were recurrent UTIs, previous hospital admission, diabetes mellitus and previous fluoroquinolone use. In another study, it was reported that ESBL-producing *E. coli* caused UTIs more frequently in females than males, with

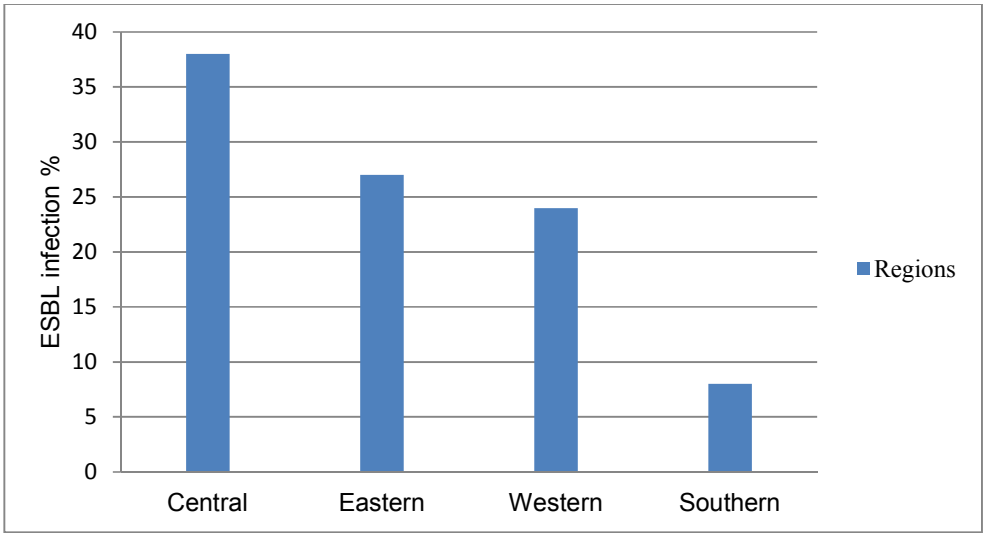

Fig. 1. Prevalence of ESBL infection in different regions in Saudi Arabia [17]

Table 1. The most common risk factors for ESBLs producers in different regions in Saudi Arabia

Region	Risk factors					
Central	Gander	Hospitalization	Recurrent ICU	Renal disease	Surgical	Invasive diagnosis procedures
Eastern	Mechanical ventilation	urinary catheter	Hospital admission	Cephalosporins	Fluoroquinolones	
Western	Older patientsn (>50 years)		ICU patients	Gander	Surgical ward	
Southern	Elderly (71-80 years)		Children (≤1-10 years)	Gander	Chronic disease (diabetes)	

rates of 67.5% and 32.5%, respectively [21]. Moreover, almost 70% of these infections were accrued in adults, compared to the pediatric age group at 32% [21]. Invasive diagnosis procedures are another risk factor that leads to the prevalence of ESBL infections (Table 1) [23].

Several studies have concluded that CTX-M (especially CTX-M-15) is the main ESBL enzyme in *E. coli*, while the SHV enzyme (particularly 1, 5 and 12) is predominant in *K. pneumoniae* [18]. A study by Al-Mijalli (2016) indicated that OXA was the most common gene in ESBL bacteria, followed by CTX-M, TEM and SHV, respectively (Table 2) [24]. ESBL-producer bacteria, particularly *E. coli* and *K. pneumoniae*, excrete TEM and SHV enzymes, both of which are the most predominant in these organisms [25].

Table 2. The most common genotypes for ESBLs producers in different regions in Saudi Arabia

Region	Genotype of ESBL
Central	OXA, CTX-M , TEM, SHV
Eastern	CTX-M, SHV, TEM
Western	CTX-M, TEM, SHV
Southern	CTX-M

In 2010, Al-Agamy and his colleagues isolated 400 specimens of *K. pneumoniae* and ESBL-producer *K. pneumoniae* was [220/400 (55%)], collected from Riyadh hospitals [19]. The BlaSHV gene was found most frequently in the positive samples (97.3%), followed by blaTEM (84%). BlaCTX-M was found the least frequently (34.15), with CTX-M-1 and CTX-9-like gene.

The two types of CTX-M first reported in Saudi Arabia by Al-Agamy et al. (2010) were the CTX-M-15-like gene and the CTX-M-14/18-like gene. Al-Obied et al. (2008) suggest that the *K. pneumoniae* LO10 (SHV-12 genotype) was the reason for the spread of ESBL infections in the neonatal unit at the Security Forces Hospital [26]. Yezli et al.'s study [18] was the first to describe the outbreak of carbapenem-resistant *K. pneumoniae* in Central Saudi Arabia. A prospective study performed in King Khalid Hospital between 2006 and 2010 (with 1,076 positive samples of ESBL) showed that carbapenems accompanied with amikacin is the treatment of choice for ESBL infections [11]. Another study found that the *K. pneumoniae* ESBL-producer was highly sensitive (100%) to imipenem [27].

About 19% of Enterobacteriaceae have the ability to resist the majority of beta-lactam antibiotics, particularly ESBL-producing *E. coli* [15]. Trimethoprim-sulfamethoxazole, ciprofloxacin and gentamicin were the least effective in the treatment of ESBL infections, compared to carbapenems, amikacin and nitrofurantoin (Table 3). A study by Baby (2012) recommended that it was necessary to change ESBL-treatment to another group, such as carbapenems, due to the high resistance of ESBL-producing bacteria [23]. The ability of ESBL-producing *K. pneumoniae* to resist cephalosporins may be due to the presence of the SHV gene [19].

2.2 Eastern Region

Kandeel [10] indicates that UTIs are the most common infection caused by ESBLs. Different regions in Saudi Arabia have difference rates of ESBLs. For example, the Central region (Riyadh) had the highest incidence of ESBL infections (36%), while the Southern region (Abha) had the lowest rate (11%) and the Eastern province had a rate of approximately 27% [10]. A 2014 study performed in King Khaled Hospital in Hafer-Albaten to investigate the spread of ESB-L-producing *K. pneumoniae* concluded that this bacterium was present in approximately 54% of patients [28]. Another study by Hassan and Abdalhamid [29] was carried out in the Eastern region of Saudi Arabia

Table 3. Antibiotics susceptibility and resistance patterns of ESBLs produced by *E.coli* in different regions in Saudi Arabia

Antimicrobial agents	Region			
	Central		Eastern	
	Al-Mously et al., 2016 (S)	Somily et al., 2014 (R)	Kandeel, 2014 (S)	Alsultan et al., 2013 (S)
Amikacin (AK)	97%	3.83%	85%	ND
Ampicillin (AMP)	ND	ND	ND	0(0)
Amoxicillin/clavulanate (AMC)	ND	ND	ND	ND
Cefuroxime (CXM)	ND	ND	ND	0
Cefoxitin(FOX)	ND	ND	ND	70%
Cefotaxime(CTX)	ND	ND	ND	18%
Ceftazidime (CAZ)	ND	ND	ND	35%
Cefepime (FEB)	ND	ND	ND	76%
Ciprofloxacin (CIP)	28.7%	68%	50%	21%
Gentamicin (CN)	59.1%	47%	52%	36%
Imipenem (IPM)	99.8	ND	80%	100%
Meropenem (MEM)	99.8	ND	80%	100%
Nitrofurantoin (F)	92.2	5.99%	ND	ND
Piperacillin/Tazobactam (TZP)	82.8	ND	83%	80%
Trimethoprim/ Sulfamethoxazole	24.9%	ND	34%	21%
Tigecycline (TGC)	ND	ND	77%	100%

S: sensitive, R: resistance, ND: No data.

(Dammam) and showed that the prevalence of *E. coli* and *K. pneumoniae* was remarkable, at 35.8% and 25.2%, respectively [29]. The prevalence of ESBLs in the Eastern region was therefore similar to that recorded in the Southern region of Saudi Arabia (27.3%) in 2001. A study of 6,750 positive samples of GNB carried out by Khanfar et al. [17] in Dhahran (Eastern region) concluded that 409 of the organisms (6%) were ESBL-producers, which were found in 143 of the inpatient (15%) and 266 of the outpatients (4.5%). *E. coli* was the most common bacteria, then *K. pneumoniae*, followed by *K. oxytoca*. In addition, this study concluded that *K. pneumoniae* accounted for the largest proration (60%) of the ESBL-organism that was isolated in the hospital, in comparison to the community-acquired infection. In contrast, there was no difference in the rate of *E. coli* infection between the nosocomial and community-acquired ESBL infections [17].

It is possible that people of many nationalities living in the same area contributes to the prevalence of ESBL infection. A number of studies have indicated that the presence of a high percentage of foreign workers in Saudi Arabia by more than patients who infected with Saudi society [30]. Similarly, the reason for the wide spread of CTX-M in the Arab Gulf States, such as Kuwait, is the presence of immigrants from countries where this type of enzyme is endemic [19]. Kandeel (2014) identified some important risk factors that are consistent with other studies, such as mechanical ventilation and the use of a urinary catheter (Table 1) [10].

On the other hand, a central venous catheter, age, sex and recent surgery were found not to be associated with infections caused by ESBL bacteria. Hospital admission was one of the most important factors in contracting an ESBL infection, which could happen within 48 hours. The use of cephalosporins and fluoroquinolones were also associated with ESBL infections [10]. Some research has referred to the fact that older patients (> 60 years) were more susceptible to ESBL infections than others [17]. In addition, an important risk factor that plays a role in increasing the transmission of ESBL organisms was the use of devices in hospital departments, particularly in intensive care [17].

In 2005, a study was conducted on 2,302 isolated organisms in Amana Hospital (Eastern region) and the results showed that approximately 8.9% (204/2,302) were ESBL-positive and Foley catheter infections accounted for the majority of these cases [64.2% (131/204)] [31]. In addition, inpatients and outpatients accounted for less than 43% and 13%, respectively [31]. ESBL-producing bacteria have

the ability to resist different antibiotic agents, such as fluoroquinolone family, leading to the consideration that this treatment may be considered a risk factor for ESBL infections [30].

A research project performed at King Khalid General Hospital, Hafer Al-Batin showed that the most prevalent ESBL-producing bacteria was *E. coli* with rates possibly exceeding 60% of isolated samples, while *K. pneumoniae* was the second most prevalent [10]. A study investigating the molecular features of ESBL bacteria (Hassan 2014) indicates that the CTX-M genotype occurred more frequently than SHV, at 97.4% and 23.1% respectively (Table 2) [29]. The TEM genotype was not detected in this study. However, another study performed in the same area showed that *K. pneumoniae* had a high rate of the SHV genotype, while in *E. coli* the TEM enzyme was the most common [7].

Al-Agamy and his colleagues [32] studied the outbreak (16 cases) of *K. pneumoniae* among newborns in an intensive care unit in Al-Qatif Hospital (Eastern region). They discovered that there were three types of genes carried by *K. pneumoniae*, CTX-M, TEM-1 and SHV-1, and that the reason for the infection was the CTX-M-15-producing *K. pneumoniae*.

In recent years, studies have indicated the ability of some types of ESBLs to resist the carbapenem antibiotic group, at rates of up to 20%. However, ESBL organisms showed sensitivity to amikacin [10]. Another study also recommended the use of amikacin due to its effectiveness against *K. pneumoniae* [29]. Despite the evidence of the resistance of ESBL bacteria to carbapenems, they remain the drug of choice to treat ESBL infections. Nevertheless, some researchers have reported that tigecycline and piperacillin-tazobactam may become an appropriate treatment for ESBL infections in the future [7].

Several studies have concluded that there is a need to stop using the third generation of cephalosporins, such as sulfamethoxazole-trimethoprim, ciprofloxacin, levofloxacin and gentamicin due to the high resistance shown by ESBL-producing bacteria to these types of treatment (Table 3) [7]. Furthermore, *E. coli* (CTX-M genotype) has demonstrated the ability to resist imipenem with increasing frequency (20%). Combination drugs, such as amoxicillin-clavulanic may be an inappropriate choice for the treatment of ESBL infections [17]. However, a study of 204 ESBL-positive samples carried out by Kader [31] indicated that imipenem and meropenem gave excellent results for the treatment of ESBL infections, with a success rate of more than 89%.

2.3 Western Region

A cross-sectional study by Elhassan et al. (2016) performed in Al-Madenah (Western region) concluded that ESBL-producing Enterobacteriaceae represented almost 24% of GNB compared to other regions of Saudi Arabia [33]. In addition, produce ESBL-producing *E.coli* was the most common organism [189/359 (52.61%)], followed by *K.pneumoniae* [87/359 (24.2%)]. The ESBL group accounted for less than a quarter of the Enterobacteriaceae [28/140 (20%)] and such infections were found to be more common among non-Saudis than Saudis, at 67.72% and 32.28%, respectively [33]. As in previous studies, *E. coli* was the most prevalent, then *K. pneumoniae*, but the rate of this spread may vary from one region to another [34]. Millions of Muslims come to Saudi Arabia from around the world each year to perform Umrah or Hajj, which may have contributed to the emergence of OXA-48 and NDM carbapenamases and ST131 [19,35].

A study of the existence of ESBL genes in *P. aeruginosa* conducted in the Western region (2015) indicated that this gene was present in about 26% of the total bacteria isolated. The *blaGES* gene was the most prevalent ESBL gene and no TEM or SHV genotypes were found in any samples [36]. A study in Makkah showed that the appearance of ESBL-producing *K. pneumoniae* was slightly higher than *E. coli*, at 24.4% and 23.1%, respectively [8].

In recent years, a study carried out in the Western province of Saudi Arabia (Jeddah) concluded that older patients (> 50 years) and patients in the intensive care unit were more likely to be infected with ESBL bacteria. Furthermore, gender, a stay in intensive care unit and the surgical ward all affected the rates of ESBL infections [34]. The major genotype of ESBL in the Western region (Al-Madenah) was CTX-M at 74.1% [33]. Other genotypes, such as TEM and SHV, also appeared, at 31.8% and 14.1%, respectively [33]. The ESBL producers have a high ability to resist non-beta-lactam treatment [33]. Tigecycline, imipenem, meropenem and amikacin were four antibiotics that were shown to be highly effective against

ESBL-producing bacteria and multi-drug resistant Enterobacteriaceae (Table 4) [34].

2.4 Southern Region

A study conducted in Southern Saudi Arabia (2015) indicated that among 269 GNB specimens, 91 (33%) were ESBL-producing *E. coli*, while 23 were *K. pneumoniae* (8%) and other ESBL bacteria accounted for ten samples (3%) [37]. The same study pointed out the patients most frequently infected with GNB were women, at approximately 75%. Furthermore, children (≤ 1–10 years) and the elderly (71–80 years) were more susceptible to ESBL infection than other age groups. In addition, patients with chronic diseases, such as diabetes, were more likely to be infected with ESBL bacteria than patients without these diseases [37].

Meropenem was the drug of choice to treat both GNB and ESBL organisms. Furthermore, nitrofurantoin proved to be a suitable treatment to overcome an *E. coli* infection (75%) and other GNBs (70%), but not for *K. pneumoniae* (14%) [37].

3. ESBL DETECTIO TECHNIQUE

According to studies published in Saudi Arabia, most of the samples used in the detection of ESBLs are urine specimens (followed by blood specimens). Other samples have also tested positive for the presence of ESBL-producing bacteria such as swabs from different areas of patients' bodies. Due to the diversity of the enzymatic characteristics of the β-lactamases, the biggest challenge for clinical microbiology laboratories is to recognize ESBL-producing organisms [38]. Several tests can be used to diagnose ESBL infections. Screening tests and confirmation tests are two important steps in the detection of ESBL enzymes [39].

3.1 Screening Tests

3.1.1 Disk diffusion methods

According to the guidelines of the Clinical and Laboratory Standard Institute (CLSI) (2012), *K. pneumoniae*, *K. oxytoca*, *E.coli* and *P. mirabilis* can be detected by disk diffusion methods. Observing specific zones of antibiotic sensitivity such as cefpodoxime, ceftazidime, aztreonam, cefotaxime and ceftriaxone is a simple way of determining ESBL production. To confirm a positive result of ESBL production, the zone diameter of an isolated organism with an antibiotic should be less than or equal to 17 mm when a cefpodoxime disk (10-µg) is used [40].

Table 4. Antibiotics susceptibility and resistance patterns of ESBLs produced by *E. coli* in different regions in Saudi Arabia

Antimicrobial agents	Region		
	Western		Southern
	Elhassan et al., 2016 (R)	Zaman et al., 2015 (S)	El-Kersh et al., 2015 (S)
Amikacin (AK)	32%	89%	88%
Ampicillin (AMP)	95%	ND	20%
Amoxicillin/clavulanate (AMC)	ND	ND	37%
Cefuroxime (CXM)	ND	ND	47%
Cefoxitin(FOX)	ND	71%	71%
Cefotaxime(CTX)	ND	ND	56%
Ceftazidime (CAZ)	ND	ND	56%
Cefepime (FEB)	ND	14%	57%
Ciprofloxacin (CIP)	72%	21%	56%
Gentamicin (CN)	24%	57%	75%
Imipenem (IPM)	ND	100%	ND
Meropenem (MEM)	ND	100%	99%
Nitrofurantoin (F)	ND	85%	75%
Piperacillin/Tazobactam (TZP)	ND	53%	66%
Trimethoprim/ Sulfamethoxazole	71%	32%	47%
Tigecycline (TGC)	ND	100%	ND

S: sensitive, R: resistance, ND: No data.

3.1.2 Dilution methods

The CLSI suggests the use of dilution methods to screen for ESBL-producing Enterobacteriaceae; however, the use of 8 µg/ml or more of cefpodoxime MIC is a more clinically useful screening test for cefpodoxime [40].

3.2 ESBL Disk Confirmation Tests

3.2.1 Double disk synergy tess (approximation test)

According to Livermorea and Brown [41], Muller-Hinton agar plates should be inoculated with the test organisms. Ceftazidime and amoxicillin/clavulanic acid disks should then be placed 30 mm apart (center to center) and incubated at 37°C for 24 hours. Any enhancement of the inhibition zone in the area between the disks indicates a positive result.

3.2.2 E-test strip

The E-test Strip can be used to confirm ESBLs results. In this test, the organism being tested is spread onto a Muller-Hinton agar plate. If the ratio (MIC) of amoxicillin/clavulanic acid with ceftazidime is more than eight, the result is positive [38].

3.3 Molecular Detection Methods

The molecular test for ESBL detection is the most important method for studying bacterial genetics. Polymerase chain reaction (PCR) is a common molecular method used to determine ESBL genotypes such as CTX-M, TEM and SHV [42].

4. ESBL SPREAD AND PREVENTION

Direct contact among people with ESBL infections, particularly in hospitals, and touching surfaces contaminated with ESBL-producing bacteria are common ways of causing the spread of ESBL infections. The most important methods for preventing the prevalence of ESBL include:

- Applying infection control policies properly in hospitals (e.g., health workers should follow hygiene and cleanliness guidelines in relation to medical equipment, rooms, corridors and all facilities inside hospital departments);
- Hospitals exploring the rate of ESBL prevalence on a regular basis;
- Isolating patients with ESBL infections in separate rooms;
- Ensuring that medications are not overused and diagnoses are correct;
- In the case of the spread of ESBL infections, conducting PCR tests to detect genotypes of bacteria;
- Keeping food clean (several studies have shown that food is a source of ESBL infection); and
- Increasing awareness of ESBL infection transmissions and educating individuals on how to avoid such infections to reduce the prevalence of ESBL-producing bacteria in environments.

5. SUMMARY

The majority of studies that have been published in Saudi Arabia in relation to ESBL infection concluded that the incidence of ESBL infections in all regions in Saudi Arabia is increasing with a difference in the ratio. In addition, the presence of positive cases of ESBL infections outside hospitals suggests that the cause of the infections may be common among people in the community. Regarding antimicrobial agents, the cephalosporin group has failed to treat ESBL and thus it may be appropriate to discontinue its use in the treatment of cases. The carbapenem family is the best choice for treating cases of ESBL; however, it should be noted that strains of *K. pneumoniae* that are able to resist this kind of antimicrobial agent are emerging. Risk factors contributing to the spread of ESBL infection include gander, age, chronic disease and previous treatments. On the other hand, it is very important to focus on effective methods of prevention (e.g., implementing programs to explore the disease and following-up) to limit the spread of infection. Also, it is necessary to have strict infection control procedures in place at hospitals to reduce the excessive use of drugs and avoid the emergence of new strains that have the ability to resist antibiotics.

6. CONCLUSION

In conclusion, ESBL-producing organisms are a real challenge for health and safety in both communities and health organizations. Despite the lack of ESBL infection research published in Saudi Arabia, we conclude that the increasing number of ESBL bacteria that have the ability to resist several antibiotic agents in different regions of Saudi Arabia and the inappropriate application of infection control policies lead to an

increase in the prevalence of infections in some hospitals and health centers. Therefore, all risk factors associated with ESBL infection in health environments should be considered in order to reduce ESBL-producing bacteria, particularly in provinces where the ESBL infection is increasing significantly. In the future, research needs to be conducted in all parts of Saudi Arabia to determine the prevalence of ESBL-producing organisms and their genotypes.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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