

The Burden of Infections with Extended Spectrum Beta-Lactamase-Producing Pathogen on Home Health Care Services

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Abstract

Citation: Al Seraya AS, Bin Haikel KA. The Burden of Infections with Extended Spectrum Beta-Lactamase-Producing Pathogen on Home Health Care Services. Open Access Maced J Med Sci. 2026 Feb 12; 14(1):11-14. <https://doi.org/10.3889/oamjms.2026.12039>

Keywords: outpatients' intravenous antimicrobial therapy (opat); antimicrobial resistance; multi-drug resistance; home health care; extended spectrum beta-lactamase (ESBL)

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Received: 24-Feb-2025

Revised: 11-Sep-2025

Accepted: 5-Dec-2025

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Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: Extended-spectrum beta-lactamase (ESBL) producing pathogens are a growing health threat due to their resistance to most of the commonly used antimicrobial agents.

AIM: In this paper, we aimed to assess the prevalence of those pathogens among patients who received care in the home parenteral antimicrobial therapy program. We also aimed to examine the burden of those pathogens on the home health care services and discuss the options to minimize this burden.

METHODS: This retrospective cohort study was conducted in the Adult Home Health Care Service at King Abdulaziz Medical City in Riyadh, Saudi Arabia. We studied all patients referring to the home health care parenteral antimicrobial program in the period from January 1, 2019 to December 31, 2021. Patients' data were retrieved from their electronic medical records. We classified patients as a patient with ESBL infection and a patient with a non-ESBL infection based on their cultures.

RESULTS: A total of 253 patients, of whom 144 (56.9%) were females, were accepted into the home parenteral antimicrobial therapy during the specified period. Of these, 121 (47.8%) were treated with an infection with ESBL-producing bacteria. *Escherichia coli* (92.76.0%) and *Klebsiella pneumoniae* (23.19.0%) were the most commonly isolated ESBL pathogens. Female gender, a previous history of UTI or ESBL infection, cognitive impairment and BPH in men were all associated with a higher rate of ESBL infections ($P < 0.05$). Infection caused by ESBL-producing pathogen was not associated with a significantly increased rate of complications, readmission or mortality ($P \geq 0.05$).

CONCLUSION: Almost half of the patients treated in the home parenteral antimicrobial program are infected with an ESBL-producing pathogens. However, we did not find any significant increase in adverse clinical outcomes associated with those infections in our sample. The burden on the HHC services that comes with these infections is mostly related to the limited choices of antimicrobials and to the high rate of recurrence.

Introduction

Extended-spectrum-beta-lactamase (ESBL) is a group of enzymes produced by some strains of gram negative bacteria, rendering them highly resistant to most of the commonly used antibacterial agents. As reported by the CDC, infections with ESBL-producing Enterobacteriaceae have been increasing since 2012 [1]. In its report for antimicrobial resistance threat in the United States, the Center of Disease Control and Prevention (CDC) classifies ESBL-producing Enterobacteriaceae as a "serious threat" and carbapenem resistant Enterobacteriaceae as an "urgent threat" [1]. In Saudi Arabia, a study conducted at a tertiary center in Riyadh examined 17,105 samples between 2006 and 2010 and reported 6.3% prevalence

rate of ESBL-producing pathogens, mostly in urine samples [2].

Another report from the same period stated that 33% of urinary tract infections with *Escherichia coli* are caused by ESBL-producing *E. coli* [3]. A more recent study reported the prevalence of 67% of multidrug resistant *E. coli* and 33% of ESBL-producing *E. coli* in urine isolates [4]. This topic is relevant to home health care services today since they are dealing with those pathogens within their home antimicrobial programs. In this paper, we aim to examine this issue and its impact on care from the point of view of home health care specialists. We also try to investigate the role that the home health care departments can play toward the resolution of this current threat.

Materials and Methods

This retrospective cohort study was conducted in the Adult Home Health Care Service at King Abdulaziz Medical City (KAMC) in Riyadh, Saudi Arabia. We studied all patients referred to the home parenteral antimicrobial program in the period from January 1, 2019 to December 31, 2021. We included all the accepted patients during this period. Patients' data were retrieved from their electronic medical record. The study was approved by the institutional review board of King Abdullah International Medical Research Center in KAMC (RYD-22-419812-128030).

The data were analyzed through SPSS software version 24.0 (NY: IBM Corp.). Continuous variables were presented as mean and standard deviation (mean \pm SD), while percentages and frequencies were used to describe the categorical variables. The statistical analysis included Chi-square test that was used to measure the association between the two groups (the group with ESBL infection and the group with non-ESBL infection), the risk factors, and the clinical outcomes. P values less than 0.05 were considered statistically significant.

Results

As seen in Table 1, a total of 253 patients received therapy in the program during the identified period. Almost half of those patients were infected with an ESBL pathogen. Females were affected almost twice as much as males. The mean age of patients seen with ESBL was 75 years. Fifty-five percent of those patients were followed by HHC for other services.

Table 1: Patient Characteristics

Variable	ESBL	All
Female	ESBL: 77 (63.6%)	All: 144 (56.9%)
Male	ESBL: 44 (36.4%)	All: 109 (43.1%)
Total	ESBL: 121 (47.8%)	All: 253 (100%)
Age (Mean \pm SD)	ESBL: 74.5 \pm 13.8	All: 72.2 \pm 15.5
Registered to other HHC programs	ESBL: 67 (55.4%)	All: 129 (51.0%)
Deaths	ESBL: 5 (4.1%)	All: 12 (4.7%)

Table 2 presents the risk factor and their association with having an ESBL infection. Female gender, a history of urinary tract infection (UTI), cognitive impairment, and benign prostatic hyperplasia (BPH) in males were significantly associated with having an ESBL infection.

Table 2: Risk Factors in Patients with ESBL Infections

Risk Factor	ESBL	All	P Value
Female gender	77 (53.5%)	144	0.04
UTI history	115 (55.6%)	207	0.00
ESBL history	98 (73.7%)	133	0.00
DM	89 (49.2%)	181	0.48
CKD	49 (54.4%)	90	0.12
Cognitive impairment	41 (57.0%)	72	0.07
BPH*	21 (60.0%)	35	0.00
Catheter*	10 (50.0%)	20	0.33

* For male patients only

As seen in Table 3, complications and mortality in both groups were similar; however, patients with

ESBL infections had significantly higher rates of ER visits ($p = 0.02$).

Table 3: Complications in Patients with ESBL Infections During Therapy

Complication	ESBL	All	P Value
Complications	19 (42.2%)	45	0.41
Persistent infection	10 (52.6%)	19	0.66
Sepsis	3 (33.3%)	9	0.38
Readmission	31 (62.0%)	50	0.67
ER visits	40 (60.6%)	66	0.02
Deaths	5 (42.7%)	12	0.66

As shown in Table 4, *E. coli* and *K. pneumoniae* were seen in over 90% of cases.

Table 4: ESBL Pathogens and Susceptibility

Pathogen	Frequency (%)
<i>Escherichia coli</i>	92 (76.0%)
Pan resistant (<i>E. coli</i>)	3 (3.3%)
<i>Klebsiella pneumoniae</i>	23 (19.0%)
Pan resistant (<i>Klebsiella</i>)	4 (17.4%)
<i>Serratia marcescens</i>	2 (1.7%)
<i>Pseudomonas aeruginosa</i>	2 (1.7%)
<i>Enterobacter cloacae</i>	1 (0.8%)
<i>Morganella morganii</i>	1 (0.8%)
Total	121 (100%)

Table 5 summarizes the diagnoses of patients with ESBL infections. Over 80% of our patients suffered from UTI or a urosepsis. Osteomyelitis was seen in 12% of patients.

Table 5: Diagnoses of Patients with ESBL Infection

Diagnosis	Frequency (%)
UTI	85 (70.2%)
Urosepsis	18 (14.9%)
Osteomyelitis	15 (12.4%)
Pneumonia	2 (1.7%)
Liver abscess	1 (0.8%)
Total	121 (100%)

Table 6 presents the antimicrobial agents that were used with those infections. Carbapenems (namely ertapenem and meropenem) were used to treat 90% of cases. Ceftazidime with avibactam and Tigecycline were used mainly in cases of carbapenem resistance.

Table 6: Antimicrobial Agents Used in ESBL Patients

Antimicrobial Agent	Frequency (%)
Ertapenem	92 (76.0%)
Meropenem	18 (14.9%)
Tigecycline	6 (13.2%)
Ceftazidime	5 (4.1%)
Total	121 (100%)

Discussion

Magnitude of the problem

During the period of 1/1/2019 to 31/12/2021, we have seen 119 patients (out of 253) with ESBL-producing pathogen infection that is proven by culture. Over 80% of those patients had a history of ESBL infection prior to this presentation. While receiving home care, 19 patients had complications and 20 had to be readmitted to the hospital. Three patients had sepsis while receiving home therapy, and 3 patients died. All ESBL patients had to be treated with parenteral antimicrobials, mainly ertapenem and

meropenem. However, a small, worrisome set of patients had a carbapenem resistant pathogen; therefore, IV tigecycline or ceftazidime/avibactam were used.

Burden of the Infection

ESBL patients represent almost half of the patients served by the HHC parenteral antimicrobial program. Those patients constitute a challenge to HHC on many levels. Current evidence suggests carbapenems to be the antimicrobial of choice for ESBL infections, owing to their effectiveness in treating the infection and their enhancement of survival rates [5]. Most of our patients were treated with either a course of ertapenem or meropenem. Ertapenem can be given once daily; however, it requires an infusion over 30 minutes, meaning longer HHC visits. Meropenem on the other hand is injected over 5 minutes, but requires multiple doses per day, mandating multiple daily visits. Challenges associated with carbapenems use include their parenteral route, high costs and susceptibility to resistance [6]. However, the duration of therapy is usually similar to the duration in non ESBL infections. Patients with ESBL infections have higher mortality and poorer outcomes compared to others infected with non-ESBL pathogens [7, 8]. ESBL patients are more likely to be hospitalized and to be admitted to ICU [9]. ESBL infections had been associated with severe infections as well as bacteremia [10]. Sepsis and bacteremia are feared complications that are associated with higher mortality [7, 8]. Recurrence of infection is also another factor that generously contributes to the burden of the infection [11].

Approaching the issue

HHC management of ESBL infections has been successful in treating patients with the added benefit of preventing transmission of infection to other patients as well as cutting the costs of management. Nevertheless, various measures can be taken to ensure the continuity of care and address this serious health threat on the level of HHC.

Preventive Measures

As in all cases of bacterial resistance, ESBL-producing bacteria thrive and evolve whenever antibacterial agents are misused. The implementation of antimicrobial stewardship (AMS) programs is vital to fight against the spread of ESBL infections. ESBL pathogens can also be transmitted through hands of patients and health care practitioners, which necessitates teaching patients, caregiver and HHC staff the importance of hand hygiene, especially when dealing with ESBL infected patients.

Decolonization therapy for patients who are carrier to ESBL pathogens is suggested to lower the infection rate and subsequently lower the morbidity and mortality rate without an increase in antimicrobial resistance [12]. However, data are still insufficient to recommend routine decolonization for patients carrying these pathogens [12].

Long-term nitrofurantoin has been prescribed to patients with recurrent ESBL infections; however, it carries a significant risk of toxicity and inducing resistance [13]. Fosfomycin and methenamine hippurate have been also used to prevent recurrent UTIs with some evidence supporting their effectiveness [7, 13]. Methenamine hippurate is specifically promising due to its safety profile and lack of resistance risk [7].

Addressing Risk Factors

Many risk factors for acquiring ESBL infections have been identified; however, the majority of them are non-modifiable. Risk factors include female sex, age older than 65 years, diabetes mellites, urinary catheterization, recurrent UTIs and prior administration of antibiotics [10]. Most of our patients have more than one of these risk factors, which might be a reason behind their high rate of recurrence. However, it is important to mention that patients without any of the documented risk factors might acquire the infection as well [7].

Early Initiation of Therapy

Many studies have investigated the impact of failing to provide sufficient antimicrobial therapy within 72 hours of infection on the patient's outcomes. A study described delay in early treatment as an independent predictor of death [14]. The length of delay in adequate treatment was also found to significantly increase the mortality rate and adverse clinical outcomes [7, 10, 14, 15]. It might be beneficial for the patient in HHC to have a system of dealing with patients with recurrent ESBL infections that can identify the infection and treat it early. Initiation of therapy by HHC has also the added benefit of preventing the spread of infection to the health care facilities and to the other hospitalized patients.

Use of New Technologies

Utilization of new technologies in HHC service might be a way to reduce costs and enhance patients' safety and satisfaction at home. One technology that can be used in the parenteral antimicrobial program is the 5 of 7 elastomeric infusion devices. Those devices, or pumps, can be easily operated by the patients or their caregivers without interfering with the patients' activities or sleep. They reduce the visits and the workload of the HHC staff, reduce the costs, and

enhance patients' satisfaction [16]. They can be specifically beneficial when administering a medication with frequent daily doses or a medication that needs to be administered over a long period of time.

Limitations

The limitation of the study is the comparison between the patients who required IV treatment for a significant infection and patients who had to be treated with IV antimicrobial agents merely for their susceptibility results - who might otherwise have been treated with oral agents and have not been referred to HHC services. This might result in underestimating the outcomes of an infection with an ESBL-producing pathogen.

Conclusions

Infection with ESBL-producing pathogens, acquired from the health care facilities and from the community, is on the rise. Home health care services are increasingly dealing with these infections and with patients carrier to these pathogens. The burden on HHC services from those infections is unlikely to subside, thus it is time for decision makers to think about the best strategies to lower this burden and provide the best care to the infected patients.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. King Abdullah International Medical Research Center (KAIMRC) issued approval IRB/1941/22. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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