

Gastrointestinal Tract Colonization Rate of Extended-Spectrum Beta-Lactamase- and Carbapenemase-Producing Enterobacteriaceae and Associated Factors Among Hospitalized Patients in Arba Minch General Hospital, Arba Minch, Ethiopia

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Background: The incidence of hospital-acquired enterobacteria that produce extended-spectrum beta-lactamases (ESBLs) is on the rise worldwide. Colonization of gastrointestinal tract by extended-spectrum beta-lactamase Enterobacteriaceae, a prominent causative agent, results in life-threatening infections.

Objective: To determine the rate of gastrointestinal colonization by extended-spectrum beta-lactamase- and carbapenemase-producing Enterobacteriaceae and also to elucidate the antibiotic susceptibility profile and associated risk factors among hospitalized patients in Arba Minch General Hospital, Ethiopia.

Methodology: A facility-based cross-sectional study was conducted in Arba Minch General Hospital from May 2018 to July 2019. Sociodemographic data and associated factors were collected using a pre-tested-structured questionnaire. Stool specimens were collected using sterile stool cups. Each sample was then inoculated onto MacConkey agar. Bacterial isolates were identified using various biochemical tests. Screening and confirmatory tests for extended-spectrum beta-lactamase- and carbapenemase-producing Enterobacteriaceae were performed using the modified Kirby–Bauer disc diffusion technique. Statistical package for Social Science was used to analyze the data. The P-value ≤ 0.05 was considered as statistically significant.

Results: A total of 421 hospitalized patients were enrolled in this study of which there were 240 (57%) females. The mean age of the study participants was 28.8 with SD of 15.7. Majority of participants were in the age range of 25–40 years 179 (42.5%). About 146 (34.7%) participants were found to be colonized by extended-spectrum beta-lactamase-producing Enterobacteriaceae. The predominant ESBL-producing isolates were *Escherichia coli* 62 (42.46%) followed by *Klebsiella pneumoniae* 60 (41.09%). Six (1.43%) carbapenemase-producing *K. pneumoniae* were isolated. ESBL-producing Enterobacteriaceae showed higher resistance against tetracycline (91.1%) and cotrimoxazole (93.84%). Colonization of the gastrointestinal tract by ESBL showed statistically significant association with regard to chronic diseases ($p < 0.001$) and the administration of oral antibiotics after admission ($p = 0.020$).

Conclusion: The overall colonization rate of the gastrointestinal tract by extended-spectrum beta-lactamase-producing Enterobacteriaceae was prominent. The extended-spectrum beta-lactamase-producing isolates exhibited a higher level of resistance against the commonly used antibiotics which further needs greater attention.

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Introduction

Drug resistance is an increasing public health problem worldwide. Antibiotic resistance among Gram-negative bacilli is a rapidly increasing conundrum due to the organisms' ability to mutate and to acquire and transmit plasmids and other mobile genetic elements encoded with resistance genes. Beta-lactam antibiotics are among the most commonly used antibiotics which include penicillins, cephalosporins and carbapenems and the emergence of resistance to these agents had resulted in a major clinical crisis. Infections caused by drug-resistant organisms pose important challenges during the treatment of both common and life-threatening diseases.^{1,2}

β -lactamase production is one of the most important mechanisms of resistance displayed by the Gram-negative bacilli to penicillins and cephalosporins. Extended-spectrum beta-lactamases (ESBLs) are enzymes capable of hydrolyzing many beta-lactam antibiotics including penicillins and cephalosporins, thereby protecting ESBL-producing bacteria from the action of these groups of drugs. Carbapenems are the drug of choice for infections caused by these bacteria.²⁻⁴ Cephamycins and carbapenems are the only beta-lactam families that remained fully effective against extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL-PE). Combinations with beta-lactam inhibitors like clavulanic acid can restore the activity of several beta-lactams. However, nowadays these ESBL-PE are becoming increasingly resistant to carbapenems due to the production of carbapenemase. *Klebsiella pneumoniae* is the major carbapenemase producer worldwide. Besides, species of *Acinetobacter* and *Pseudomonas* are also becoming resistant to carbapenems due to mono-therapy.^{5,6,7}

ESBL-producing bacteria can be transmitted through fecal-oral route and/or via direct person to person contact. In a hospital setting, the transmission can be among patients, from patients to health-care workers, or/and to visitors. Especially when health-care workers contract the bacterial infections, there exists a chance of disseminations to a larger population. Therefore, hospitalized patients are considered as the main source of the causative agent, ESBL-PE.⁸

The incidence of MDR is increasing globally and even there are reports of pan drug-resistant (PDR) isolates. The World Health Organization (WHO) has declared infections

caused by multidrug-resistant bacteria as an emerging global health problem.^{3,9}

MDR Gram-negative bacteria are a major public health threat. For more than two decades, the incidence of hospital-acquired enterobacteria that produce ESBLs has increased worldwide. The widespread occurrence of ESBL-producing bacteria not only affects the choice of antibiotics but may also cause excessive morbidity, mortality and economic crisis.^{10,11}

The rates of gastrointestinal tract colonization caused by ESBL-PE vary considerably in different geographical areas and also change over time. For instance, in various European countries reported carriage rates fall between 8% and 28%. And in recent years, the higher prevalence rate had been reported, viz., 50.5%, 63.3% and 69.3% in China, Egypt, and Thailand, respectively. The rates are found to be increasing over time especially in low-income countries including Ethiopia.^{12,13}

In hospitalized patients, ESBL-PE has become the most common type and is highly prevalent in developing regions of the subtropics. According to some reports, the international/local travel may contribute substantially and certain proportion of visitors reach the ESBL burdened destinations resulting in the contraction of ESBL-PE. They may spread the bacteria to their close contacts and local hospitals and contribute further to the dissemination of MDR bacteria worldwide.^{7,14}

Most commonly, patients infected with ESBL-producing organisms are more at risk. This is because frequently they are treated with antibiotics to which the organisms exhibit a high level of resistance. The mortality rates in infections caused by ESBL-producing bacteria are higher and some studies even show that the rate may range from 42% to 100%.¹⁵ On the other hand, infections caused by carbapenems resistant organisms are associated with mortality rates up to 70%. The spread of carbapenems resistant *Enterobacteriaceae* (CRE) in health-care settings is another important medical problem. Most of the nations are at risk of falling victim to the emergence of CRE. Therefore, infection prevention and control system should be strengthened to combat the spread of such resistant bacteria.¹⁶

ESBLs also add to the burden on health-care systems causing prolonged hospital stay. Report from Europe revealed that there could be more than 2700 deaths and excess burden of 18.1 million euro (in cost-wise), and also

more than 120,000 days of hospital stay. ESBL-PE often displays MDR phenotypic characteristics, further limiting the therapeutic options.^{17,18}

Survey of the literature indicated that little is known about the gastrointestinal carriage of ESBLs producers and antibiotic susceptibility patterns in Ethiopia, with only one study, which was conducted in Addis Ababa, Ethiopia. Therefore, this study was conducted to investigate the colonization rate of the gastrointestinal tract with ESBL-PE, antibiotics susceptibility pattern and also to identify associated risk factors of carriage rate among hospitalized patients in Arba Minch General Hospital, Arba Minch, Ethiopia.

Materials and Methods

Study Design, Area and Period

A facility-based prospective cross-sectional study was conducted from May 2018 to July 2019 at Arba Minch General Hospital which is located in Arba Minch town the south of Addis Ababa. It was established in 1961 during the period of Emperor Haile Selassie and was the only hospital in the town at that time, and even today continues to serve a large number of patients annually, around 1000,000 individuals visit the hospital. The hospital has different wards including medical inpatient, surgical, emergency, gynec-obstetrics, and neonatal/pediatric. There are more than 300 beds that are actively serving. The hospital serves for both outpatients and inpatients. Annually there are more than 10,000 admissions including those admitted for less than 48 hrs and for more than 48 hrs.

Population

Source population

All the patients who were admitted into Arba Minch General Hospital.

Study Population

Entire patients who were admitted to medical, surgical, gynecology and pediatrics wards for more than 48 hrs in Arba Minch General Hospital were our study population.

Sample Size Determination and Sampling Technique

Sample Size Determination

The sample size was determined by using a single population proportion formula. P-value of 0.52 from a previous study done in Ethiopia was opted.¹⁹ After considering 95% of confidence interval ($Z_{\alpha/2} = 1.96$) and 5% of marginal

error ($d=0.05$), the initial sample size of 383 was computed using the following expression:

$$n = \frac{(Z_{\alpha/2})^2 * P(1 - P)}{d^2} = 3.84 * 0.52(1 - 0.52)/(0.05)^2 = 383$$

Finally, by considering the 10% of contingency, 38 subjects were added and the final sample size was consolidated as 421.

Sampling Technique

A total of 421 patients were included in this study. A systematic random sampling technique was used to recruit the study participants. The first participant was selected by lottery method and by using the formula ($K = 880/421 = 2.09$). Therefore, every two individuals were taken. Individual participants were selected randomly in every Kth interval during the study period. We have included participants from four wards (Medical inpatient, surgical, pediatrics and gynecology) proportionally.

Eligibility Criteria

The inclusion criteria for the study subjects was the patients who were admitted to medical, surgical, gynecology and pediatric wards of Arba Minch General Hospital for more than 48 hrs. The exclusion criteria for the study subjects were: (1) Patients who took antibiotics on the day of sample collection, (2) Patients who are admitted for less than 48 hrs.

Data Collection and Laboratory Investigation

Data Collection

On the starting day of data collection, patients who were admitted to the hospital 48 hrs ago were recruited by taking written consent from each one individually. Details pertaining to the socio-demographic data (age, residence and occupation), clinical history (existing antibiotic treatment, previous antibiotic therapy if any, previous history of hospitalization for longer period and also the incidence of earlier colonization by any multidrug-resistant bacteria) were collected by using a pre-tested-structured questionnaire.

Sample Collection

Two stool specimens were collected from each patient using sterile stool cups after 48 hrs of admission and just before discharging him/her from the hospital. The collected stool specimens were then transported to the Microbiology and Parasitology laboratory of College of

Medicine and Health Sciences, Arba Minch University (within 1 hr of collection).

Laboratory Investigation

Bacterial Isolation

Stool samples were inoculated onto MacConkey agar and then incubated for 24 hrs at 37°C. After incubation, bacterial growth was observed and pure cultures of bacterial isolates were subsequently subjected to species identification and confirmation. Biochemical (indole, oxidase, TSI, citrate, urease, LDC, motility, and H₂S gas production), morphological, and physiological characteristics of isolated bacteria were determined by adopting standard laboratory methods as described elsewhere. Corresponding American Type Culture Collection strains were utilized as reference standards to validate the biochemical identification.²⁰

Screening of ESBL- and Carbapenemase-Producing Enterobacteriaceae

Phenotypic characterization of ESBL-PE was performed for the screening of patients. Screening for the presence of ESBL or carbapenemase production was done according to CLSI guidelines.²¹

Confirmatory Test for ESBL Production

ESBL phenotypic confirmatory test was performed by standard disc diffusion technique using indicator drugs. Briefly, organism suspected for the production of ESBL was spread onto a Mueller-Hinton agar by preparing a suspension equivalent to 0.5 CFU McFarland standards. Two indicator antibiotic discs were then placed 15 mm apart (center to center). One of the discs contains amoxicillin/clavulanic acid and the other contains an expanded-spectrum cephalosporin (ceftriaxone, cefotaxime or ceftazidime). After 24 hrs of incubation, if the zone of inhibition in between the discs were enhanced, the test was considered positive. The carbapenemase production of *K. pneumoniae* was confirmed by meropenem/cloxacillin combination discs test technique. The test was considered positive if an increase in the inhibition zone by 5 mm was observed compared to the inhibition zone of carbapenems alone. *K. pneumoniae* CCUG 56233 was used as a positive control for carbapenemase production and *K. pneumoniae* ATCC 25955 obtained from EPHI was used as a negative control in all phenotype tests.²¹

Antibiotic Susceptibility Testing

Antimicrobial susceptibility testing was performed by Kirby-Bauer disk diffusion technique on Mueller-Hinton agar according to CLSI guidelines (CLSI, 2017). Antibiotics

(Oxoid Ltd Basingstoke, Hampshire, UK) which are recommended by CLSI for susceptibility test such as aztreonam (15 µg), ciprofloxacin (5 µg), chloramphenicol (30µg), trimethoprim-sulfamethoxazole (co-trimoxazole) (1.25/23.75 µg), amikacin (10µg), tetracycline (30µg), gentamycin (10µg), tobramycin (10 µg), meropenem (10 µg), imipenem (10 µg), and ceftoxitin (30 µg) were included. The bacteria that were resistant for three or more classes of antibiotics were considered as multidrug-resistant (MDR).²²

Quality Assurance

Data quality was ensured from collection up to the final laboratory identification by following a standard operating procedure. Culture media was prepared according to manufacturer's instruction, and the sterility was checked by incubating 5% of the prepared media at 35–37°C overnight and also by observing the bacterial growth. Those batches of the media that show the growth was discarded and prepared again. The performance of the prepared media was also checked by inoculating control strain *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603, which were obtained from Ethiopian Public Health Institute (EPHI). The performance of antibiotic discs were checked by using *Enterococcus faecalis* ATCC 29122 and co-trimoxazole disc. Five percentage of the questionnaire was pretested prior to the data collection and process was supervised on a daily basis. Incompletely filled questionnaires were discarded.

Statistical Analysis

Data were entered, edited, cleaned and analyzed by using Statistical Package for Social Sciences (SPSS) software Version 21.0. Descriptive statistics were calculated according to the objectives of study such as frequency, mean and standard deviations. Binary logistic regression analysis was used to determine the association between colonization rate and associated factors. All variables with P<0.25 in the bivariate analysis were included in the final model/multivariate analysis. P ≤0.05 was considered as a statistically significant association. Finally, the magnitude of the association among different variables in relation to the outcome variable was measured by the odds ratio with a 95% confidence interval. Compiled results were presented in the form of text, tables or graphs.

Ethical Considerations

The study protocol was ethically approved by the institutional review board of Arba Minch University, College of

Medicine and Health Sciences (Ref. No. CMHS/10635/21). This study was conducted in accordance with the declaration of Helsinki. Besides, separate permission was procured from Arba Minch General Hospital administrators. Formal written consent was obtained from each study participant. Confidentiality was strictly maintained from sample collection up to the final report writing.

Operational Definitions

Previous antibiotics treatment – History of antibiotic treatments for the last one year if any.

Prolonged hospitalization – Hospitalization for more than two weeks

Presence of chronic disease – Diseases like HIV, diabetes mellitus and hypertension

Habit of handwashing – (Less frequent – participants who never wash their hands at all and who wash their hands once a day, Frequent – participants who wash their hands two to three times a day, More frequent – participants who have the habit of washing their hands more than three times a day).

Results

Socio-Demographic Characteristics

A total of 421 hospitalized patients were included in this study of which there were 240 (57%) females. The mean age of the study participant was 28.8 years with SD of ± 15.7 . Majority of participants were in the age range of 25–40 years 179 (42.5%). Half of the study participants were rural dwellers 211 (50.1%), whereas, most of them had the habit of eating raw foods, 389 (92.4%). Number of participants who had the habit of eating more than one type of raw foods were 167 (39.7%). Also, chronic diseases were found in 126 (38.5%) patients (Table 1).

Fecal Carriage Rate of ESBL-PE

Among the total 421 admitted patients, 140 (33.25%) were found to be colonized by ESBL-PE. Majority of the carriers about 92 (69.02%) were rural dwellers. Among the carriers, 74 (50.68%) were males. Patients with a family income of below 1000 birr per month and participants who have had the habit of eating raw foods showed higher carriage rates of ESBL-PE (Table 2). It was found that the predominant ESBL-producing organism was *E. coli* 62 (44.28%) followed by *K. pneumoniae* 60 (42.85%) (Figure 1). On the

Table 1 Socio-Demographic Characteristics of Hospitalized Patients at Arba Minch General Hospital, 2019

Variables	Category	Frequency	Percentage
Sex	Male	181	43
	Female	240	57
Age	0–15	83	19.7
	16–25	90	21.4
	26–40	179	42.5
	41–60	59	14
	>60	10	2.4
Residence	Urban	210	49.9
	Rural	211	50.1
Educational level	Illiterate	162	38.5
	Preschool	44	10.5
	Primary school	112	26.6
	Secondary school	34	8.1
	College and above	69	16.4
Occupational status	Farmer	97	23
	Student	88	20.9
	Merchant	20	4.8
	Employee	73	17.3
	House wife	85	20.2
	Others	15	3.6
	No job	43	10.2
Family income	<1000 ETB	251	59.6
	1000–2000 ETB	111	26.4
	>2000 ETB	59	14
Habit of eating raw food	Yes	389	92.4
	No	32	7.6
Chronic disease	Yes	126	38.5
	No	295	61.5
Ward patient admitted	Medical inpatient	207	49.2
	Surgery	103	24.5
	Gynecology	40	9.5
	Pediatrics	71	16.9

Abbreviation: ETB, Ethiopian birr.

Table 2 Prevalence and Association of ESBL-PE Colonization Rate with Demographic and Clinical Factors Among Hospitalized Patients in Arba Minch General Hospital, 2019

Variable Categories		Colonization with ESBL-PE	Multivariate Analysis		
		Positive N (%)	AOR	95% CI	P-value
Sex	Male	74(50.68)	1		
	Female	72(49.32)	0.973	0.419–2.261	0.949
Age	0–15	29(19.86)	0.167	0.013–2.116	0.167
	16–25	40(27.39)	0.047	0.005–0.465	0.009
	26–40	55(37.67)	0.295	0.037–2.352	0.249
	41–60	17(11.64)	0.506	0.057–4.479	0.450
	>60	5(3.42)	1		
Residence	Urban	54(39.98)	1		
	Rural	92(69.02)	2.23	1.47–3.37	<0.001
Educational level	Illiterate	52(35.62)	-	-	-
	Preschool	14(9.58)	-	-	-
	Primary school	50(34.24)	-	-	-
	Secondary school	0	-	-	-
	College and above	30(20.55)	-	-	-
Occupational	Farmer	45(30.82)	-	-	-
	Student	45(30.82)	-	-	-
	Merchant	5(3.42)	-	-	-
	Employee	15(10.27)	-	-	-
	House wife	17(11.64)	-	-	-
	Others	5(3.42)	-	-	-
	No job	14(9.58)	-	-	-
Family income	<1000 ETB	98(67.12)	1.386	0.310–6.205	0.669
	1000–2000 ETB	30(20.55)	5.658	1.160–27.610	0.032
	>2000 ETB	18(12.33)	1		
Raw food eating	Yes	128(87.67)	21.072	5.194–85.493	<0.001
	No	18(12.33)	1		
Admission ward	Medical	70(47.95)	-	-	-
	Surgery	39(26.71)	-	-	-
	Gynecology	13(8.90)	-	-	-
	Pediatrics	24(16.44)	-	-	-
Chronic disease	Yes	72(49.32)	0.136	0.048–0.380	<0.001
	No	74(50.68)	1		
Prev. hospitalization	Yes	43(29.45)	0.312	0.141–0.690	0.004
	No	103(70.55)	1		
Hospital stay	Days	104(37.14)	-	-	-
	One week	36(30.77)	-	-	-
	Two weeks	0	-	-	-
	Three weeks	0	-	-	-
	Month or more	6(50.00)	-	-	-
Handwashing habit	Less frequent	38(26.04)	0.134	0.030–0.593	0.008
	Frequent	90(61.64)	0.261	0.085–0.799	0.019
	More frequent	18(12.32)	1		

(Continued)

Table 2 (Continued).

Variable Categories		Colonization with ESBL-PE	Multivariate Analysis		
		Positive N (%)	AOR	95% CI	P-value
Presence of latrine at home	Yes	68(45.57)	1		
	No	78(53.43)	3.380	1.410–8.100	0.006

Notes: Prev. – previous, (-): not included in multivariate analysis since P-value >0.25 in bivariate analysis.

Abbreviation: ETB, Ethiopian birr.

other hand, only six (1.43%) isolates of carbapenemase-producing *K. pneumoniae* were identified.

ESBL-PE Colonization Rate and Associated Factors

Multivariate analysis revealed that colonization of the gastrointestinal tract by ESBL showed statistically significant association with the presence of chronic diseases ($p < 0.001$, AOR=0.136, 95% CI=0.048–0.380), prolonged previous history of hospitalization ($p = 0.004$, AOR=0.312, 95% CI=0.141–0.69), administration of oral antibiotics after admission ($p = 0.020$, AOR= 2.882, 95% CI=1.179–7.043), residence in rural area ($p < 0.001$, AOR=2.23, 95% CI= 1.47–3.37) and habit of handwashing ($p = 0.008$, AOR= 0.13, 95% CI= 0.03–0.59) (Table 2).

Antimicrobial Susceptibility Pattern

Totally, nine antibiotics were tested against ESBL-PE by using the Kirby–Bauer disc diffusion technique. ESBL-producing *Enterobacteriaceae* showed a higher resistance against tetracycline (91.1%), cotrimoxazole (93.84%), chloramphenicol (69.18%) and less resistance against aztreonam (4.11%) and amikacin (4.79%). The isolates of *K. pneumoniae* showed higher resistance against tetracycline (91.70%), cotrimoxazole (96.7%), and chloramphenicol (73.3%). In the case of *E. coli*,

resistance was produced against tetracycline, cotrimoxazole (93.5%), and ciprofloxacin (72.6%) (Table 3).

Multidrug Resistance Pattern of ESBL-PE

In this study, the overall prevalence of MDR bacteria (resistant to three or more classes of antibiotics tested) was 99 (70.71%). Most of the Gram-negative enteric bacteria were resistant to at least one of the antibiotics tested (Table 4).

Discussion

The incidence of MDR is increasing globally and even there are reports of PDR isolates. Recently, WHO has declared infections caused by multidrug-resistant bacteria as an emerging global health problem.^{3,9} The incidence of hospital-acquired enterobacteria that produce ESBLs had increased worldwide. The widespread presence of ESBL-producing bacteria not only affects the choice of antibiotics but also may cause excessive morbidity, mortality and economic crisis on a global scale.^{10,11}

In this study, the overall colonization rate of the gastrointestinal tract by ESBL-PE was high 140 (33.25%) 95% CI (29.36%–42.67%). This data is comparable with results of a study reported in India 43%.²³ Our results showed higher carriage rate compared to studies conducted in Turkey 24%,²⁴ Israel 8%,²⁵ India 9.3%²⁶ and USA 2%,²⁷ but lower than the rates found in other studies conducted in Ethiopia 52%,¹⁹ Ecuador 56%,²⁸ Morocco 58%,²⁹ Egypt 68%,³⁰ and Cambodia 61.9%.³¹ The possible reason for the variability of colonization rate found among different studies could be attributed to variations in the socioeconomic status of the population included and the study design.

The predominant ESBL-PE was *E. coli* (44.28%), followed by *K. pneumoniae* (42.85%), *Citrobacter* species (8.57%) and *Enterobacter* species (4.3%). This is in line with previous studies conducted in Ethiopia,¹⁹ Turkey,²⁴ Ecuador,²⁸ and Egypt.³⁰ However, in studies conducted in Morocco,^{29,32} India^{23,26} and the USA,²⁵ the isolates of *K. pneumoniae* were found to be the predominant ESBL producer.

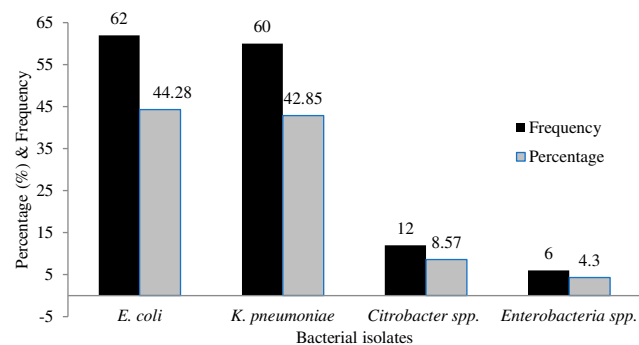


Figure 1 Frequency of ESBL-producing bacteria.

Table 3 Antimicrobial Resistance Pattern of ESBL-PE Isolates Among Hospitalized Patients in Arba Minch General Hospital, 2019

Bacteria	Antibiotics								
	TE	AK	CIP	CN	TOB	SXT	C	FOX	AZT
<i>E. coli</i> (N=62)	93.5	6.5	72.6	30.6	27.4	93.5	66.7	9.7	1.6
<i>K. pneumoniae</i> (N=60)	91.7	3.4	53.4	36.6	35.0	96.7	73.3	16.7	8.4
<i>E. aerogenes</i> (N=6)	67.7	0	66.7	33.3	16.7	100	66.6	16.7	0
<i>Citrobacter</i> spp. (N=12)	91.7	0	50.0	58.3	41.7	83.4	75.0	16.7	0
Total (N=140)	91.1	4.79	68.49	35.62	35.51	93.84	69.18	14.38	5.12

Abbreviations: TE, tetracycline; AK, amikacine; CIP, ciprofloxacin; CN, gentamycin; TOB, tobramycin; SXT, trimethoprim-sulfamethoxazole; C, chloramphenicol; FOX, ceftiofloxime; AZT, aztreonam.

Table 4 Multidrug Resistance Pattern of ESBL-PE Isolates Among Hospitalized Patients in Arba Minch General Hospital, 2019

Bacteria	Multiple Antibiotics Resistance						Total
	R0	R1	R2	R3	R4	R5 and Above	
<i>E. coli</i>	1	7	14	14	17	9	62
<i>K. pneumoniae</i>	2	3	8	20	15	12	60
<i>E. aerogenes</i>	0	2	1	2	0	1	6
<i>Citrobacter</i>	0	2	1	5	2	2	12
Species							
Total isolates	3	14	24	41	34	24	140

Abbreviations: R0, bacterial isolates sensitive to all antibiotics; R1, resistant against one class of antibiotics; R2, resistant against two classes; R3, resistant against three classes; R4, resistant against four classes; R5 and above, resistant against five or more classes of antibiotics.

In the present study, the colonization rate of carbapenemase-producing *K. pneumoniae* was 6(1.43%) 95% CI (0.83–3.54%). This is in accordance with the results of two similar studies reported in Ethiopia (2%)¹⁹ and in Morocco (1.8%).³² However, the study conducted in Egypt and Cambodia reported higher rates of colonization with carbapenemase such as 5% and 7.5%, respectively.^{30,31}

In the present study, the gastrointestinal colonization rate with ESBL-PE has statistical correlation with various factors such as prolonged hospitalization, poor handwashing habits, presence of chronic diseases and habit of eating raw foods. Similar studies conducted in the USA, Israel, and Ecuador had shown that prolonged hospital stays are significantly associated with ESBL carriage rate.^{25,27,28} These factors could contribute to the transmission and/or dissemination of resistant bacteria among patients in the hospital setup. Probably they may also contribute to the onset of outbreaks both in hospital and in the community. On the other hand, the study conducted in Turkey showed that catheterization and surgical procedures were associated with the colonization of ESBL-PE in the gastrointestinal tract.²⁴ Furthermore, the

study done in Ethiopia also showed a greater extent of ESBL colonization within lower age group, specifically neonates.¹⁹

Administration of oral antibiotics after admission also showed a statistically significant association with gastrointestinal colonization rate by ESBL-PE. This is in concordance with a study conducted related to antibiotic treatment in Israel.²⁵ Conversely, studies done in the USA revealed previous exposure to antibiotics and it showed a statistically significant association with colonization rate.^{27,33}

In the present study, ESBL-PE showed higher resistance to commonly used antibiotics. This was in consonance with the findings obtained from studies done in India²³ and Ethiopia.¹⁹ Besides, the results of our study revealed lower resistance against ceftiofloxime (14.38%), aztreonam (5.16%) and amikacin (4.79%). Another study performed in Ethiopia showed higher resistance rates against aztreonam, and ceftiofloxime such as 97% and 28%, respectively. Moreover, ESBL-producing *E. coli* and *K. pneumoniae* showed a higher level of resistance against tetracycline, cotrimoxazole, chloramphenicol, and ciprofloxacin. These observations are well-nigh similar to several studies conducted in Ethiopia¹⁹ and other locales of the world.^{23,24,27,29,30} The higher level of resistance showed by the isolates may be due to the overuse or irrational use of antibiotics. This finally makes the treatment of infection caused by ESBL-producing bacteria a very challenging task.

The overall prevalence of MDR ESBL-producing isolates that colonized the gastrointestinal tract was 99 (70.71%). This result is comparable to the findings of studies done in Ethiopia¹⁹ and Sweden 68%.⁶ However, this value is higher compared to the data obtained from a study reported in Egypt 47.83%.³⁰ However, it was much lower than the overall prevalence reported from in Tanzania 94%.³ Most of the ESBL-PE can display co-resistance to non-beta-lactam antibiotics. Such variations in the drug resistance pattern may be

attributed to the difference in rational use of antibiotics in clinical setups.

Conclusion

The overall colonization rate of the gastrointestinal tract by ESBL-PE among hospitalized patients at Arba Minch General Hospital was higher (34.7%). The predominant isolates of ESBL-producing bacteria were *E. coli* and *K. pneumoniae*. ESBL-producing isolates showed higher degree of resistance against the commonly used antibiotics such as tetracycline, cotrimoxazole, ciprofloxacin, and chloramphenicol which need a great attention from the concerned bodies at different levels. The carriage rate of ESBL-PE among hospitalized patients is increasing, so that it needs a nationwide survey with a large population size. Besides, awareness should be created in hospitals on how such drug-resistant bacteria develop the mechanism of resistance, spread and also the hospital should work on infection prevention strategies, especially on hospital-acquired drug-resistant bacteria. Finally, further in-depth studies pertaining to the molecular characterization of ESBL strains are warranted.

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Author Contributions

All authors have contributed in designing, data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors declared that they have no conflicts of interest in this work.

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