Heliyon 9 (2023) e20072

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Carriage of β-lactamase and carbapenemase-producing *Enterobacteriaceae* in hospitalized patients at debre tabor comprehensive specialized hospital

Teklehaimanot Kiros [a,*], Debaka Belete [c], Tesfaye Andualem [a], Lemma Workineh [a], Mekdes Tilahun [a], Tahir Eyayu [a], Birhanu Getie [a], Tegenaw Tiruneh [a], Saymon Kiflom [d], Shewaneh Damtie [a], Tsehaynesh Gebreyesus [b]

[a] *Department of Medical Laboratory Sciences, College of Health Sciences and School of Medicine, Debre Tabor University, Debre Tabor, Ethiopia*
[b] *Amhara Public Health Institute, Bahrdar, Ethiopia*
[c] *Department of Medical Microbiology, School of Biomedical and Laboratory Sciences, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia*
[d] *College of Natural and Computational Sciences, Mekelle University, Mekelle, Ethiopia*

ARTICLE INFO

Keywords:
Antimicrobial resistance
Enterobacteriaceae
Hospitalization
Stool culture
Determinants
Ethiopia

ABSTRACT

Background: Antimicrobial resistance has remained global public health threat. Carriage with drug-resistant bacterial pathogens, particularly beta-lactamase and carbapenemase-producing *Enterobacteriaceae* is among the most concerning. The purpose of this study was to look into the magnitude, antimicrobial resistance patterns, and associated risk factors among hospitalized patients.

Methods: A facility-based cross-sectional study was conducted on 383 hospitalized patients at Debre Tabor Comprehensive Specialized Hospital between September 2022 and May 2023. A pre-tested structured questionnaire was used to collect sociodemographic and clinical data. The data on the etiologic agent was collected using standard bacteriological techniques. Briefly, stool specimens were collected aseptically into sterile, leak-proof stool cups. The stool sample was inoculated onto MacConkey agar and incubated aerobically at 37 °C for 24 h. The species isolation and antimicrobial resistance patterns were then performed adhering to bacteriological procedures. In the analysis, a p-value of <0.05 was considered statistically significant.

Results: There were 383 study participants, and men made up the majority (55.6%). The study participants' mean age was 33 ± 18 years. Three hundred and seventy-seven (88%) of the study's participants had no previous history of antibiotic use. There were 102 (26.6%) and 21 (5.5%) cases of gastrointestinal carriage caused by *Enterobacteriaceae* that produce beta-lactamase and carbapenemase, respectively. In total, 175 isolates of *Enterobacteriaceae* were detected. *E. coli* (n = 89) and *K. pneumoniae* (n = 51) were the most frequently recovered. In this study, 46 (79.3%) and 8 (13.8%) isolates of *E. coli* that produce beta-lactamase were resistant to ampicillin and amoxicillin/clavulanic acid, respectively. Furthermore, participants who had previously used antibiotics experienced a two-fold increase in exposure to gastrointestinal tract carriage by carbapenemase-producing *Enterobacteriaceae* [AOR, 95% CI (2.01, 1.06–2.98), p = 0.001].

Conclusions: The emergence of drug-resistant pathogens is a growing concern. An increase in the prevalence of drug-resistant infections in hospitalized patients is warranting further investigation.

* Corresponding author.
E-mail address: tkt0932@gmail.com (T. Kiros).

https://doi.org/10.1016/j.heliyon.2023.e20072
Received 23 August 2022; Received in revised form 10 September 2023; Accepted 11 September 2023
Available online 12 September 2023

1. Introduction

Antimicrobial resistance has remained a major public health concern worldwide. Because of the serious consequences for human and animal health, robust intervention policies, such as antimicrobial stewardship programs, national surveillance, and global collaboration programs are essential for mitigating antimicrobial resistance dynamics and informing appropriate containment strategies to health experts across the ecosystem [1].

Drug-resistant bacterial pathogens have become a major global health threat, with β-lactamase and carbapenemase-producing *Enterobacteriaceae* being among the most concerning. These bacteria are able to produce enzymes that break down antibiotics, rendering them ineffective and making infections difficult to treat. In addition, the lack of development of new antibiotics has exacerbated the problem. Without effective antibiotics, common infections could become life-threatening, and routine medical procedures such as surgeries and chemotherapy could become too risky to perform. Therefore, it is important to promote the responsible use of antibiotics and invest in research for new treatments [2–4].

The World Health Organization (WHO) has issued a warning about the importance of global cooperation in combating antimicrobial resistance and establishing a priority for global health action plans across all world member states. Unless the development of a powerful drug to promote careful management of various infections caused by a multidrug-resistant pathogen is secured, many pathogens are steadily developing a robust defense strategy to ensure their survival. WHO published a list of antibiotic-resistant bacteria with the goal of developing and researching new antibiotics in 2017. The report classified bacterial drug resistance as critical, high, or medium based on drug resistance, fatality rate, global distribution, socioeconomic burden, and availability of preventive and therapeutic modalities. *Acinetobacter baumannii* (*A. baumannii*), *Pseudomonas aeruginosa* (*P. aeruginosa*), and the diverse *Enterobacteriaceae* family are all members of the critical-priority group [5,6].

β-lactamase, plasmid-mediated AmpC β-lactamase, and carbapenemase-producing *Enterobacteriaceae* are bacteria that have developed resistance to commonly used antibiotics such as penicillin and cephalosporins. These bacteria pose a significant threat to public health as they can cause severe infections that are difficult to treat. The emergence of these resistant strains is a result of the overuse and misuse of antibiotics, leading to the selection of resistant strains. It is crucial to implement measures to prevent the spread of these bacteria. This includes proper infection control practices in healthcare settings, appropriate use of antibiotics, and increased surveillance and monitoring of antibiotic resistance. Additionally, research into new antibiotics and alternative treatments is necessary to combat the growing threat of carbapenemase-producing *Enterobacteriaceae* [7,8].

Many of the *Enterobacteriaceae* are able to produce extended-spectrum beta-lactamase (ESBL) enzymes, which hydrolyze the majority of beta-lactams. They are also encoded by a mobile genetic element, such as transposons and plasmids, which facilitates conferring resistance to additional antimicrobial agents. As their prevalence keeps increasing, ESBL-producing *Enterobacteriaceae* (ESBL-PE) is considered a serious public health threat [9].

The most crucial enabler of beta-lactam resistance among many Gram-negative bacteria is known to be ESBL synthesis. The group of bacterial enzymes known as beta-lactamases hydrolyze beta -lactam antibiotics, rendering them ineffective for treating nosocomial and community-acquired infections such as urinary tract infections, bloodstream infections, respiratory tract infections, wound infections, and gastrointestinal tract infections. As a result, the post-antibiotic period is accompanied by antibiotic resistance to beta-lactam and carbapenems. This makes these organisms the most important contributor to therapy failure and rising medical costs globally [7,10].

The main structure or the functional properties of the enzymes are used to categorize beta-lactamases. The protein sequence provides the simplest method of categorization. Beta-lactamases are divided into four molecular classes (A- D) primarily based on distinctive and conserved amino acid patterns. A functional classification, as opposed to the structural approach, offers a better chance to link these diverse groupings of enzymes to clinical relevance, such as by offering selected resistance to different classes of antibiotics [11–14].

The swift spread of *Enterobacteriaceae* that produce carbapenemase (CP-E) has continued to be the biggest threat to global health, with serious clinical and socioeconomic repercussions [15]. It has outgrown the capacity of health care systems and reached pandemic proportions in some places, such as the African continent. Although the distribution of resistance genes varies among various clinical isolates, *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*)- and other carbapenemase-producing organisms resistance genes have a greater propensity to clonally propagate. Due to this, *K. pneumoniae* strains which produce carbapenemase, have been identified as having a high degree of transmission potential between clinical and community health care settings [16–19]. Furthermore, the "AmpC" genes found on the chromosomes of *Enterobacteriaceae* species including *Citrobacter freundii*, *Enterobacter cloacae*, and *Aeromonas* species are the source of plasmid-mediated AmpC beta-lactamase producing *Enterobacteriaceae* (PABL). They have become the major concerns in health care settings due to their ability to rapidly spreading antibiotic resistant genes. This leads to an increased in the use of last resort antibiotics which further fuels the development of drug resistance. This heightens the urgent need for new antibiotics and alternative treatment to combat antibiotic resistance [20]. Compared to ESB, PABLs have a wider range of resistance [21–23]. Similar to this, hospitalized patients admitted to various wards are mostly documented to carry and acquire ESBL-PE, PABL, and CP-E infections [24–26].

The intestinal carriage of antibiotic-resistant bacteria in hospitalized patients is a major contributor to the spread of infections. Studying carriage patterns can help identify high-risk patients and implement targeted interventions to prevent cross-transmission. This can ultimately lead to better patient outcomes and reduce the burden of multidrug resistance in healthcare settings [2,27]. To the best of our knowledge, very little is known about the prevalence and risk factors for ESBL-PE and CP-E among hospitalized patients, even in the absence of published data on PABL in Ethiopia. Early precise identification of fecal carriers is essential for the development

of a robust mitigation strategy and the prevention of nosocomial outbreaks caused by such bacteria. Moreover, understanding the current epidemiological picture of the isolate will enable to develop clinical guidelines and infection prevention measures. Furthermore, to de-escalate the disastrous effect of superbugs, rapid surveillance and accurate identification are therefore necessary.

2. Methods and materials

2.1. Study design, area and period

A hospital-based prospective cross-sectional study was carried out among hospitalized patients between September 2022 and May 2023 at Debre Tabor Comprehensive Specialized Hospital, Northwest, Ethiopia. The latitude and longitude of this historic town are 11°51′N 38°1′E, and its elevation is 2706 m above sea level. Only one public hospital, three health centers, six health posts, and four private medical facilities are located in the Town. The hospital is currently offering an extensive service to inpatients and outpatients in average for 8333 patients per week (emergency, medical, surgical, obstetric/gynecologic, orthopedic, pediatric wards, emergency triage assessment and treatment and intensive care units).

2.2. Source population

All patients who were admitted to various wards and units comprised the source population. As the study population, all patients admitted to various wards including the intensive care unit, pediatric, gynecologic, medical, and surgical wards for ≥48 h.

2.3. Eligibility criteria

All hospitalized patients of any age group, suspected of gastrointestinal complaints, and admitted for ≥48 h when the data was being collected were included. Patients who underwent same-day therapy, surgery, or were seen in the outpatient department during the survey were excluded. Stool samples collected twice from the same subject were rejected. Additionally, individuals who were unable to give their consent and who had received antibiotic therapy in the previous few weeks prior to the data collecting period were removed from the study. Furthermore, registered participants with incomplete medical data, such as a past history of antibiotic use were disqualified from the study.

2.4. Sample size calculation

The sample size for this study was determined using a formula for the estimation of a single population proportion as given below. The prevalence, p = 34.7% which was taken from a previously done study [28] by using a 95% confidence interval, Zα/2 = 1.96, the margin of error 0.05 then, the required sample size for the study using a single population proportion formula was determined as denoted below:

$$n = (Z\,\alpha/2)^2\,P\,(1-P)\,/\,d2$$

where,

n = the required sample size.

Z = standard normal distribution value at 95% confidence level of a/2 = 1.96.

P = proportion of fecal carriage among hospitalized patients = 0.347

d = margin of error = 5%

By substituting the above values, it gives

n = $(1.96)^2$0.347 (1–0.347)/0.05^2 = 348.2. By adding a 10% non-response rate, n ~383. Hence**,** the total sample size required for this study was 383 admitted patients. In this study, the convenient sampling method was employed to select the study population.

2.5. Study variables

The dependent variables include isolates of *Enterobacteriaceae,* the magnitude of ESBL-PE, PABL, CP-E, and their antibiogram patterns; whereas socio-demographic variables, and clinically related characteristics were considered independent study variables.

2.6. Operational definitions

Fecal carriage: Bacterial colonization of the gastrointestinal tract (GIT) caused by ESBL-PE, PABL and CP-E with their detection in feces [7,25,28,30–34].

Sensitive (S): Bacterial isolates are inhibited by the usually achievable concentration of antimicrobial agents [35].

Resistant (R): Bacterial isolates uninhabited by the usually achievable concentration of the agent with normal dosage [35].

Extended-spectrum beta-lactamase-producing *Enterobacteriaceae* (ESBL-PE): The bacteria that produce the enzyme that confers resistance to most β-lactam antibiotics, but is inhibited by β-lactamase inhibitor [35].

Carbapenemase-producing *Enterobacteriaceae* (CP-E): The bacteria that produce enzymes that can hydrolyze carbapenems or

are non-susceptible to meropenem and ertapenem, and showed positive results when confirmed by phenotypic test [35].

AmpC β-lactamases producing *Enterobacteriaceae* (PABL): The bacteria that produce the enzyme that is non-susceptible to cephalosporins, cefoxitin, and also not inhibited by β-lactamase inhibitors [35].

3. Data collection methods

All study participants, including the care givers, received written information and/or orientations prior to data collection. This would allow participants to decide whether to continue with the study or discontinue it entirely after being informed of its aim. Convenient sampling was used on the volunteers who were selected for the study. The authors created pre-designed and pre-tested questions before the actual data collection in order to guarantee the questionnaire's completeness, clarity, and simplicity. Based on the study's goal, volunteers were chosen at random to participate at the study. After that, each study participant was given a modified version of a carefully created questionnaire to complete in order to evaluate socio-demographic characteristics and clinical related factors (**Supplementary file-1**). Moreover, using standard bacteriological testing, the etiologic agents for gastrointestinal carriage caused by isolates of *Enterobacteriaceae* capable of expressing ESBL-PE, PABL, and CP-E were performed.

3.1. Sample collection

Three hundred and eighty-three specimens were obtained from hospitalized patients by aseptically collecting one sample of stool from each study participant. Stool samples were collected aseptically in accordance with standard operating procedures after participants gave their agreement to participate in the study. Collected stool and rectal swabs for the research of gastrointestinal pathogens was transported using Cary-Blair transport medium when necessary.

3.2. Stool culture

Stool samples were collected into a clean, leak-proof container, then suspended in 5 ml of 0.9% normal saline and vortexed for at least 30 s. A loop full of an aliquot of the fecal sample was plated onto MacConkey agar media using standard bacteriological procedure. Finally, cultures were incubated for 24 h in an aerobic environment at 37 °C [28,29,36].

All positive cultures were identified to species level by colony characteristics such as morphology for size, consistency, shape, and pattern of biochemical profiles using standard microbiological procedures. For the identification of *Enterobacteriaceae*, a battery of biochemical tests was used, including indole production, gas production, lactose fermentation, citrate utilization, glucose utilization, motility test, urease test, bile solubility, lysine utilization in lysine decarboxylase, and oxidase test [25,26,32].

The screening for ESBL producing isolates was done using standard Kirby-Bauer disk diffusion method with cefotaxime, ceftriaxone, and ceftazidime. Freshly grown pure colonies on MacConkey agar media were suspended in normal saline, and the suspension's turbidity was set to 0.5 McFarland's standard. A sterile cotton swab was used to inoculate the suspension onto Mueller-Hinton agar (MHA). The above three antibiotic discs are then placed 25 mm center to center and incubated aerobically at 37 °C for 24 h. Finally, isolates with decreased susceptibility to cefotaxime (zone diameter of 27 mm), ceftazidime (zone diameter of 22 mm), and ceftriaxone

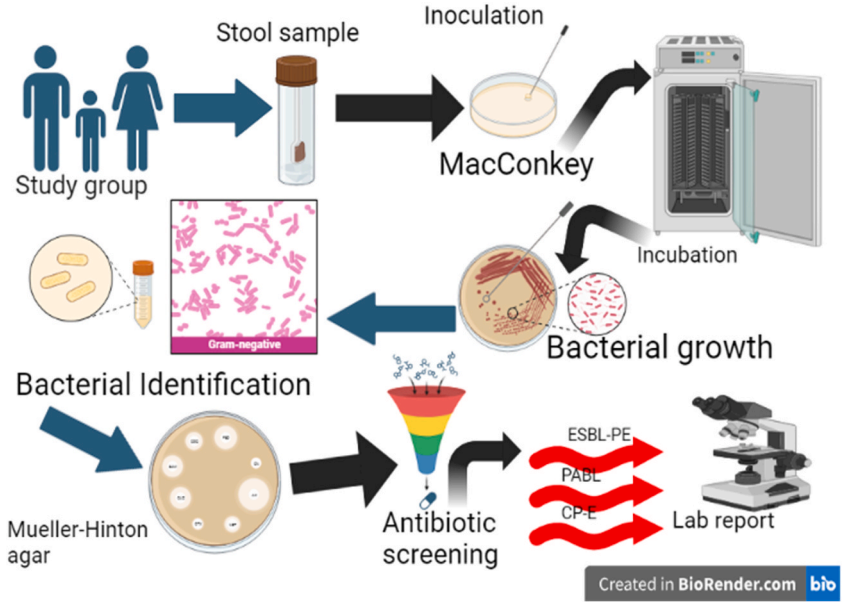

Fig. 1. Schematic diagram depicting the lab workflow of the study.

(zone diameter of 25 mm) around the disks were suspected of producing ESBLs and subjected to further testing. Similarly, all isolates that grew in cefotaxime and/or ceftazidime containing media were tested for PABL activity using cefoxitin discs. Isolates with low susceptibility to cefoxitin (zone diameter of 18 mm) were considered for PABL production [35,37]. CP-E, on the other hand, was screened using meropenem disks. In this regard, if a colony suspension of isolated bacteria is inoculated onto MHA with meropenem disks after 24-h incubation at 37 °C, if the zone of inhibition is 19 mm, and the isolates are considered CP-E [35,37,38]. The combination disc test was used to confirm ESBL-producing isolates according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [35].

A susceptibility disc containing amoxicillin-clavulanate was placed in the center of an MHA, with cefotaxime and/ceftazidime discs placed 15 mm from the amoxicillin-clavulanate disc, and incubated at 37 °C for 24 h. Then, any improvement in the inhibition zone of any of these discs on the side facing the amoxicillin-clavulanate disc was interpreted as ESBL positive compared to the antibiotics alone was considered positive for ESBL production [25,26]. Similarly, PABL activity was confirmed using the cefoxitin-cloxacillin combined disk method, as previously described [39,40]. The test is based on cloxacillin's inhibitory effect on AmpC beta-lactamase. Antibiotic disks containing 30 μg cefoxitin or 30 μg cefoxitin plus 200 μg cloxacillin were used. A difference of 5 mm between the cefoxitin-cloxacillin inhibition zones and the cefoxitin alone zones was interpreted as positive PABL production [26,40]. Furthermore, the modified carbapenem inactivation method was used to confirm isolates of CP-E accordance with CLSI guidelines [35]. The entire laboratory algorism for this study is also summarized in **Figure-1**.

3.3. Antibiotic susceptibility testing (AST)

According to CLSI guidelines, the AST was performed on MHA using the Kirby-Bauer disk diffusion technique [35]. In brief, a loop full of bacterial colony was taken from a pure culture and transferred to a tube containing 4–5 ml of 0.9% normal saline and gently mixed until it formed a homogeneous suspension. To standardize the inoculum size, the suspension's turbidity was adjusted to the density of a McFarland 0.5 standard. After dipping a sterile cotton swab into the suspension, the excess was removed by gently rotating the swab against the surface of the tube. The bacteria were then distributed evenly across the entire surface of MHA using the swab [28,35–37,41].

The following antibiotics were used; ceftriaxone (CTR,30 μg), cefotaxime (CTX,30 μg), ceftazidime (CAZ,30 μg), cefoxitin (FOX,30 μg), amoxicillin/clavulanic acid (AMX, 20/10 μg), ampicillin (AMP,10 μg), ciprofloxacin (CIP,5 μg), chloramphenicol (CHL,30 μg), aztreonam (AZT,15 μg), gentamicin (GM,10 μg)), tetracycline (TET,30 μg), trimethoprim-sulfamethoxazole (STX,1.25/23.75 μg), cefepime (CPM,30 μg) and meropenem (MEM,10 μg). In the meantime, the diameters of the zone of inhibition around the discs were measured using a ruler and the isolates are classified as sensitive, intermediate, and resistant according to the 2019 CLSI guideline [35].

3.4. Data quality assurance

Internal quality control (QC) measures for questionnaires, specimen collection, and the final laboratory work-up were implemented through a standard operating procedure to ensure the reliability of the study findings. All materials, equipment, reagents, and procedures were properly regulated. Before collecting data, a structured questionnaire was developed to assess socio-demographic characteristics, clinical data, and associated risk factors. Before the actual data collection process, about 5% of the questionnaire was pre-tested among randomly selected volunteer participants. To maintain consistency, the questionnaire was first prepared in the local language (Amharic), then translated to English and then back to Amharic. Furthermore, the study's progress was monitored on a daily basis by assigned supervisors.

The culture media was prepared in accordance with the manufacturer's recommendations. Above all, the sterility of culture media was tested by incubating 5% of the batch/prepared media overnight at 37 °C to look for potential contamination. To ensure testing performance of the potency of antimicrobial discs, standard reference bacteria strains such as *K. pneumoniae* (ATCC 700603) and *E. coli* (ATCC-25922) were tested weekly as controls on biochemical tests and agar plates including MHA with antimicrobial discs. Furthermore, to test ESBL production, *K. pneumoniae* (ATCC 700603) and *E. coli* (ATCC-25922) were used as positive and negative controls, respectively, whereas *K. pneumoniae* (ATCC BAA1705) and (ATCC BAA 1706) were used as positive and negative quality controls, respectively for carbapenemase production.

3.5. Data processing and statistical analysis

All data were entered into epi info manager version7.2.0.1 and analyzed taking care of completeness, consistency, and coding using SPSS version 20. The statistical analysis for the descriptive statistics was performed. For associated risk assessments of independent variables with the outcomes, odds ratios (OR) with 95% confidence intervals (95% CI) were calculated. All variables with a $p < 0.25$ in the bivariate logistic analysis were included in the multivariate logistic regression model for risk factor analysis using adjusted odds ratio (AOR) and 95%confidence intervals. In the final model, a p-value <0.05 was taken as a statistically significant association. Finally, the findings of the study we presented using texts and tables.

3.5.1. Ethical clearance

Debre Tabor University, College of Health Sciences, Research and Ethical Review Committee approved this study (letter reference number: CHS/3579/2021). To protect individuals' privacy, all results were kept confidential, and the study process was carried out

using coding. Finally, study participants who had vulnerability to fecal carriage were linked to their physicians in order to receive appropriate treatment.

4. Results

4.1. Socio-demographic characteristics

Of the total of 383 study participants included in this study, the majority [213 (55.6%)] were male participants. The age category of the study participants has shown that about 130 (34%) were in the age group of 36–50 years followed by the 21–35 years age group (23.5%). In this study, the mean age of the study subjects was 33 ± 18 years. Regarding marital status, the majority [230 (60%)] were married (Table-1).

5. Clinical characteristics

Semi-structured questionnaires were used to collect the hospitalized patients' clinical characteristics. In total, 337 (88%) and 157 (41%) of the study population had no prior history of antibiotic use and gastrointestinal tract symptom, respectively (**Table-2**).

5.1. Prevalence of bacterial carriage

Using screening and confirmatory tests based on standard bacteriological techniques, the gastrointestinal colonization caused by ESBL-PE, PABL, and CP-E among hospitalized subjects was identified. As a result, 102 (26.6%), 21 (5.5%), and 52 (13.6%) of the participants had positive for ESBL-PE, PABL, and CP-E, respectively.

In this study, 383 stool samples were screened for the fecal carriage of gastrointestinal colonization. A total of 175 isolates of *Enterobacteriaceae* were found. *E. coli* (n = 89) and *K. pneumoniae* (n = 51) were the two *Enterobacteriaceae* species that were most frequently recovered from hospitalized patients who were thought to have colonized their gastrointestinal tracts. In addition, 58 (56.9%) of the 102 ESBL-PE infected people had ESBL-producing *E. coli* colonization (**Table-3**). *Citrobacter freundii*, however, was only found in small amounts [1 (0.98%)]. There were 21 cases of PABL, and it was reported that 14 (66.7%), 3 (14.3%), and 4 (19%) participants had colonized with PABL-producing *E. coli*, *K. pneumoniae*, and *K. oxytoca*, respectively.

6. Antibiogram profile

In this study, five species of *Enterobacteriaceae* were found from hospitalized patients. These isolates' antibiogram profiles and enzyme production were examined in comparison to fourteen antibacterial compounds from various anti-infective agent classes. The majority of the agents are aminoglycosides (gentamicin), beta-lactam combination group (amoxicillin/clavulanic acid, ampicillin), cephalosporins of the second generation of extended-spectrum (cefoxitin), third generation of cephalosporins (ceftriaxone, cefotaxime, and ceftazidime), fourth generation of cephalosporins (cefepime), monobactam. According to the antibacterial resistance pattern for

Table 1
Sociodemographic characteristics of hospitalized patients at Debre Tabor Comprehensives specialized Hospital, Northwest Ethiopia.

Characteristics	Group	Frequency (n = 383)	Percentage (%)
Gender	Male	213	55.6
	Female	170	44.4
Age (year)	≤5	70	18.3
	6–20	66	17.2
	21–35	90	23.5
	36–50	130	34
	≥51	27	7
Educational status	No formal education	70	18.3
	Primary (1–8 grade)	74	19.3
	Secondary (9-12)	180	47
	Tertiary (college and above)	59	15.4
Marital status	Single	58	15
	Married	230	60
	Divorced	67	18
	Widow	28	7
Occupational status	Civil servant	53	13.8
	Merchant	83	21.7
	Student	92	24
	Farmer	55	14.4
	Others[a]	100	26.1
Residence	Urban	256	66.8
	Rural	127	33.2

[a] Includes self-employed, housewife, daily labourer, jobless.

Table 2
Clinical characteristics of study participants who were admitted to different wards in Debre Tabor Comprehensives specialized Hospital.

Characteristics	Category	Frequency	Percentage (%)
Gastrointestinal symptoms	Yes	157	41
	No	226	59
Previous antibiotic history	Yes	46	12
	No	337	88
Prolonged hospitalization	Yes	27	7
	No	356	93
Previous hospitalization	Yes	82	21
	No	301	79
Admission ward	Medical	110	28.7
	Surgical	78	20.4
	Gynecology	70	18.3
	Pediatrics	55	14.3
	Intensive care unit	58	15
	Others	16	4.2
Underlying comorbidity	Yes	18	4.7
	No	365	95.3
Frequent hand-washing habit	Yes	307	80.2
	No	76	19.8

Table 3
Distribution of bacterial isolates among hospitalized subjects.

Strains	No of isolates (n = 175)	Proportions of *Enterobacteriaceae*					
		Total ESBL-PE producers (n = 102)		Total PABL producers (n = 21)		Total CP-E producers (n = 52)	
		ESBL Positive n (%)	ESBL Negative n (%)	PABL Positive n (%)	PABL Negative n (%)	CP-E Positive n (%)	CR-E Negative n (%)
E. coli	89	58 (65.1)	31 (34.9)	14 (66.7)	7 (33.3)	31 (34.8)	58 (65.2)
K. pneumoniae	51	34 (66.7)	17 (33.3)	3 (14.3)	18 (85.7)	16 (31.4)	35 (68.6)
E. cloacae	8	3 (37.5)	5 (62.5)	–	–	1 (12.5)	7 (87.5)
K. oxytoca	19	6 (31.6)	13 (68.4)	4 (19.1)	17 (80.9)	2 (10.5)	17 (89.5)
C. freundii	8	1 (12.5)	7 (87.5)	–	–	2 (25)	6 (75)

ESBL-producing *E. coli* (n = 58), every isolate was completely resistant to trimethoprim-sulfamethoxazole, tetracycline, and chloramphenicol. Similar to this, 52 (89.7%) and 53 (91.4%) of the ESBL-*E. coli* isolates were resistant to the tested fluoroquinolone (ciprofloxacin) and aminoglycoside (gentamicin). Ampicillin and amoxicillin/clavulanic that are known to inhibit the synthesis of cell wall were found to be effective against 46 (79.3%) and 50 (86.2%) ESBL-producing isolates of *E. coli*, respectively. However, of the 34 isolates of ESBL-*K. pneumoniae*, 24 (70.6%) and 15 (44.1%) were resistant to amoxicillin/clavulanic acid and ampicillin, respectively. Given that ESBL-*C. freundii* (n = 1), *K. oxytoca* (n = 6), and *E. cloacae* (n = 3) were 1(100%), 6(100%), and 2 (66.7%) susceptible for cefoxitin, respectively. Unfortunately, third-generation cephalosporins like cefotaxime, ceftriaxone, and ceftazidime have shown much higher resistance in both ESBL-producing isolates of *K. pneumoniae* and *E. coli*. Furthermore, 96 (94.1%) of all ESBL-PE isolates have demonstrated meropenem resistance. The monobactam group (aztreonam), the fourth generation of extended-spectrum cephalosporins (cefepime), and the carbapenems (meropenem) were generally the antibacterial agents of choice for treating bacterial colonization (**Table-4**). According to the current findings, *C. freundii* (n = 2) and *E. cloacae* (n = 1) were completely susceptible to the monobactam group (aztreonam) while *K. oxytoca* (n = 2) was completely resistant to aztreonam (**Table-5**). *E. cloacae* (n = 1) was completely resistant to meropenem, but the majority of carbapenemase-producing *E. coli* [23 (74.2%)] and *K. pneumoniae* [(10 (62.5%)] were susceptible to it. Similar to this, all CP-E isolates have demonstrated complete resistance to both tetracycline and chloramphenicol. *C. freundii* and *E. cloacae* were not PABL producers. All *E. coli* isolates tested positive for cefoxitin, ceftriaxone, and cefepime. Against all PABL isolates, the second-generation cephalosporines (cefoxitin) has demonstrated 100% sensitivity (**Table-6**).

6.1. Risk factor analysis

All of the variables were analyzed for this study. To determine the risk factors connected to fecal carriage among hospitalized patients, the bivariate logistic regression analysis was performed. Bivariate logistic regression analysis determined which variables were statistically significant, and these variables were then integrated into the multivariate logistic regression model.

In the binary logistic analysis (Table 7), study groups with a history of antibiotic use were statistically associated with ESBL-PE, PABL, and CP-E carriage (p-values of 0.01, 0.03, and 0.05, respectively). The multivariate logistic regression model was fitted and variables with a p-value 0.05 or less in the bivariate logistic regression analysis were included to determine the risk factors. In the multivariate analysis (**Table-8**), having a prior history of antibiotic use increases the likelihood of exposure to CP-E gastrointestinal tract colonization by twofold [AOR, 95% CI (2.01, 1.06–2.98), p = 0.001].

Table-4
Antimicrobial resistance patterns of ESBL-producing isolates of *Enterobacteriaceae* among hospitalized patients at Debre Tabor Comprehensives specialized Hospital, Northwest Ethiopia.

Isolates (n = 102)	P	Antimicrobial disks tested against the ESBL-producing isolates of *Enterobacteriaceae* (n = 102)													
		CTR n (%)	CTX n (%)	CAZ n (%)	FOX n (%)	AMX n (%)	AMP n (%)	CIP n (%)	CHL n (%)	AZT n (%)	GM n (%)	TET n (%)	SXT n (%)	CPM n (%)	MEM n (%)
E. coli (n = 58)	S	12 (20.7)	9 (15.5)	8 (13.8)	38 (65.5)	12 (20.7)	50 (86.2)	5 (8.6)	0	19 (32.8)	6 (10.3)	0	0	53 (91.4)	54 (93.1)
	R	46 (79.3)	49 (84.5)	50 (86.2)	20 (34.5)	46 (79.3)	8 (13.8)	53 (91.4)	58 (100)	39 (67.2)	52 (89.7)	58 (100)	58 (100)	5 (8.6)	4 (6.9)
K. pneumoniae (n = 34)	S	0	21 (61.8)	3 (8.8)	27 (79.4)	10 (29.4)	19 (55.9)	0	0	34 (100)	4 (11.8)	3 (8.8)	0	21 (61.8)	34 (100)
	R	34 (100)	13 (38.2)	31 (91.2)	7 (20.6)	24 (70.6)	15 (44.1)	34 (100)	34 (100)	0	30 (88.2)	31 (91.2)	34 (100)	13 (38.2)	0
C. freundii (n = 1)	S	1 (100)	1 (100)	1 (100)	1 (100)	0	1 (100)	0	0	1 (100)	1 (100)	0	0	1 (100)	1 (100)
	R	0	0	0	0	1 (100)	0	1 (100)	1 (100)	0	0	1 (100)	1 (100)	0	0
E. cloacae (n = 3)	S	3 (100)	2 (66.7)	0	2 (66.7)	2 (66.7)	2 (66.7)	1 (33.3)	0	3 (100)	0	1 (33.3)	0	2 (66.7)	3 (100)
	R	0	1 (33.3)	3 (100)	1 (33.3)	1 (33.3)	1 (33.3)	2 (66.7)	3 (100)	0	3 (100)	2 (66.7)	3 (100)	1 (33.3)	0
K. oxytoca (n = 6)	S	3 (50)	1 (16.7)	2 (33.3)	6 (100)	0	4 (66.7)	0	1 (16.7)	0	0	1 (16.7)	1 (16.7)	3 (50)	4 (66.7)
	R	3 (50)	5 (83.3)	4 (66.7)	0	6 (100)	2 (33.3)	6 (100)	5 (83.3)	2 (33.3)	6 (100)	5 (83.3)	5 (83.3)	3 (50)	2 (33.3)
Total n (%)	S	19 (18.6)	34 (33.3)	14 (13.7)	74 (72.5)	24 (23.5)	76 (74.5)	6 (5.9)	1 (1)	57 (55.9)	86 (84.3)	5 (4.9)	1 (1)	80 (78.4)	96 (94.1)
	R	83 (81.4)	68 (66.7)	88 (86.3)	28 (27.5)	78 (76.5)	26 (25.5)	96 (94.1)	101 (99)	45 (44.1)	16 (15.7)	97 (95.1)	101 (99)	22 (21.6)	6 (5.9)

P-pattern, S-Sensitive, R- Resistance, Ceftriaxone (CTR), Cefotaxime (CTX), Ceftazidime (CAZ), Cefoxitin (FOX), Amoxicillin/Clavulanic acid (AMX), Ampicillin (AMP), Ciprofloxacin (CIP), Chloramphenicol (CHL), Aztreonam (AZT), Gentamicin (GM)), Tetracycline (TET), Trimethoprim-Sulfamethoxazole (STX), Cefepime (CPM), and Meropenem (MEM).

Table-5
Antimicrobial Resistance patterns of carbapenemase-producing isolates of *Enterobacteriaceae* among hospitalized patients at Debre Tabor Comprehensives specialized Hospital, Northwest Ethiopia.

Isolates (n = 52)	P	Antimicrobial disks tested against the carbapenemase-producing isolates of *Enterobacteriaceae* (n = 52)													
		CTR n (%)	CTX n (%)	CAZ n (%)	FOX n (%)	AMX n (%)	AMP n (%)	CIP n (%)	CHL n (%)	AZT n (%)	GM n (%)	TET n (%)	SXT n (%)	CPM n (%)	MEM n (%)
E. coli (n = 31)	S	10 (32.3)	4 (12.9)	0	21 (76.7)	8 (25.8)	3 (9.7)	0	0	16 (51.6)	0	0	0	3 (9.7)	23 (74.2)
	R	21 (76.7)	27 (87.1)	31 (100)	10 (32.3)	23 (74.2)	28 (90.3)	31 (100)	31 (100)	15 (48.4)	31 (100)	31 (100)	31 (100)	28 (90.3)	8 (25.8)
K. pneumoniae (n = 16)	S	7 (43.8)	10 (62.5)	0	12 (75)	2 (12.5)	2 (12.5)	1 (6.3)	0	14 (87.5)	0	0	1 (6.3)	15 (93.8)	10 (62.5)
	R	9 (56.2)	6 (37.5)	16 (100)	4 (25)	14 (87.5)	14 (87.5)	15 (93.8)	16 (100)	2 (12.5)	16 (100)	16 (100)	15 (93.8)	1 (6.3)	6 (37.5)
C. freundii (n = 2)	S	2 (100)	2 (100)	2 (100)	2 (100)	1 (50)	1 (50)	0	0	2 (100)	1 (50)	0	0	2 (100)	2 (100)
	R	0	0	0	0	1 (50)	1 (50)	2 (100)	2 (100)	0	1 (50)	2 (100)	2 (100)	0	0
E. cloacae (n = 1)	S	1 (100)	0	0	0	0	0	1 (100)	0	1 (100)	1 (100)	0	0	1 (100)	1 (100)
	R	0	1 (100)	0	1 (100)	1 (100)	1 (100)	0	1 (100)	0	0	1 (100)	1 (100)	0	0
K. oxytoca (n = 2)	S	1 (50)	1 (50)	1 (100)	0	1 (50)	1 (50)	0	0	0	0	0	0	1 (50)	1 (50)
	R	1 (50)	1 (50)	0	2 (100)	1 (50)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	1 (50)	1 (50)
Total n (%)	S	21 (40.4)	17 (32.7)	3 (5.8)	35 (67.3)	12 (23.1)	7 (13.5)	2 (3.8)	0	33 (63.5)	2 (3.8)	0	1 (2)	22 (42.3)	37 (71.2)
	R	31 (59.6)	35 (67.3)	49 (94.2)	17 (32.7)	40 (76.9)	45 (86.5)	50 (96.2)	52 (100)	19 (36.5)	50 (96.2)	52 (100)	51 (98)	30 (57.7)	15 (28.8)

Table-6

Antimicrobial Resistance patterns of plasmid-mediated AmpC β-lactamase-producing isolates of *Enterobacteriaceae* recovered hospitalized patients at Debre Tabor Comprehensives specialized Hospital, Northwest Ethiopia.

Isolates (n = 21)	P	Antimicrobial disks tested against the plasmid-mediated AmpC β-lactamase-producing isolates of *Enterobacteriaceae* (n = 21)													
		CTR n (%)	CTX n (%)	CAZ n (%)	FOX n (%)	AMX n (%)	AMP n (%)	CIP n (%)	CHL n (%)	AZT n (%)	GM n (%)	TET n (%)	SXT n (%)	CPM n (%)	MEM n (%)
E. coli (n = 14)	S	14 (100)	4 (28.6)	0	14 (100)	7 (50)	1 (7.1)	0	0	7 (50)	0	0	0	14 (100)	7 (50)
	R	0	10 (71.4)	14 (100)	0	7 (50)	13 (92.9)	14 (100)	14 (100)	7 (50)	14 (100)	14 (100)	14 (100)	0	7 (50)
K. pneumoniae (n = 3)	S	0	1 (33.3)	0	3 (100)	1 (33.3)	1 (33.3)	0	1 (33.3)	0	1 (33.3)	1 (33.3)	0	0	2 (66.7)
	R	3 (100)	2 (66.7)	3 (100)	0	2 (66.7)	2 (66.7)	3 (100)	2 (66.7)	3 (100)	2 (66.7)	2 (66.7)	3 (100)	3 (100)	1 (33.3)
K. oxytoca (n = 4)	S	4 (100)	0	4 (100)	4 (100)	2 (50)	1 (25)	0	0	2 (50)	0	0	0	2 (50)	1 (25)
	R	0	4 (100)	0	0	2 (50)	3 (75)	4 (100)	4 (100)	2 (50)	4 (100)	4 (100)	4 (100)	2 (50)	3 (75)
Total n (%)	S	18 (85.7)	5 (23.8)	4 (19)	21 (100)	10 (47.6)	3 (14.3)	0	1 (4.8)	9 (42.9)	1 (4.8)	1 (4.8)	0	16 (76.2)	10 (47.6)
	R	3 (14.3)	16 (76.2)	17 (81)	0	11 (52.4)	18 (85.7)	21 (100)	20 (95.2)	12 (57.1)	20 (95.2)	20 (95.2)	21 (100)	5 (23.8)	11 (52.4)

Table-7
Bivariate logistic regression analysis for the risk factor associated with carriage due to positivity of ESBL-PE, PABL, and CP-E among hospitalized patients, Northwest, Ethiopia.

Study variables	Categories	Bivariate analysis for ESBL-PE, PABL, and CP-E among hospitalized patients								
		ESBL-PE			PABL			CP-E		
		Frequency (%)	COR (95% CI)	p-value	Frequency (%)	COR (95% CI)	p-value	Frequency (%)	COR (95% CI)	p-value
Gender	Male	65 (30.5)	0.63 (0.43–2.08)	0.058	11 (5.2)	1.11 (0.23–1.81)	0.051	23 (13.5)	0.95 (0.11–1.14)	0.085
	Female	37 (21.8)	1		10 (5.9)	1		29 (13.6)	1	
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Age	≤5	13 (18.6)	1		3 (4.3)	1		14 (20)	1	
	6–20	24 (36.4)	0.14 (0.56–3.56)	0.312	1 (1.5)	2.02 (0.04–3.09)	0.555	8 (12.1)	1.08 (0.55–1.58)	0.177
	21–35	20 (22.2)	2.01 (1.81–3.71)	0.125	5 (5.6)	0.90 (0.50–1.20)	0.310	5 (5.6)	1.35 (0.44–4.65)	0.881
	36–50	30 (23.1)	2.28 (0.71–4.33)	0.156	7 (5.4)	1.06 (0.08–1.15)	**0.01**	7 (5.4)	1.22 (1.06–7.31)	0.598
	≥51	15 (55.6)	0.58 (0.27–3.76)	0.09	5 (18.5)	4.09 (1.13–6.60)	**0.041**	18 (66.7)	1.04 (0.39–2.75)	**0.035**
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Educational status	No formal education	38 (54.3)	0.18 (0.02–0.97)	0.813	6 (8.6)	1.04 (0.63–1.73)	0.741	32 (45.7)	2.11 (1.02–4.58)	0.773
	Primary (1–8 grade)	18 (24.3)	0.12 (0.05–0.92)	0.437	4 (5.4)	3.01 (2.04–4.01)	0.651	9 (12.2)	0.12 (0.08–2.37)	0.181
	Secondary (9-12)	21 (11.7)	1.02 (0.91–2.06)	0.052	3 (1.7)	0.36 (0.08–2.03)	**0.027**	4 (5)	2.01 (0.99–3.07)	0.155
	Tertiary (college and above)	25 (42.4)	1		8 (13.6)	1		7 (11.9)	1	
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Marital status	Single	9 (15.5)	1.27 (1.05–4.67)	0.092	2 (3.4)	1.37 (0.44–3.92)	**0.011**	11 (19)	0.90 (0.04–1.11)	0.220
	Married	55 ((23.9)	1		11 (4.8)	1		14 (6.1)	1	
	Divorced	26 ((38.8)	0.28 (0.71–2.33)	0.325	7 (10.4)	5.01 (2.10–6.09)	0.099	17 (23.4)	2.11 (0.98–5.03)	0.670
	Widow	12 (42.9)	0.44 (0.17–2.76)	**0.03**	1 (3.6)	2.11 (1.11–4.09)	0.058	10 (35.7)	0.71 (0.86–2.97)	0.880
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Occupational status	Civil servant	22 (41.5)	1		5 (9.4)	1		13 (24.5)	1	
	Merchant	27 (32.5)	0.47 (0.22–3.01)	0.652	3 (3.6)	5.05 (2.09–6.08)	0.665	14 (16.9)	3.11 (3.01–4.04)	0.221
	Student	7 (7.6)	0.54 (0.09–2.01)	**0.01**	1 (1.1)	2.05 (1.09–3.08)	0.640	8 (8.7)	1.11 (0.01–4.04)	0.330
	Farmer	36 (65.5)	1.03 (0.99–4.05)	0.441	9 (16.4)	0.15 (1.06–1.01)	0.990	6 (10.9)	0.99 (0.05–2.09)	0.441
	Others*	10 (10)	0.13 (0.05–1.09)	0.555	3 (3)	0.41 (0.01–1.88)	0.066	11 (11)	1.93 (0.09–2.06)	0.223
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Residence	Urban	61 (23.8)	1		12 (4.7)	1		17 (13.4)	1	
	Rural	41 (32.3)	1.05 (0.07–3.01)	**0.021**	9 (7.1)	0.77 (0.61–2.03)	0.057	35 (13.7)	0.22 (0.99–1.99)	0.559
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
GIT complains	Yes	49 (31.2)	2.05 (0.01–4.21)	0.244	9 (5.7)	0.61 (0.60–1.66)	0.442	28 (17.8)	1.92 (0.99–2.11)	0.080
	No	53 (23.5)	1		12 (5.5)	1		24 (10.6)	1	
	Total	102 (26.6)			21 (5.5)			52 (13.6)		

(*continued on next page*)

Table-7 (*continued*)

Study variables	Categories	Bivariate analysis for ESBL-PE, PABL, and CP-E among hospitalized patients								
		ESBL-PE			PABL			CP-E		
		Frequency (%)	COR (95% CI)	p-value	Frequency (%)	COR (95% CI)	p-value	Frequency (%)	COR (95% CI)	p-value
Previous antibiotic history	Yes	23 (50)	2.16 (1.09–6.50)	**0.01**	13 (28.3)	0.81 (0.11–2.05)	**0.03**	23 (50)	0.99 (0.35–2.01)	**0.05**
	No	79 ((23.4)	1		8 (2.4)	1		29 (8.6)	1	
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Prolonged hospitalization	Yes	11 (40.7)	0.11 (0.01–1.08)	**0.021**	4 (14.8)	0.70 (0.21–1.05)	0.999	15 (55.6)	1.12 (0.31–1.89)	0.451
	No	91 (25.6)	1		17 (4.8)	1		37 (10.4)	1	
	Total	102 (26.6)			21 (5.5)			52 (13.6)		
Admission ward	Medical	44 ((40)	0.61 (0.02–1.01)	0.881	5 (4.5)	1.12 (0.91–2.09)	0.441	15 (13.6)	2.01 (2.06–3.04)	0.332
	Surgical	26 (33.3)	0.55 (0.01–0.89)	**0.001**	3 (3.8)	1.32 (0.76–2.45)	0.840	7 (9)	1.01 (0.88–2.22)	0.055
	Gynecology	5 (7.1)	1.13 (0.01–3.06)	0.507	2 (2.9)	0.45 (0.21–1.38)	0.770	5 (7.1)	1.34(1.02–2.98)	0.562
	Pediatrics	6(10.9)	1		1(1.8)	1		10(18.2)	1	
	ICU	20(34.5)	0.45(0.02–1.19)	0.801	7(12.1)	3.22(1.06–7.31)	0.222	13(22.4)	1.04(0.39–2.75)	0.054
	others	1(6.25)	1.67 (1.08–2.17)	0.661	3(18.75)	0.52(0.143–0.96)	0.330	2(12.5)	1.04(0.91–1.89)	0.771
	Total	102 (26.6)			21(5.5)			52(13.6)		
Underlying comorbidity	Yes	5(27.8)	0.14 (0.52–6.12)	**0.001**	1(5.6)	0.99(0.22–1.65)	0.058	4(22.2)	1.01(0.04–1.15)	0.150
	No	97(26.6)	1		20(5.5)	1		48(13.2)	1	
	Total	102 (26.6)			21(5.5)			52(13.6)		
Frequent hand washing habit	Yes	55(17.9)	1.19 (0.33–2.32)	**0.01**	13(4.2)	1.91(0.88–1.44)	0.221	16(5.2)	1.04(0.44–1.89)	0.276
	No	47(61.8)	1		8(10.5)	1		36(47.4)		
	Total	102 (26.6)			21(5.5)			52(13.6)		

COR-Crude odds ratio, CI-Confidence interval.

Table-8
Multivariate logistic regression analysis for the factors associated with gastrointestinal tract colonization due to ESBL-PE, PABL, and CP-E among hospitalized patients, Northwest, Ethiopia.

Study variables	Categories	Multivariate analysis for GIT colonization due to ESBL-PE, PABL, and CP-E								
		ESBL-PE			PABL			CP -E		
		Number (%)	AOR (95%CI)	p-value	Number (%)	AOR (95%CI)	p-value	Number (%)	AOR (95%CI)	p-value
Marital status	Single	9(15.5)	1.11 (0.08–3.04)	0.07	2(3.4)	1.22 (0.51–2.05)	0.593	11(19)	1.03 (0.01–1.22)	0.996
	Married	55((23.9)			11(4.8)			14(6.1)		
	Divorced	26((38.8)	0.41 (0.22–0.93)	0.331	7(10.4)	2.01 (1.03–3.09)	0.441	17(23.4)	1.04 (0.71–2.05)	0.552
	Widow	12(42.9)	0.29 (0.13–4.01)	0.217	1(3.6)	2.78 (0.555.58)	**0.03**	10(35.7)	0.92 (0.33–2.55)	0.110
	Total	102 (26.6)			21(5.5)			52(13.6)		
Previous antibiotic history	Yes	23(50)	1.04 (0.21–4.67)	**0.004**	13(28.3)	1.99 (0.05–2.07)	**≤0.001**	23(50)	2.01 (1.06–2.98)	**0.001**
	No	79((23.4)			8(2.4)			29(8.6)	1	

AOR-Adjusted odds ratio.

7. Discussion

One of the most complicated global public health issues is antimicrobial resistance. Due to antibiotic overuse and/or misuse in human medicine or animal health, many antimicrobial drugs are losing their therapeutic efficacy. Due to the growth and spread of drug-resistant microorganisms, surgical infections, diarrheal illnesses, bloodstream infections, and sexually transmitted diseases are now providing a serious health problem [42].

Antimicrobial resistance may also have detrimental effects on socioeconomic conditions and clinical outcomes, among other things. This is why infections, particularly those brought on by ESBL-PE, PABL, and CP-E, have become a major focus of numerous clinical guidelines, research, and national and international programs aiming to combat threats to maternal, child, and reproductive health, as well as to diseases that are spread through contaminated food and water, and unclean environments [16].

Enterobacteriaceae are responsible for urinary tract infections, septicemia, pneumonia, peritonitis, and meningitis. The hospital setting is an ideal home for resistance genes transmission via the mobile genetic elements. As a result, hand-to-hand contact, tainted food, and inadequate waste disposal systems can all contribute to the spread of germs that are resistant to antibiotics. This could make it easier for resistance genes to move from hospital effluents to nearby healthcare facilities, patients, and staff [29,43].

In the present study, the overall prevalence of gastrointestinal colonization due to ESBL-PE was much higher (26.6%) than the findings in Amsterdam 8.6% [44], Czech Republic 8.2% in hospitalized patients and 3.2% in community subjects, respectively [45], another study in Denmark among surgical patients 6% [46], 17.7% in French hospitals [47] and 13.7% [48] among HIV-infected children in Zimbabwe. A relatively higher carriage comparing the present study was reported including 37.8% in Nepal [24], another facility-based cross-sectional study (n = 97) in the Republic of Korea at 37% [49], a prospective observational study in Morocco among 164 neonates hospitalized in the neonatal intensive care unit 58.0% [30] and a study among children (n = 408) in Guinea-Bissau 32.6% [33]. Moreover, much higher than the current carriage was reported in a study in Egypt 68% [50], Tanzania among hospitalized and healthy community children 50.4% and 11.6%, respectively [51] and studies in Ethiopia such as (Addis Ababa) 52% [29], Arba Minch 34.7% [28] and in Debre Berhan hospital 47.3% [52]. Fairly similar to our current study, the present finding is relatively in line with a hospital-based cross-sectional study(n = 347) in the Republic of Korea 28.2% [53] and another study in the community of Northern Cyprus (n = 500) which revealed ESBL-PE was detected in 107 (21.4%) [54]. The variation of the present study with the previously done result may be due to the difference in the study design, study population (community-onset and/or hospitalized carriage) and the sample size [3,14,55,56]. Bacterial colonization is also common in people with community onset gastrointestinal problems [25,54].

In this study, gastrointestinal colonization with CP-E was found to be 13.6%. A hospital-based cross-sectional study in Korea to investigate the rates of transmission of CP-E among patients (n = 347) admitted to ICUs has shown 0.3% overall fecal carriage with an acquisition rate of 2.9% [53]. Moreover, five out of the total hundred participants were positive for CP-E colonization in a community-based onset gastrointestinal carriage in Egypt [50]. In the present study, the overall prevalence of PABL was 5.5% (n = 21). Similar to our study, a 3.0% (n = 15) was reported from Egypt [57] but, a relatively higher PABL l (9%) was reported in one study in Denmark among surgical patients [46]. The possible explanation for the discrepancy in the gastrointestinal colonization with other previously done studies may be attributed to the difference in the study design, source of reservoirs [16] sample size, target population, methodological variations [24,48], and socioeconomic condition.

Regarding the distributions of *Enterobacteriaceae* which are responsible for gastrointestinal colonization, *K. pneumoniae* (66.7%), *E. coli* (65%) followed by *E. cloacae* (37.5%) were the most pre-dominant ESBL-producing isolates. *K. pneumoniae* (68.6%) was the most

prominent isolate for CP-E followed by other species of *Enterobacteriaceae*. A study in Amsterdam revealed that *E. coli* (91%%), *K. pneumonia* (7.6%), and *E.cloacae* (0.7%) [44] were mostly detected isolates. Similarly in French, ESBL- *E. coli* (71.4%) followed by *K. pneumoniae* 14.3% [47] and another study in Pakistan had shown that *E. coli* (81.02%) and *K. pneumoniae* (18.98%) were the most frequently detected isolates [45]. Another study in Tanzania reported that *E. coli* and *K. pneumoniae* were responsible for the carriage due to ESBL-PE, PABL and CP-E which account for about 94% of the cases [51]. ESBL-*E.coli* 68% and *K. pneumoniae* 32% [29] and ESBL- *E.coli* 62 (42.46%) and *K. pneumoniae* 60 (41.09%) were also the most predominant clinical isolates [28]. A study among different types of hospital wards including medical, surgical, and intensive care unit (ICU) in French hospitals have revealed that ESBL-*E. coli* 71.4% followed by *K. pneumoniae* 14.3% were the most common isolates responsible for intestinal colonization [47]. Similar to our finding, in Morocco, 66.3% of ESBL-*K. pneumoniae* was the most predominant isolate [30]. Another comparative study on the carriage of ESBL-PE and CP-E at a University hospital in Morocco has shown that the prevalence of *K. pneumoniae* 70% and *E. cloacae* 30% [31]. The reason for the variability can be attributed to the variation in the local pathogen distribution or resistance profile, the type of the target population and the type of method employed [58]. Furthermore, asymptomatic carriage of ESBL-producing isolates like *K. pneumoniae* may serve as the source of subsequent infections [16,43,59,60].

Another important element of this study was the antibiogram profile of the isolates. In the current study, all isolates of ESBL-producing *E. coli* were 100% resistant to chloramphenicol, tetracycline and trimethoprim-sulfamethoxazole. Likewise, 52 (89.7%) and 53 (91.4%) of them were resistant to gentamicin and ciprofloxacin, respectively. Added that 46 (79.3%) and 50 (86.2%) ESBL-producing isolates of *E. coli* were resistant and susceptible to amoxicillin/clavulanic acid and ampicillin, respectively. Similarly, 24 (70.6%) and 15 (44.1%) isolates of ESBL-*K. pneumoniae* were resistant to amoxicillin/clavulanic acid and ampicillin, respectively. Other species like ESBL-*C. freundii*, *K. oxytoca* and *E. cloacae* were 1 (100%), 6 (100%) and 2 (66.7%) susceptible to cefoxitin, respectively. However, both ESBL-producing isolates of *E. coli* and *K. pneumoniae* have shown much higher resistance to third-generation cephalosporins including cefotaxime, ceftriaxone, and ceftazidime. Moreover, all isolates of ESBL-PE have shown a 96 (94.1%) resistance to meropenem. In the current study, C. *freundii* and *E. cloacae* have shown 100% susceptibility to aztreonam but *K. oxytoca* was 100% resistant against Aztreonam. In the study, 74.2% and 62.5% carbapenemase-producing *E. coli* followed by *K. pneumoniae* were susceptible to meropenem but *E. cloacae* was 100% resistant. In addition, all isolates of CP-E have shown a 100% overall resistance to chloramphenicol and tetracycline. Regarding the PABL, all isolates of *E. coli* have shown susceptibility to cefoxitin, ceftriaxone and cefepime. Comparing and contrasting with the previous studies, one study in Zimbabwe [48] indicated that 50% of all ESBL-PEs were resistant to amoxicillin-clavulanate, 100% to co-trimoxazole, 45.8% to chloramphenicol, and 91.6% to ceftriaxone. Another cross-sectional study on the carriage of ESBL-producing *E. coli* (n = 83) and *K. pneumoniae* (n = 91) in the Guinea-Bissau [33] has shown that co-resistance to ciprofloxacin, trimethoprim-sulfamethoxazole, and aminoglycosides was common; indicating that 38.5% were co-resistant to these classes plus ESBLs. Added that the ESBL-PE has shown higher resistance against tetracycline 91.1% and cotrimoxazole 93.84% [28]. In addition, among the ESBL-PE isolates (*E. coli* and *K. pneumoniae*), 98.3%, 80.7% and 73.3% resistance to ampicillin, gentamicin and tetracycline, respectively were reported; while ESBL-*E.coli* and ESBL-*K. pneumoniae* have shown a 90.2% sensitivity to the carbapenem (meropenem) class of antimicrobials [52]. Moreover, ESBL and PABL co-producing isolates of *E. coli* were resistant to ciprofloxacin; while one isolate of ESBL-positive *E. coli/K. pneumoniae* was co-resistant to erythromycin. However, resistance against ciprofloxacin and erythromycin has been shown in one isolate of ESBL and PABL co-harboring of *K. pneumoniae* [54]. The possible explanation for the variation in the level of AST can be attributed due to the difference in the resistance-encoding gene and their subgroup like blaCTX-*M*-1 [33], CTX-M, OXA, TEM, and SHV enzymes [48], study population [61], local habits of antimicrobial usage [62], the infection control and prevention practices, variation in the method selection [49,58] as well as the socioeconomic conditions of countries [5].

Risk factor analysis was performed to identify the factors associated with intestinal colonization. In this study, both bivariate and multivariate logistic regression analysis was performed. As a result, the previous antibiotic history has shown a statistically significant association (p-value <0.05) with the risk of developing fecal carriage among hospitalized patients. Study participants with the previous history of antibiotics were two times a greater risk of developing a carriage due to CP-E (p-value = 0.001) comparing those having no experience of antibiotics. In the meantime, gastrointestinal carriage due to ESBL-PE and PABL has revealed a statistically significant association with the previous antibiotic history. Similar to the present study, other studies [25,52,54] were also reported (p-value <0.05). This may be due to prolonged hospitalization, especially in the intensive care unit [49] that may increase the rate of antimicrobial consumption [28] like cephalosporin [63].

7.1. Strengths and limitations

This study provides sufficient baseline data regarding the magnitude and antimicrobial profile of ESBL-PE, PABL, and CP-E in our set up. In order to control and treat nosocomial bacterial infections caused by the multidrug resistant strains, these findings are important to assist the choices of appropriate antibacterial drugs. Additionally, it will help local public health authorities to modify their infection prevention and control programs by fostering a greater understanding of the value of early screening and precise detection utilizing phenotypic approaches designed to lessen the impact of antimicrobial resistance. The current study also discusses the socioeconomic, bacteriological, and clinical aspects of the rise in intestinal carriage of drug resistant strains of *Enterobacteriaceae*. Similarly, recording local epidemiological and bacteriological data to inform empirical therapy and encourage the prudent use of antibiotics is crucial in the fight against the rise of antimicrobial resistance. Moreover, it will support the introduction of antimicrobial stewardship initiatives to improve active antimicrobial resistance surveillance in our system.

On the other hand, this study had several limitations. Due to the lack of standardized detection methods across nations, the intensive spread of drug resistant species of *Enterobacteriaceae* has reminded challenging to intervene. In the industrialized world, state

of the art facilities including metagenomic approaches, and deep machine learning are common, but in the third world, traditional microbiological culture methods are widely utilized for the screening of the emergence of superbugs. Consequently, such phenotypic methods could not determine the type of beta-lactamase and carbapenemase producing genes as well as their virulence. The socio-economic constraints will also hinder genome sequencing analysis to target the species-specific encoding genes that allow conferring resistance against a variety of antibiotics.

Furthermore, because this was a single-center cross-sectional study, the final findings may not accurately reflect the national figure but warrant further investigation. Last but not least, in light of the epidemiological, bacteriological, and clinical data, performing method evaluation to all of these screening assays using molecular tests as the gold standard is quite important in subsequent research.

8. Conclusions and recommendations

In this investigation, ESBL-PE caused a much higher gastrointestinal colonization than PABL and CP-E. The monobactam group (aztreonam), the fourth generation of extended-spectrum cephalosporins (cefepime), and the carbapenems (meropenem) were the antibacterial agents of choice for treating intestinal colonization. In this study, all CP-E isolates have demonstrated complete resistance to both tetracycline and chloramphenicol.

C. freundii and *E. cloacae* did not produce PABL activity in our investigation. However, cefoxitin, ceftriaxone, and cefepime were all effective against all isolates of PABL-*E. coli*. To prevent the transmission of drug resistant superbugs in the hospital environment, the screening activity should be expanded to include nearby patients in the hospital ward once a patient has been identified as colonized with ESBL-PE, PABL, and CP-E.

Despite the fact that antimicrobial stewardship programs have been developed successfully in countries with abundant resources, efforts to reduce antimicrobial overuse and misuse in humans and in animals are generally weak in impoverished countries. In nations like Ethiopia, infection control practices should be implemented to stop the spread of drug resistance. Furthermore, the current gaps in antimicrobial resistance research knowledge should be filled by developing novel antimicrobials and advanced assays through integrated, holistic, and cross-disciplinary collaboration approaches of a national and international organization to advance science and make the general public aware of the current epidemiological picture of the threat posed by antimicrobial resistance.

Declarations

Ethics approval and consent to participate

Not applicable.

Author contribution statement

Teklehaimanot Kiros: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Tsehaynesh Gebreyesus: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Debaka Belete; Mekdes Tilahun; Shewaneh Damtie: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tesfaye Andualem; Tahir Eyayu: Analyzed and interpreted the data; Wrote the paper.

Lemma Workineh; Birhanu Getie; Tegenaw Tiruneh; Saymon Kiflom: Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We extend our gratitude to Debre Tabor Comprehensive Specialized hospital health care community for their substantial support throughout the study course. We are also indebted to thank the study participants for their voluntary participation. Furthermore, we greatly appreciate online writing tools including Quill Bot, Paperpal, Trinka and Grammerly to prepare our manuscript.

Abbreviations and Acronyms

AST Antimicrobial susceptibility Testing

ATCC American Type Culture Collection
CLSI Clinical and Laboratory Standards Institute
CP-E Carbapenemase-Producing *Enterobacteriaceae*
ESBL Extended-Spectrum Beta-lactamases
ESBL-PE ESBL-Producing *Enterobacteriaceae*
MHA Mueller-Hinton agar
PABL AmpC β-lactamases Producing *Enterobacteriaceae*
WHO World Health Organization

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e20072.

References

[1] W.H. Organization, Antimicrobial Resistance: Global Report on Surveillance, World Health Organization, 2014.
[2] J.D. Pitout, et al., Emergence of Enterobacteriaceae producing extended-spectrum β-lactamases (ESBLs) in the community, J. Antimicrob. Chemother. 56 (1) (2005) 52–59.
[3] A.N. Bulabula, A. Dramowski, S. Mehtar, Maternal colonization or infection with extended-spectrum beta-lactamase-producing Enterobacteriaceae in Africa: a systematic review and meta-analysis, Int. J. Infect. Dis. 64 (2017) 58–66.
[4] M.S. Butler, et al., Analysis of the clinical pipeline of treatments for drug-resistant bacterial infections: despite progress, more action is needed, 21, Antimicrobial agents and chemotherapy 66 (3) (2022), e01991.
[5] A. Chioro, et al., Antimicrobial Resistance: a Priority for Global Health Action, SciELO Public Health, 2015.
[6] E. Tacconelli, et al., Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis, Lancet Infect. Dis. 18 (3) (2018) 318–327.
[7] J.D. Pitout, K.B. Laupland, Extended-spectrum β-lactamase-producing Enterobacteriaceae: an emerging public-health concern, Lancet Infect. Dis. 8 (3) (2008) 159–166.
[8] M.S. Mulani, et al., Emerging strategies to combat ESKAPE pathogens in the era of antimicrobial resistance: a review, Front. Microbiol. 10 (2019) 539.
[9] M.E. Flokas, et al., Prevalence of ESBL-producing Enterobacteriaceae in pediatric bloodstream infections: a systematic review and meta-analysis, PLoS One 12 (1) (2017), e0171216.
[10] L. Cao, et al., Prevalence and molecular characteristics of mcr-1 colistin resistance in Escherichia coli: isolates of clinical infection from a Chinese University Hospital, Infect. Drug Resist. 11 (2018) 1597.
[11] K. Bush, J.F. Fisher, Epidemiological expansion, structural studies, and clinical challenges of new β-lactamases from gram-negative bacteria, Annu. Rev. Microbiol. 65 (2011) 455–478.
[12] B. Karen, A. George, Updated functional classification of b-lactamases, Antimicrob. Agents Chemother. 54 (3) (2010) 969–976.
[13] F. Moges, et al., High prevalence of extended-spectrum beta-lactamase-producing gram-negative pathogens from patients attending Felege hiwot comprehensive specialized hospital, bahir dar, amhara region, PLoS One 14 (4) (2019), e0215177.
[14] S. Sangare, et al., Prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae isolated from blood cultures in Africa, Med. Maladies Infect. 45 (9) (2015) 374–382.
[15] M.E. Flokas, et al., Prevalence of ESBL-producing Enterobacteriaceae in paediatric urinary tract infections: a systematic review and meta-analysis, J. Infect. 73 (6) (2016) 547–557.
[16] L. López-Cerero, B. Almirante, Epidemiology of infections caused by carbapenemase-producing Enterobacteriaceae: reservoirs and transmission mechanisms, Enferm. Infecc. Microbiol. Clín. 32 (2014) 10–16.
[17] S. Ghafourian, et al., Extended spectrum beta-lactamases: definition, classification and epidemiology, Curr. Issues Mol. Biol. 17 (1) (2015) 11–22.
[18] I. Iroha, et al., Extended spectrum beta-lactamase (EBSL) in E. coli isolated from a tertiary hospital in Enugu State, Nigeria, Pakistan J. Med. Sci. 25 (2) (2009) 279–282.
[19] T. Toy, et al., Multicountry distribution and characterization of extended-spectrum β-Lactamase–associated gram-negative bacteria from bloodstream infections in sub-saharan africa, Clin. Infect. Dis. 69 (Supplement_6) (2019) S449–S458.
[20] Y. Li, et al., Prevalence of plasmid-mediated AmpC β-lactamases in a Chinese university hospital from 2003 to 2005: first report of CMY-2-type AmpC β-lactamase resistance in China, J. Clin. Microbiol. 46 (4) (2008) 1317–1321.
[21] F.J. Pérez-Pérez, N.D. Hanson, Detection of plasmid-mediated AmpC β-lactamase genes in clinical isolates by using multiplex PCR, J. Clin. Microbiol. 40 (6) (2002) 2153–2162.
[22] Y.S. Park, et al., Risk factors and clinical features of infections caused by plasmid-mediated AmpC β-lactamase-producing Enterobacteriaceae, Int. J. Antimicrob. Agents 34 (1) (2009) 38–43.
[23] C. Pitart, et al., First outbreak of a plasmid-mediated carbapenem-hydrolyzing OXA-48 β-lactamase in Klebsiella pneumoniae in Spain, Antimicrobial agents and chemotherapy 55 (9) (2011) 4398–4401.
[24] S.H. Subramanya, et al., Low rate of gut colonization by extended-spectrum β-lactamase producing Enterobacteriaceae in HIV infected persons as compared to healthy individuals in Nepal, PLoS One 14 (2) (2019).
[25] H. Abdallah, et al., Fecal carriage of extended-spectrum β-lactamase-and carbapenemase-producing Enterobacteriaceae in Egyptian patients with community-onset gastrointestinal complaints: a hospital-based cross-sectional study, Antimicrob. Resist. Infect. Control 6 (1) (2017) 62.
[26] W. Hassan, A. Hashim, R. Domany, Plasmid mediated quinolone resistance determinants qnr, aac (6′)-Ib-cr, and qep in ESBL-producing Escherichia coli clinical isolates from Egypt, Indian J. Med. Microbiol. 30 (4) (2012) 442.
[27] N. Prim, et al., Prevalence of colistin resistance in clinical isolates of Enterobacteriaceae: a four-year cross-sectional study, J. Infect. 75 (6) (2017) 493–498.
[28] A. Aklilu, et al., 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, Infect. Drug Resist. 13 (2020) 1517–1526.
[29] K. Desta, et al., High gastrointestinal colonization rate with extended-Spectrum β-lactamase-producing Enterobacteriaceae in hospitalized patients: emergence of Carbapenemase-Producing K. pneumoniae in Ethiopia, PLoS One 11 (8) (2016), e0161685.
[30] B. Arhoune, et al., Rectal carriage of extended-spectrum β-lactamase-and carbapenemase-producing Enterobacteriaceae among hospitalised neonates in a neonatal intensive care unit in Fez, Morocco, Journal of global antimicrobial resistance 8 (2017) 90–96.
[31] D. Girlich, et al., High rate of fecalfecalfecal carriage of extended-spectrum β-lactamase and OXA-48 carbapenemase-producing Enterobacteriaceae at a university hospital in Morocco, Clin. Microbiol. Infection 20 (4) (2014) 350–354.

[32] V. Husickova, et al., Carriage of ESBL-and AmpC-positive Enterobacteriaceae in the gastrointestinal tract of community subjects and hospitalized patients in the Czech Republic, Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 156 (4) (2012) 348–353.
[33] J. Isendahl, et al., Fecal carriage of ESBL-producing E. coli and K. pneumoniae in children in Guinea-Bissau: a hospital-based cross-sectional study, PLoS One 7 (12) (2012).
[34] P. Nordmann, Carbapenemase-producing Enterobacteriaceae: overview of a major public health challenge, Med. Maladies Infect. 44 (2) (2014) 51–56.
[35] C.L.S. Institute, Performance Standards For Antimicrobial Susceptibility Testing [S]. CLSI Supplement M100, Clinical and Laboratory Standards Institute Wayne, PA, 2018.
[36] M. Worku, et al., Extended-Spectrum Beta-Lactamase and Carbapenemase Producing Enterobacteriaceae Among Patients with Gastrointestinal Complaints in North West Ethiopia, 2019.
[37] D. Beyene, et al., Multidrug-resistant profile and prevalence of extended spectrum β-lactamase and carbapenemase production in fermentative Gram-negative bacilli recovered from patients and specimens referred to National Reference Laboratory, Addis Ababa, Ethiopia, PLoS One 14 (9) (2019).
[38] R.S. Giriyapur, et al., Comparison of disc diffusion methods for the detection of extended-spectrum beta lactamase-producing Enterobacteriaceae, J. Lab. Phys. 3 (1) (2011) 33.
[39] S. Polsfuss, et al., Practical approach for reliable detection of AmpC beta-lactamase-producing Enterobacteriaceae, J. Clin. Microbiol. 49 (8) (2011) 2798–2803.
[40] T.Y. Tan, et al., Evaluation of screening methods to detect plasmid-mediated AmpC in Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis, Antimicrob. Agents Chemother. 53 (1) (2009) 146–149.
[41] E.C.o.A.S. Testing, EUCAST Disk Diffusion Method for Antimicrobial Susceptibility Testing, 2017. Version 6.0.
[42] A. Valverde, et al., CTX-M-15-non-ST131 Escherichia coli isolates are mainly responsible of fecalfecalfecal carriage with ESBL-producing Enterobacteriaceae in travellers, immigrants and those visiting friends and relatives, Clin. Microbiol. Infection 21 (3) (2015), 252. e1-252. e4.
[43] P. Nordmann, T. Naas, L. Poirel, Global spread of carbapenemase-producing Enterobacteriaceae, Emerg. Infect. Dis. 17 (10) (2011) 1791.
[44] E. Reuland, et al., Prevalence and risk factors for carriage of ESBL-producing Enterobacteriaceae in Amsterdam, J. Antimicrob. Chemother. 71 (4) (2016) 1076–1082.
[45] M. Shafiq, et al., Prevalence of plasmid-mediated Ampc β-Lactamases in Escherichia coli and Klebsiella pneumoniae at tertiary care hospital of Islamabad, Pakistan, European Journal of Microbiology 3 (4) (2013) 267–271.
[46] L. Jakobsen, et al., Fecal carriage of extended-spectrum and AmpC β-lactamase-producing Enterobacteriaceae in surgical patients before and after antibiotic prophylaxis, Diagn. Microbiol. Infect. Dis. 86 (3) (2016) 316–321.
[47] B. Pilmis, et al., Carriage of ESBL-producing Enterobacteriaceae in French hospitals: the PORTABLSE study, J. Hosp. Infect. 98 (3) (2018) 247–252.
[48] S.S. Wilmore, et al., Carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae in HIV-infected children in Zimbabwe, J. Med. Microbiol. 66 (5) (2017) 609.
[49] Y.J. Ko, et al., Risk factors of fecal carriage with extended-spectrum β-lactamase-producing Enterobacteriaceae in hospitalized patients, Am. J. Infect. Control 41 (12) (2013) 1241–1243.
[50] H. Abdallah, et al., Fecal carriage of extended-spectrum β-lactamase-and carbapenemase-producing Enterobacteriaceae in Egyptian patients with community-onset gastrointestinal complaints: a hospital-based cross-sectional study, Antimicrob. Resist. Infect. Control 6 (1) (2017) 1–7.
[51] M.G. Tellevik, et al., High prevalence of fecalfecalfecal carriage of ESBL-producing Enterobacteriaceae among children in Dar es Salaam, Tanzania, PLoS One 11 (12) (2016).
[52] D. Shenkute, et al., High magnitude of fecal carriage of extended-spectrum beta-lactamase-producing Enterobacteriaceae at Debre berhan comprehensive specialized hospital, Ethiopia, Infect. Drug Resist. 15 (2022) 2445.
[53] J. Kim, et al., Rates of fecal transmission of extended-spectrum β-lactamase-producing and carbapenem-resistant Enterobacteriaceae among patients in intensive care units in Korea, Annals of laboratory medicine 34 (1) (2014) 20–25.
[54] E. Ruh, et al., Extended-spectrum β-lactamase, plasmid-mediated AmpC β-lactamase, fluoroquinolone resistance, and decreased susceptibility to carbapenems in Enterobacteriaceae: fecal carriage rates and associated risk factors in the community of Northern Cyprus, Antimicrob. Resist. Infect. Control 8 (1) (2019) 98.
[55] G. Peirano, C.H. van Greune, J.D. Pitout, Characteristics of infections caused by extended-spectrum β-lactamase–producing Escherichia coli from community hospitals in South Africa, Diagn. Microbiol. Infect. Dis. 69 (4) (2011) 449–453.
[56] G.S. Tansarli, et al., Proportion of extended-spectrum β-lactamase (ESBL)-producing isolates among Enterobacteriaceae in Africa: evaluation of the evidence—systematic review, J. Antimicrob. Chemother. 69 (5) (2014) 1177–1184.
[57] E. Ruh, et al., Extended-spectrum β-lactamase, plasmid-mediated AmpC β-lactamase, fluoroquinolone resistance, and decreased susceptibility to carbapenems in Enterobacteriaceae: fecal carriage rates and associated risk factors in the community of Northern Cyprus, Antimicrob. Resist. Infect. Control 8 (1) (2019) 1–10.
[58] K. Yamada, et al., Comparison of the Modified-Hodge test, Carba NP test, and carbapenem inactivation method as screening methods for carbapenemase-producing Enterobacteriaceae, J. Microbiol. Methods 128 (2016) 48–51.
[59] G. Patel, R.A. Bonomo, Status report on carbapenemases: challenges and prospects, Expert review of anti-infective therapy 9 (5) (2011) 555–570.
[60] S. Kumar, B.R. Singh, An Overview of Mechanisms and Emergence of Antimicrobials Drug Resistance, 2013.
[61] A. Amare, et al., High prevalence of fecal carriage of Extended-spectrum beta-lactamase and carbapenemase-producing Enterobacteriaceae among food handlers at the University of Gondar, Northwest Ethiopia, PLoS One 17 (3) (2022), e0264818.
[62] M. Ferri, et al., Antimicrobial resistance: a global emerging threat to public health systems, Crit. Rev. Food Sci. Nutr. 57 (13) (2017) 2857–2876.
[63] A. Kiremitçi, et al., Prevalence and risk factors of fecal carriage of extended-spectrum β-lactamase (ESBL)-Producing Enterobacteriaceae in hospitalized and ambulatory children, Journal of Pediatric Infection/Cocuk Enfeksiyon Dergisi 5 (2) (2011).