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Increasing Resistance of Nosocomial and Community-Acquired *Escherichia coli* in Clinical Samples from Hospitals and Clinics in Sana'a City

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Abstract

Antimicrobial resistance in *Escherichia coli* presents a global challenge associated with nosocomial infections and increased mortality rates. Understanding resistance profiles is crucial for guiding treatment strategies and ensuring effective antibiotic use. This study aimed to investigate the prevalence and *in vitro* resistance of *E. coli* to community-acquired and nosocomial infections. Various clinical samples from 700 patients were cultured on MacConkey's medium and blood agar. The disk diffusion method was used to determine the antibiotic susceptibility profile of the *E. coli* isolates following the guidelines of the Clinical and Laboratory Standards Institute (CLSI). Urine, pus, seminal fluid, vaginal swabs, and other body fluids were among the clinical samples analyzed. Of the 112 *E. coli* isolates, 48.2% were from inpatients and 51.8% were from outpatients, with the majority (66%) isolated from urine samples. Higher resistance levels were observed in the urinary isolates than that in the previously recorded data from the same institutions. Notably, isolates exhibited high resistance to penicillin (98.2%), ampicillin (97.3%), first-generation cephalosporins (90.2%), erythromycin (72.2%), and roxithromycin (95.4%), whereas lower resistance was noted against piperacillin-tazobactam (25.0%), nitrofurantoin (12.5%), and imipenem (9.8%). The overall multidrug resistance rate was 62.5%, with higher rates observed in nosocomial infections (70%) compared to community-acquired isolates (55.6%). However, this difference was not statistically significant (p>0.05). This study underscores the prevalence of *E. coli* isolates (27.0%) and highlights the concerning level of resistance, particularly to older antibiotics. These findings emphasize the importance of judicious antibiotic use and ongoing surveillance.

Keywords: *E. coli*, Antibiotics, Antimicrobial Resistance, Community-acquired Infections, Nosocomial Infections, Multidrug Resistance, Urinary Isolates

INTRODUCTION

Antimicrobial resistance (AMR) is a phenomenon that has proliferated globally, leading to several major health issues with economic, social, and political repercussions.[1] Antibiotic prescriptions are effective against infections when used appropriately. Apart from incorrect choice of drugs, wrong duration, and diagnosis, prescribing antibiotics at wrong doses for bacterial infections and non-bacterial illnesses may make bacteria more resistant.[1] The burden of AMR includes increased death rates, especially in critically ill patients, prolonged hospital stays, and recurrent infections.[2]

According to a previously published study, AMR represents a significant threat to global public health, resulting in a minimum of 1.27 million deaths worldwide and contributing to as many as five million fatalities in 2019.[3]

A comprehensive review of epidemiological data on *E. coli* infections in Yemen revealed a concerning prevalence, along with alarming AMR patterns, signifying clinical implications. However, data specifically addressing the prevalence rates, antimicrobial resistance patterns, and clinical outcomes of *E. coli* infections in Yemen are lacking. The situation in Yemen may be influenced by various factors, including conflict and resource limitations, which can affect the availability and accuracy of health data.[4,5] Studies spanning from 2003 to 2020 consistently highlighted the prominence of *E. coli* as a causative agent of urinary tract infections (UTIs) and other related ailments, with prevalence rates ranging from 35.4% to 52%.[6-9] Notably, *E. coli* exhibits substantial resistance to various antibiotics, with resistance rates as high as 84.6% and 78.8% against quinolones and penicillin, respectively.[8,9] This resistance extends to critical antibiotics, such as aztreonam (61.9%), ceftriaxone (65.1%), and amoxicillin/clavulanic acid (73.2%).[5,8] The alarming increase in multidrug-resistant strains, reaching up to 53.3%, underscores the urgency of addressing AMR in Yemen.[5] Furthermore, studies have indicated that *E. coli* infections contribute significantly to mortality, with approximately 2,600 deaths associated with AMR in 2019 alone, positioning *E. coli* as one of the leading pathogens responsible for mortality in the country.[5] Clinical outcomes were further compounded by factors, such as age-standardized

mortality rates, with Yemen ranking among the highest across 21 countries in North Africa and the Middle East region.[5] Despite efforts, such as the implementation of a National AMR action plan, the persistence of high resistance rates and associated mortality underscores the need for sustained vigilance and concerted efforts to mitigate the impact of AMR on public health in Yemen.

Antibiotics are widely used in veterinary care, aquaculture, and agricultural applications.[10] The unguided and widespread use of antibiotics by different means has led to the spread of antibiotic-resistant bacteria in the environment and in hospitals.[11] The dissemination of AMR and the influence of these antibiotics on the development, transfer, and maintenance of resistance remain largely unclear. The use of antibiotics in livestock has been assumed to contribute to the emergence and spread of antibiotic-resistant bacteria, including *E. coli*, which can be transmitted to humans.[12] Several drug-resistant *E. coli* strains have been isolated from animals and food products.[13] *E. coli* can survive and adapt to various extraintestinal habitats and spread resistance between humans, animals, food products, and the environment, either by direct contact or indirectly by ingesting contaminated food or water.[14]

According to the World Health Organization (WHO) and the Center for Disease Control and Prevention (CDC), nosocomial infections or hospital-acquired is an infection that was not present at the time of admission, acquired by patients during hospitalization.[15] The term nosocomial refers to infections that occur more than 48 h after admission; otherwise, they are called community-acquired infections. Currently, nosocomial infections are defined as any systemic or localized infection that results from adverse reactions to the presence of an infectious agent(s) or its toxin(s) that was not present or incubating at the time of admission of the patient to the hospital. This includes infections that appear after discharge from the hospital (healthcare-associated infections) if they are related to prior admission. It also encompasses occupational infections among healthcare facility staff. Nosocomial infections are a major cause of morbidity and mortality, and increase the economic burden on the healthcare system.[16] *E. coli* has been associated with various nosocomial infections, including UTIs, pneumonia and bacteremia.[17] Bacterial strains associated with nosocomial infections exhibit distinct antibiotic resistance profiles compared to strains of the same bacterium related to community-acquired infections[18] although prevalence and antibiotic susceptibility patterns of nosocomial or community-acquired infections vary among locations.[17] Therefore, this study aimed to investigate the prevalence and *in vitro* resistance of *E. coli* among community and nosocomial infections among patients in suburban hospitals.

MATERIALS AND METHODS

Study design and setting

This retrospective cross-sectional study was conducted at suburban hospitals and clinics in Sana'a, Yemen, from October 2021 to March 2022. Medical records and laboratory databases were reviewed to obtain clinical specimens for bacterial cultures. Using random sampling, patient records that met the inclusion criteria were selected for data collection and analysis with duplicate specimens. This study focused on clinical samples containing gram-negative facultative anaerobic *E. coli* isolates from both outpatient and inpatient departments. Exclusion criteria encompassed individuals who had consumed any type of antibiotic within the 2 weeks preceding the date of clinical sample collection. This measure aimed to prevent the inclusion of patients potentially harboring antibiotic-resistant strains owing to recent antibiotic exposure, thereby mitigating potential confounding factors in the antimicrobial susceptibility testing results.[19]

Laboratory identification of isolates

Various clinical samples, including aspirates, blood, CSF, ear swabs, pus, seminal fluid, sputum, urine, and vaginal swabs, were obtained from clinical laboratories. To verify the presence of bacterial colonies, clinical samples were cultured in accordance with the methods described above at the respective sample collection sites on MacConkey and blood agar, and incubated at 37°C overnight. MacConkey agar, a selective and differential medium, was used to diagnose gram-negative rods and *Enterobacteriaceae* based on lactose fermentation and to culture various samples. After incubation, the morphological

Table 1. Prevalence of *E. coli* isolates based on demographic characteristics

	N	%	χ2	OR	CI	P
Gender						
Male	67	59.8	0.5	1.2	0.8-1.8	0.461
Female	45	40.2	0.5	0.9	0.5-1.3	0.461
Age groups						
0-10	6	5.6	1.1	1.6	0.7-4.1	0.298
11-20	6	5.6	0.7	1.5	0.6-3.7	0.396
21-30	23	20.4	0.5	1.2	0.7-2.0	0.504
31-40	32	28.5	0.9	0.8	0.5-1.3	0.334
41-50	22	19.5	1.2	0.7	0.4-1.3	0.278
>51	23	20.4	0.01	1.0	0.6-1.8	0.911
Locations						
Outpatients (OP)	58	51.8	1.4	1.3	0.8-2.0	0.239
Inpatients (IP)	54	48.2	1.4	0.8	0.5-1.2	0.239
Inpatients (Nosocomial infections)						
General wards	30	55.6	4.1	1.7	1.0-2.8	0.042*
Surgical wards	9	16.7	8.9	0.2	0.2-0.7	0.003*
ICU	15	27.7	0.6	0.8	0.4-1.5	0.432
Specimens						
Urine	74	66	41.8	4.3	2.7-6.8	0.001*
Pus	24	21.4	11.1	0.4	0.3-0.7	0.001*
Vaginal swab	4	3.6	0.1	1.2	0.4-4.1	0.730
Seminal fluid	3	2.7	0.1	1.2	0.3-4.7	0.806
Body fluid	2	1.8	3.3	0.3	0.1-1.2	0.069
Others	5	4.5	13.2	0.2	0.1-0.5	0.001*

N: Number, %: Percentage, χ2: Chi-square, OR: Odd ratio, CI: Confidence interval, P: Probability, *: Statistically significant, ICU: Intensive care unit, ($\chi 2 \geq 3.84$, $p < 0.05$: significant), Others: Other type of clinical samples and body fluids

properties of the colonies were identified using Gram staining and biochemical assays. The identities of *E. coli* isolates were confirmed using an API 20E diagnostic system (bioMérieux, France).

Antimicrobial susceptibility testing

The disk diffusion method was used to determine the antibiotic susceptibility profile of the *E. coli* isolates following the guidelines of the Clinical and Laboratory Standards Institute (CLSI); 0.5 McFarland standard for turbidity was achieved by emulsifying three-five colonies in sterile saline. Thirty-six antimicrobial agents were tested to assess the sensitivity of *E. coli* strains. The bacterial inhibition zones surrounding the antibiotic disks were measured and compared with the disk diffusion interpretive criteria updated annually by the CLSI. Antimicrobial disks included: ampicillin (10 µg), amoxicillin (25 µg), amoxiclav (20 µg), aztreonam (30 µg), azithromycin (15 µg), amikacin (10 µg), cefradine (30 µg), cefadroxil (30 µg), cephalothin (30 µg), cefuroxime (30 µg), ceftizoxime (10 µg), ceftazidime (30 µg), cefotaxime (30 µg), cefepime (30 µg), ciprofloxacin (5 µg), co-trimoxazole (25 µg), erythromycin (15 µg), lomefloxacin (10 µg), levofloxacin (5 µg), moxifloxacin (5 µg), nalidixic acid (30 µg), nitrofurantoin (10 µg), minocycline (30 µg), penicillin G (10 µg), (Oxoid), piperacillin (100 µg), ticarcillin (75 µg), piperacillin-tazobactam, imipenem (10 µg), roxithromycin (15 µg), tobramycin (10 µg), tetracycline (30 µg) and sulfonamide (30 µg), and chloramphenicol (30 µg). The CLSI guidelines were used to evaluate susceptibility results.[20] Multiple drug resistance (MDR) is considered if bacterial isolates become resistant to three or more antibiotics. The susceptibility testing methods were checked for quality using *E. coli* ATCC 25992/ATCC 35218.

Statistical analysis

The percentage of antibiotic resistance was analyzed in relation to patient admission, age, and sex. The Chi-square test was used to assess statistical differences between variables using the Statistical Package for the Social Sciences (SPSS) (version 21). An unpaired t-test was used to compare the differences in resistance profiles between nosocomial and community-acquired *E. coli* isolates, and statistical significance was set at $p < 0.05$.

Ethics approval

The study was conducted in accordance with the guidelines of the Declaration of Helsinki and the research ethics were reviewed and approved by the Faculty Ethics Committee of the Faculty of Medicine and Health Science at Taiz University (Ref. No. IRB-21/01/10). Patient privacy and data confidentiality were maintained in accordance with the principles of the Declaration of Helsinki.

RESULTS

Prevalence and demographic characteristics of *E. coli* isolates

A total of 700 clinical specimens were received from different wards and departments in suburban hospitals and clinics in Sana'a, Yemen, during the study period, with a request for bacterial culture. Of these, 421 (60%) were positive for bacterial growth; 112 (27%) of which were identified as *E. coli.* Irrespective of the site of infection, around 60% of identified patients with *E. coli* strains were females, particularly adults (aged > 20 years old) as compared to other age groups (Table 1).

Regardless of site of infection, the overall percentages of patients with identified *E. coli* among inpatients (52%) and outpatients (48%) was almost equally distributed. The majority (66%) of the *E. coli* isolates were identified in urine samples ($p < 0.05$ and OR=4.3). Compared to the resistance data from our previous study conducted at the same hospital, higher levels of resistance were noted among *E. coli* urinary isolates in the current study. In a previous study, resistance rates to ampicillin, amoxicillin, and co-trimoxazole among urinary *E. coli* isolates were 78%, 70%, and 42%, respectively.[7,21] In the present study, the resistance rates of urinary *E. coli* isolates to these antibiotics increased to 90%, 85%, and 52%, respectively. This suggests an increasing trend of antibiotic resistance over time among *E. coli* strains causing urinary tract infections at this medical facility. Of these, 42 and 32 urine samples were obtained from female and male patients, respectively. Increased resistance was also observed for this type of sample. Almost half of the nosocomial *E. coli* strains were obtained from surgical wards (17%) and ICU (28%), whereas the remaining percentage (55%) belonged to other general wards (Table 1).

Antibiotic resistance patterns of *E. coli* isolates

The general sensitivity of *E. coli* strains against tested antibiotics was calculated as 62.5%, although strains of this bacterium associated with nosocomial showed higher resistance profile (70%) compared to community-acquired isolates (55.6%) (Table 2). High level of resistance (98%) to both nosocomial and community-acquired *E. coli* was observed for penicillin and ampicillin drugs, whereas greater activity of piperacillin (58%), aztreonam (62%), and ticarcillin (77%) against these isolates was also recorded. However, nosocomial *E. coli* exhibited an increased resistance rate to ticarcillin (89%) and piperacillin (68%) in comparison with community-acquired isolates, which displayed 65% and 48% of resistance, respectively. The overall resistance of isolated *E. coli* strains from both inpatients and outpatients to imipenem was determined to be limited (10%), although rate of resistance was higher among inpatients (15%) when compared to outpatients (6%). First-generation cephalosporins, including cefradine and cefadroxil, showed weak activity against nosocomial and community-acquired *E. coli* isolates, with almost 90% resistance (Table 2). Nevertheless, the second-generation cephalosporins, cephalothin and cefuroxime, provided a slightly greater activity than the first-generation cephalosporins against nosocomial and community-acquired strains of *E. coli*, as the percentage of resistance was calculated as 84% and 74%, respectively. In addition, nosocomial *E. coli* isolates showed a higher rate of resistance to third-generation ceftizoxime (74%) and cefotaxime (85%) in comparison with community-acquired

Table 2. Resistance profile of community-acquired and nosocomial *E. coli* isolates

Antibiotic group	Antibiotic	Total (N=112)		NC (N=54)		CA (N=58)		χ2	OR	CI	P
		N	%	N	%	N	%				
Aminoglycosides	Amikacin	32	28.6	17	31.5	15	25.9	0.4	1.3	0.6-3.0	0.511
	Tobramycin	82	72.2	42	77.8	40	69.0	1.1	1.6	0.7-3.7	0.293
Beta-lactam inhibitors	Piperacillin-tazobactam*	28	25.0	19	35.2	9	15.5	5.8	3.0	1.2-7.3	0.016*
	Amoxiclav*	59	52.7	40	74.1	19	32.8	19.2	5.9	2.6-13.3	0.001*
Carbapenems	Imipenem	11	9.8	8	14.8	3	6.2	2.9	3.2	0.8-12.7	0.087
Cephalosporins	Cefradine	101	90.2	51	94.4	50	86.2	2.1	2.7	0.7-10.8	0.143
	Cefadroxil	101	90.2	50	92.6	51	87.9	0.7	1.7	0.5-6.2	0.407
	Cephalothin*	94	83.9	53	98.1	41	70.7	15.6	22.0	2.8-172	0.001*
	Cefuroxime*	83	74.1	49	90.7	34	58.9	15.0	6.9	2.4-19.9	0.001*
	Ceftizoxime*	68	60.7	40	74.1	28	48.3	7.8	3.1	1.4-6.8	0.005*
	Cefotaxime*	86	76.8	46	85.2	40	69.0	4.1	2.6	1.0-6.6	0.042*
	Ceftazidime*	88	78.6	47	87.0	41	70.7	4.4	2.8	1.1-7.4	0.035*
	Cefepime	49	43.8	28	51.9	21	36.2	2.8	1.9	0.9-4.0	0.095
Macrolides	Erythromycin	103	92.0	50	92.6	53	91.4	0.05	1.2	0.3-4.6	0.813
	Azithromycin	69	61.6	36	66.7	33	56.9	1.1	1.5	0.7-3.3	0.288
	Roxithromycin	108	95.4	52	96.3	56	96.6	0.005	0.9	0.1-6.8	0.942
Monobactam	Aztreonam	69	61.6	36	66.7	33	56.9	1.1	1.5	0.7-3.3	0.288
Penicillin	Penicillin G	110	98.2	54	100.0	56	96.6	1.9	2.0	1.6-2.4	0.169
	Ampicillin	109	97.3	54	100.0	55	94.8	2.3	2.0	1.6-2.4	0.090
	Ticarcillin*	86	76.8	48	88.9	38	65.5	8.6	4.2	1.5-11.5	0.003*
	Piperacillin*	65	58.0	37	68.5	28	48.3	4.7	2.3	1.1-5.0	0.030*
Quinolones	Nalidixic acid*	81	72.3	45	83.3	36	62.1	6.9	3.1	1.3-7.5	0.012*
	Nitrofurantoin	14	12.5	7	13.0	7	12.1	0.02	1.1	0.4-3.3	0.886
	Ciprofloxacin*	62	55.4	37	68.5	25	43.1	7.3	2.9	1.3-6.2	0.007*
	Lomefloxacin*	72	64.3	40	74.1	32	55.2	4.4	2.3	1.0-5.2	0.037*
	Levofloxacin	41	36.6	24	44.4	17	29.3	2.8	1.9	0.9-4.2	0.097
	Moxifloxacin	44	39.3	25	46.3	19	32.8	2.1	1.8	0.8-3.8	0.143
Tetracyclines	Tetracycline*	87	77.7	47	87.0	40	69.0	5.3	3.0	1.2-8.0	0.022*
	Minocycline*	49	43.8	30	55.6	19	32.8	5.9	2.6	1.2-5.6	0.015*
Others	Co-trimoxazole	61	54.5	29	53.7	32	55.5	0.02	0.9	0.5-2.0	0.876
	Sulfonamide*	88	78.6	47	87.0	41	70.7	4.4	2.8	1.1-7.4	0.035*
	Chloramphenicol	41	36.6	21	38.9	20	34.5	0.3	1.2	0.6-2.6	0.629

N: Number, %: Percentage, χ2: Chi-square, OR: Odd ratio, CI: Confidence interval, P: Probability, CA: Community-acquired, NC: Nosocomial, *: Statistically significant (p< 0.05)

strains of this bacterium (Table 2). Although moderate level of resistance to cefepime was observed in both nosocomial and community-acquired *E. coli* strains (44%), isolates associated with outpatients were more sensitive to this drug (36%) than those obtained from inpatients (52%).

β-lactamases inhibitors, including piperacillin-tazobactam and amoxiclav demonstrated high and moderate activity toward all *E. coli* strains respectively, although strains associated with inpatients showed more than two-times resistance rate of isolates belong to outpatients. Nosocomial and community-acquired *E. coli* strains showed reduced resistance to nitrofurantoin (12.5%), levofloxacin (37%), moxifloxacin (40%), with insignificant differences between two groups of isolates (Table 2). Conversely, high resistance of nosocomial and community-acquired *E. coli* isolates to nalidixic acid (72%) was observed, whereas the latter group of isolates was reported with lower resistance (62%) than *E. coli* strains linked with inpatients

Table 3. Antimicrobial resistance profile of *E. coli* isolates from Sana'a city hospitals and clinics, showing percentage of resistance to multiple antimicrobials

No.	Number of Antibiotics	Number of Resistant *E. coli* Isolates	Percentage of Resistant *E. coli* Isolates
1	9	2	1.8
2	10	4	3.6
3	12	1	0.9
4	14	4	3.6
5	15	2	1.8
6	16	3	2.7
7	17	5	4.5
8	18	6	5.4
9	19	7	6.3
10	20	4	3.6
11	21	3	2.7
12	22	4	3.6
13	23	7	6.3
14	24	6	5.4
15	25	6	5.4
16	26	8	7.1
17	27	5	4.5
18	28	10	8.9
19	29	9	8.0
20	30	5	4.5
21	31	5	4.5
22	32	3	2.7
23	33	1	0.9
24	34	2	1.8
	Total	112	100.0

(83%). Similarly, *E. coli* strains isolated from inpatients were less sensitive to ciprofloxacin (68.5%) and lomefloxacin (74%) in relation to the resistance profiles of community-acquired *E. coli* isolates, which were determined as 43% and 55%, respectively. Resistance of nosocomial and community-acquired *E. coli* isolates to tobramycin was more than double (72%) of that recorded for amikacin (29%). Reduced sensitivity of *E. coli* isolates to erythromycin (92%) and roxithromycin (95%) was observed, whereas slightly higher activity of azithromycin toward strains of this bacterium was noted (Table 2). Approximately 44% and 78% of the isolated bacteria were resistant to tetracycline and minocycline, respectively, with a significant difference between nosocomial and community-acquired groups. Both nosocomial and community-acquired groups of *E. coli* exhibited low to moderate resistance rate against chloramphenicol (37%) and co-trimoxazole (54%). However, a significantly higher percentage of resistance was observed when testing sulphonamide against nosocomial *E. coli* isolates (87%) and community-acquired strains (71%) (Table 2).

Multidrug resistance analysis

Our analysis revealed varying degrees of multidrug resistance among *E. coli* isolates obtained from clinical samples. The number of antibiotics to which the isolates were resistant ranged from 9 to 34, with corresponding percentages of resistant isolates ranging from 0.9% to 8.9%, as shown in (Table 3). Notably, the majority of isolates exhibited resistance to multiple antibiotics, with 100% of the isolates collectively demonstrating resistance to at least nine antibiotics. Furthermore, our findings indicate a concerning trend of increasing resistance as the number of antibiotics tested increased, with a peak observed at 28 antibiotics, where 10 isolates (8.9%) showed resistance. These results underscore the crucial need for continued surveillance and implementation of effective antimicrobial programs to mitigate the escalating threat of multidrug-resistant bacterial infections.

DISCUSSION

The prevalence and drug susceptibility patterns of nosocomial infections, including those caused by antibiotic-resistant bacteria, such as *E. coli*, exhibit regional variation.[18] The present study revealed a high proportion of *E. coli* among females, particularly in urine samples. Although a higher percentage of *E. coli* was isolated from outpatients than inpatients, the difference was not statistically significant. The distribution of isolated bacteria across wards was highest in general wards and lowest in surgical wards, which was likely influenced by factors, such as admission rates or bed capacity, infection control measures, hygiene practices, and the unique nature of care provided in the ICU and surgical wards. The higher incidence of *E. coli* infection among females may be attributed to anatomical and microbial differences between the male and female genitourinary systems.[22] Numerous studies have consistently identified *E. coli* as the predominant pathogen responsible for UTIs, comprising up to 90% of cases.[23] A study

conducted in Saudi Arabia reported a comparable distribution of isolated bacteria, with the general ward exhibiting the highest incidence of *E. coli* isolates and the surgical ward the lowest.[24]

The general antibiotic resistance profiles of the community-acquired and nosocomial *E. coli* strains showed limited variation, with high rates of resistance to penicillin, cephalosporins, ampicillin, and macrolides. This resistance pattern could be attributed to the limited activity of these antibiotics against Gram-negative bacteria and their susceptibility to β-lactamase.[25] Previous studies in neighboring regions of Yemen have reported similar resistance rates, highlighting the importance of local surveillance of AMR.[26] Conversely, the significant resistance of community-acquired and nosocomial *E. coli* to ticarcillin, piperacillin, cefazolin, cefuroxime, cefotaxime, and ceftazidime can be explained by the fact that most hospitalized patients tend to have chronic infections or encounter nosocomial infections caused by multidrug-resistant bacteria. The present study found a high rate of resistance to piperacillin and aztreonam, providing compelling evidence that the unguided use of these antibiotics, including sublethal or excessive doses, may contribute to the development of resistance. Local authorities must carefully consider this observation and take targeted actions to effectively control the spread of AMR in the area.

The resistance rate (53%) of *E. coli* isolates to amoxiclav was consistent with that of multiple studies.[27,28] In the current study, the rate of resistance of nosocomial *E. coli* strains toward amoxiclav was 72%, whereas community-acquired *E. coli* strains of this investigation were highly sensitive to amoxiclav. Extended-spectrum β-lactamase (ESBL)-producing *E. coli* is more likely to be associated with hospitals[25] with limited sensitivity to amoxiclav, as the resistance of ESBL *E. coli* to this antibiotic is highly observed.[29] Moreover, the overall resistance to imipenem was low, whereas moderate resistance of *E. coli* strains to first-generation cefradine was observed. The limited spectra of cefadroxil and cefradine did not lead to significant differences in the rates of resistance between the community-acquired and nosocomial groups. Resistance of β-lactam group was significantly ($p < 0.05$) higher in nosocomial isolates than community-acquired isolates, possibly due to the higher prevalence of β-lactamase harboring isolates in hospitals than community. Like most other antibiotic drugs, cefuroxime displayed an increased resistance among nosocomial *E. coli* (91%) isolates, whereas almost half of community-acquired strains were sensitive to the same drug, which has been reported in multiple similar studies.[27,28]

The current study showed a resistance rate between 68% and 88% for cefotaxime, ceftriaxone, and ceftazidime in *E. coli* strains, although nosocomial isolates presented as slightly higher than community-acquired. Variations in the sensitivity profiles of third-generation cephalosporins toward *E. coli* strains could be attributed to the actual degree of hydrolysis of the drugs by different β-lactamase enzymes.[25] The present study also showed that the resistance rate of *E. coli* to cefepime (43.8%) was consistent with the findings of multiple studies.[30] The lower resistance to fourth-generation cephalosporins compared to other generations may be due to the limited or restricted use of fourth-generation cephalosporins, leading to less selection pressure for resistance compared with other generation drugs.[31]

The present study revealed relative resistance of *E. coli* strains to third-generation levofloxacin (36.6%) and fourth-generation moxifloxacin (39.3%). Notably, *E. coli* isolates were observed with high resistance to examined macrolides, including roxithromycin (95.4%) and erythromycin (92%), although azithromycin showed a distinct level of resistance (61.6%). Similar sensitivity profiles have been published previously, indicating that roxithromycin and erythromycin are similar to other macrolides with limited activity against *Enterobacteriaceae* and *Pseudomonas aeruginosa*.[32] In this study, the resistance rate to co-trimoxazole among isolated *E. coli* was approximately 55%. This finding is consistent with those of previous studies conducted in Brazil and India.[33,34] Moreover, the resistance rates of between community-acquired and nosocomial *E. coli* to co-trimoxazole were likely similar (55.5%, 53.7%). The high resistance rate among nosocomial strains compared to community-acquired strains can be attributed to the prolonged hospital stay, critical health status of patients, and massive use of medical devices.

The results of our study highlighted the prevalence of multidrug-resistant *E. coli* strains in clinical settings. The observed variability in the number of antibiotics against which the isolates displayed resistance underscores the complex nature of antimicrobial resistance and the challenges it poses for clinical management.[35] Our findings revealed a notable proportion of isolates resistant to multiple antibiotics, with resistance ranging from 1.8% to 8.9% across the tested antibiotics. The presence of isolates exhibiting resistance to numerous antibiotics was particularly alarming, with 10 isolates (8.9%) showing resistance to 28 antibiotics. This emphasizes the urgent need for effective antimicrobial strategies to combat the dissemination of multidrug-resistant pathogens.[36]

The increasing trend in resistance observed as the number of antibiotics tested increased further emphasizes the magnitude of the problem.[37] This phenomenon may indicate the acquisition and accumulation of resistance mechanisms in *E. coli* populations over time. Factors, such as inappropriate antibiotic use, inadequate infection control measures, and dissemination of resistant strains within healthcare settings are likely to contribute to the observed patterns of resistance.[38] Additionally, the presence of mobile genetic elements carrying resistance genes may facilitate the spread of resistance determinants among bacterial populations, further exacerbating this problem.[35]

Our findings extend beyond clinical settings and have notable public health implications. Multidrug-resistant *E. coli* infections are associated with increased morbidity, mortality, and healthcare costs.[39] The limited treatment options available for these infections necessitate the development of novel antimicrobial agents and alternative therapeutic approaches.[40] Furthermore, concerted efforts are needed to strengthen surveillance systems, promote judicious antibiotic use, and implement infection control measures to curb the emergence and spread of multidrug-resistant pathogens.[41] Collaborative initiatives involving healthcare providers, policymakers, and the public are essential for effectively addressing this growing threat.

In this study, high rates of resistance were observed against commonly used first-line antibiotics among *E. coli* isolates. However, no data were collected on the actual antibiotic usage patterns and consumption levels at the study site. Monitoring antibiotic consumption is necessary to inform local treatment guidelines and support antimicrobial stewardship efforts. These results demonstrate the need for the regular monitoring of antibiotic resistance in Yemen to guide empirical therapies. Future studies should aim to collect comprehensive antibiotic usage data through programs, such as the Anatomical Therapeutic Chemical Classification System to allow meaningful correlations between resistance rates and antibiotic consumption.

CONCLUSION

This study highlighted the prevalence and drug resistance patterns of nosocomial *E. coli* infections in Yemen. High resistance rates, particularly to commonly used antibiotics, underscore the urgent need for antimicrobial stewardship and infection control measures. The emergence of multidrug-resistant strains poses notable clinical and public health challenges, emphasizing the importance of collaborative efforts to strengthen surveillance and promote judicious antibiotic use. Future studies should focus on collecting comprehensive antibiotic usage data to develop evidence-based treatment guidelines and strategies to effectively combat antimicrobial resistance. More comprehensive studies across different regions of the country are necessary to determine representative resistance patterns. Molecular investigation of the resistance genes is recommended for a deeper understanding of the molecular epidemiology of the collected isolates.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

TA, MAA, TKA, JCA, AA, ASB, HQ, HSG and HA conceptualized the study. MAA, TKA and HA performed data collection. TA, TKA, JCA, AA, ASB, HQ, HSG, HA applied methodology. MAA, TKA, AA, ASB, HQ, HA performed formal analysis. TA, TKA and HA performed visualization. TKA, JCA, AA, ASB, HQ and HSG performed validation. TA and HA performed project administration. TA, TKA, AA, ASB, HQ and HA wrote the original draft. TA, MAA, JCA, ASB, HQ, HSG and HA reviewed and edited the manuscript. All authors read and approved the final manuscript for publication.

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None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was apporved by the Ethics Committee, Faculty of Medicine and Health Science, Taiz University (Ref. No. IRB-21/01/10).

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