ANTIMICROBIAL SUSCEPTIBILITY PATTERNS OF *Escherichia coli* ISOLATED FROM CANCER PATIENTS IN THE NATIONAL CANCER HOSPITAL

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ABSTRACT

***Introduction**: Escherichia coli (E. coli) is one of the leading causes of infections in cancer patients. Antibiotic-resistant E. coli is a major cause of treatment failure in infected cancer patients. This study aims to determine the prevalence and antibiotic susceptibility of E. coli in cancer patients from January 2022 to December 2022 at National Cancer Hospital.*

***Materials and methods**: We performed a retrospective review of the culture results of various clinical samples.*

***Results**: A total of 283 samples were analyzed to identify E. coli and its antimicrobial profiles. The prevalence of E. coli was 15.9%. The highest isolation rate was obtained from blood samples (35.56%). The highest rate of E. coli resistance was found in ampicillin (95.56%), followed by sulfamethoxazole/trimethoprim (77.76%) and ceftazidime (64.44%). The highest rate of E. coli sensitivity was found in fosfomycin (97.78%), followed by ertapenem, imipenem, meropenem, and amikacin (95.56% each), and nitrofurantoin (93.33%). About 55.56% and 80.0% were ESBL-positive and multidrug-resistant, respectively.*

***Conclusion**: E. coli isolates showed high rates of resistance to ampicillin, sulfamethoxazole/trimethoprim, and ceftazidime. Fosfomycin, ertapenem, imipenem, meropenem, amikacin, and nitrofurantoin are considered appropriate for the empirical treatment of E. coli. Regular monitoring of E. coli resistant to antibiotics is recommended.*

***Keywords**: E. coli, antibiotics, Burns, cancer, Vietnam*

1. INTRODUCTION

Escherichia coli (*E. coli*) are part of the normal gut microbiota of humans and animals, it can also be found in water, soil, and vegetation. *E. coli* is one of the leading pathogens causing urinary tract infections, bloodstream infections, wounds infections, and other complications in humans. *E. coli* is one of the major causes of mortality from

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these infections at all ages [1].

E. coli resistant to antibiotics has been reported worldwide and the resistance rates are increasing in both developed and developing countries is a global health concern. The emergence of antibiotic-resistant *E. coli* is a major cause of treatment failure, especially in infected cancer patients. The antibiotic-resistant *E. coli* are increasing and becoming a major threat to human health worldwide [2]. The increasing of multidrug-resistant *E. coli*, extended-spectrum β-lactamases (ESBLs) *E. coli*, and cephalosporins-resistant *E. coli* are growing concerns for the treatment of *E. coli* infection.

Infection is common among cancer patients, leading to treatment failure, prolonged hospitalization, increased cost of health care, and reduced survival. Cancer patients are at high risk for antibiotic-resistant bacterial infections. The prevalence of antimicrobial-resistant bacterial strains in cancer patients was high. More than 50% of all cancer patients are infected and about 60% of deaths occur in developing countries [3]. The burden of infection is high in developing countries, especially in Vietnam. To the best of our knowledge, there are limited data regarding *E. coli* antibiotic-resistant profile in cancer patients in Vietnam. Thus, this study aims to investigate antibiotic susceptibility, ESBL production, and multi-drug resistance of *E. coli* isolates from cancer patients to provide useful information for the clinical treatment of *E. coli* infections.

2. MATERIALS AND METHODS

Study Design

This study was performed at the Tan Trieu National Cancer Hospital. All cancer patients with *E. coli*-positive cultures were enrolled, and other bacteria strains were excluded. The study was performed for 8 months, from January 2022 to September 2022. This study was approved by the ethics committee of the National Cancer Hospital, following the Declaration of Helsinki.

Bacterial Identification

E. coli species identification, antibiotic susceptibility, and ESBL producing were performed using the VITEK® 2 Compact system (bioMérieux company) using GN and AST N204 cards, respectively. The *E. coli* strain ATCC 25922 was used for routine quality-control assays. Multi-drug resistant *E. coli* was defined as a strain resistant to at least one agent in three or more antimicrobial categories.

Statistical Analysis

All data was prepared in Microsoft Excel 2013 for Windows (Microsoft Corp.). The X^2 test was performed for comparing groups using the R software version 4.2.2. The $p < 0.05$ were considered statistically significant.

3. RESULTS

Baseline characteristics

The baseline characteristics of cancer patients who are infected with *E. coli* are shown in Table 1. Over the 8-month study period from January 2022 to September 2022, a total of 45 patients met the study criteria and were analyzed.

A total of 45 (15.9%) *E. coli* were identified. The highest number of *E. coli* collected was in June (26.7%), followed by July (24.4%), and May (13.3%). Among the type of cancer, colorectal cancer was the

most frequent (35.6%), followed by uterine cancer (13.3%). Among the type of sample, blood was the most common (35.6%), followed by ascites (15.6%), and urine (13.3%). The ESBL-positive and multidrug-resistant rates were 55.6% and 80%, respectively. The mean age was 60.3 ± 12.7 years; 23 (51.1%) were male, and 22 (48.9%) were female.

There was no statistically significant difference in the proportion of *E. coli* isolated between gender (p = 0.881), ESBL producing (p = 0.456), and among units (p = 0.936). However, there was a statistically significant difference in the proportion of *E. coli* isolated between MDR (p < 0.001), among the sample (p < 0.001), and type of cancer (p < 0.001).

Table 1. The baseline characteristics of cancer patients with *E. coli* infected

Variables	Overall (n = 45)	P-value
Month		0.0339*
January	5 (11.1%)	
March	5 (11.1%)	
April	5 (11.1%)	
May	6 (13.3%)	
June	12 (26.7%)	
July	11 (24.4%)	
August	1 (2.2%)	
Type of cancer		< 0.001**
Biliary tract cancer	1 (2.2%)	
Bladder cancer	3 (6.7%)	
Brain cancer	1 (2.2%)	
Breast cancer	2 (4.4%)	
Colon cancer	1 (2.2%)	
Colorectal cancer	16 (35.6%)	
Esophageal cancer	1 (2.2%)	
Kidney cancer	1 (2.2%)	
Liver cancer	3 (6.7%)	
Lung cancer	2 (4.4%)	
Oral cancer	1 (2.2%)	
Ovarian cancer	2 (4.4%)	
Prostate cancer	1 (2.2%)	
Spine cancer	1 (2.2%)	
Stomach cancer	2 (4.4%)	
Ureters cancer	1 (2.2%)	

Variables	Overall (n = 45)	P-value
Uterine cancer	6 (13.3%)	
Gender		0.881
Female	22 (48.9%)	
Male	23 (51.1%)	
Unit		0.936
General internal medicine	14 (31.1%)	
General surgery	15 (33.3%)	
ICU	16 (35.6%)	
Sample		< 0.001**
Abscess fluid	2 (4.4%)	
Ascites	7 (15.6%)	
Biliary drainage	2 (4.4%)	
Blood	16 (35.6%)	
Colorectal drain	1 (2.2%)	
Sputum	4 (8.9%)	
Surgical fluid	5 (11.1%)	
Urine	6 (13.3%)	
Urine drainage	1 (2.2%)	
Uterus drain	1 (2.2%)	
ESBL		0.456
Negative	20 (44.4%)	
Positive	25 (55.6%)	
Multidrug resistance (MDR)		< 0.001**
MDR	36 (80.0%)	
Not MDR	9 (20.0%)	
Age		
Mean (SD)	60.3 (12.7)	
Median [Min, Max]	61.0 [15.0, 80.0]	

Antimicrobial Susceptibility

A total of 45 *E. coli* strains were collected. The antibiotic susceptibility of the 45 *E. coli* strains to 16 antibiotics is presented in Table 2. Based on the CLSI 2018 criteria, the highest resistance rate of *E. coli* was to Ampicillin (43; 95.56%), followed by Sulfamethoxazole/Trimethoprim (35; 77.78%), Ceftazidime (29; 64.44%), Ciprofloxacin and Norfloxacin (62.22% each). All isolates were not resistant to

nitrofurantoin. The highest sensitive rate was found in Fosfomycin (97.78%), followed by Ertapenem, Imipenem, Meropenem, Amikacin (95.56% each), and Nitrofurantoin (93.33%).

Based on CLSI (2018), the antibiotic agents were classified as shown in Table 2. We defined multidrug resistance in *E. coli* as resistance to at least three distinct antibiotic classes and estimated this rate was 80% (36/45).

Table 2. The antibiotics susceptibility of 45 *E. coli* isolates

Antimicrobial Class	Antimicrobial agents	Antibiotics susceptibility n (%)		
		R	S	I
β-Lactams	Ampicillin	43 (95.56)	2 (4.44)	0 (0)
β-Lactams	Amoxicillin-clavulanate	17 (37.78)	22 (48.89)	6 (13.33)
β-Lactams	Piperacillin-Tazobactam	6 (13.33)	37 (82.22)	2 (4.44)
Cephems	Cefotaxime	27 (60)	17 (37.78)	1 (2.22)
Cephems	Ceftazidime	29 (64.44)	15 (33.33)	1 (2.22)
Cephems*	Cefepime*	26 (57.78)	18 (40)	0 (0)
Carbapenems	Ertapenem	2 (4.44)	43 (95.56)	0 (0)
Carbapenems	Imipenem	2 (4.44)	43 (95.56)	0 (0)
Carbapenems	Meropenem	2 (4.44)	43 (95.56)	0 (0)
Aminoglycosides	Amikacin	2 (4.44)	43 (95.56)	0 (0)
Aminoglycosides	Gentamicin	20 (44.44)	24 (53.33)	1 (2.22)
Fluoroquinolones	Ciprofloxacin	28 (62.22)	15 (33.33)	2 (4.44)
Fluoroquinolones	Norfloxacin	28 (62.22)	15 (33.33)	2 (4.44)
Fosfomycin	Fosfomycin	1 (2.22)	44 (97.78)	0 (0)
Nitrofurans	Nitrofurantoin	0 (0)	42 (93.33)	3 (6.67)
Folate pathway antagonists	Sulfamethoxazole-Trimethoprim	35 (77.78)	10 (22.22)	0 (0)

** One missing value*

ESBL-Producing *E. coli*

The ESBL-Producing *E. coli* profiles are shown in Table 3 and Table 4. The rate of ESBL-Producing *E. coli* was 55.6%. There was no significant ($p > 0.05$) different between ESBL positive and ESBL negative in relation to month, diagnosis, gender, unit, sample, and MDR.

Table 3. The ESBL-Producing *E. coli* profiles

Variables	ESBL negative (n = 20)	ESBL positive (n = 25)	Overall (n = 45)	*p*-value
ESBL				< 0.001
Negative	20 (100%)	0 (0%)	20 (44.4%)	
Positive	0 (0%)	25 (100%)	25 (55.6%)	
Month				0.648
January	4 (20.0%)	1 (4.0%)	5 (11.1%)	
March	4 (20.0%)	1 (4.0%)	5 (11.1%)	
April	2 (10.0%)	3 (12.0%)	5 (11.1%)	
May	1 (5.0%)	5 (20.0%)	6 (13.3%)	
June	5 (25.0%)	7 (28.0%)	12 (26.7%)	
July	3 (15.0%)	8 (32.0%)	11 (24.4%)	
August	1 (5.0%)	0 (0%)	1 (2.2%)	
Diagnosis				0.994
Biliary tract cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Bladder cancer	2 (10.0%)	1 (4.0%)	3 (6.7%)	
Colon cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Colorectal cancer	5 (25.0%)	11 (44.0%)	16 (35.6%)	
Esophageal cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Kidney cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Liver cancer	2 (10.0%)	1 (4.0%)	3 (6.7%)	
Lung cancer	1 (5.0%)	1 (4.0%)	2 (4.4%)	
Prostate cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Spine cancer	1 (5.0%)	0 (0%)	1 (2.2%)	
Stomach cancer	1 (5.0%)	1 (4.0%)	2 (4.4%)	
Uterine cancer	3 (15.0%)	3 (12.0%)	6 (13.3%)	
Brain cancer	0 (0%)	1 (4.0%)	1 (2.2%)	
Breast cancer	0 (0%)	2 (8.0%)	2 (4.4%)	
Oral cancer	0 (0%)	1 (4.0%)	1 (2.2%)	
Ovarian cancer	0 (0%)	2 (8.0%)	2 (4.4%)	
Ureters cancer	0 (0%)	1 (4.0%)	1 (2.2%)	
Gender				0.566
Female	8 (40.0%)	14 (56.0%)	22 (48.9%)	
Male	12 (60.0%)	11 (44.0%)	23 (51.1%)	
Unit				0.454

Variables	ESBL negative (n = 20)	ESBL positive (n = 25)	Overall (n = 45)	*p*-value
General internal medicine	4 (20.0%)	10 (40.0%)	14 (31.1%)	
General surgery	6 (30.0%)	9 (36.0%)	15 (33.3%)	
ICU	10 (50.0%)	6 (24.0%)	16 (35.6%)	
Sample				0.958
Abscess fluid	1 (5.0%)	1 (4.0%)	2 (4.4%)	
Ascites	2 (10.0%)	5 (20.0%)	7 (15.6%)	
Biliary drainage	1 (5.0%)	1 (4.0%)	2 (4.4%)	
Blood	9 (45.0%)	7 (28.0%)	16 (35.6%)	
Colorectal drain	1 (5.0%)	0 (0%)	1 (2.2%)	
Sputum	2 (10.0%)	2 (8.0%)	4 (8.9%)	
Urine	3 (15.0%)	3 (12.0%)	6 (13.3%)	
Uterus drain	1 (5.0%)	0 (0%)	1 (2.2%)	
Surgical fluid	0 (0%)	5 (20.0%)	5 (11.1%)	
Urine drainage	0 (0%)	1 (4.0%)	1 (2.2%)	
MDR				0.0796
MDR	13 (65.0%)	23 (92.0%)	36 (80.0%)	
Non MDR	7 (35.0%)	2 (8.0%)	9 (20.0%)	

The majority of the isolates were resistant to β-lactam antimicrobial agents; the resistance rates were significantly higher than those observed in other antibiotics classes. There was a significantly different between the proportion of ESBL positive and ESBL negative resistant to cephems ($p < 0.001$). However, no significantly different was observed in other antibiotics classes (Table 4).

Table 4. Resistance rate of ESBL-positive and ESBL-negative *E. coli* strains.

Antibiotics	ESBL Negative (n = 20)	ESBL Positive (n = 25)	Overall (n = 45)	*p*-value
β-Lactams	32 (34.78)	34 (23.13)	66 (27.62)	
Ampicillin	18 (90.0%)	25 (100%)	43 (95.6%)	0.37
Amoxicillin-clavulanate	11 (55.0%)	6 (24.0%)	17 (37.8%)	0.07
Piperacillin-Tazobactam	3 (15.0%)	3 (12.0%)	6 (13.3%)	1.00
Cephems	4 (4.35)	49 (33.33)	53 (22.18)	
Cefotaxime	2 (10.0%)	25 (100%)	27 (60.0%)	<0.001
Cefepime	2 (10.0%)	24 (96.0%)	26 (57.8%)	<0.001
Carbapenems	6 (6.52)	0 (0)	6 (2.51)	

Antibiotics	ESBL Negative (n = 20)	ESBL Positive (n = 25)	Overall (n = 45)	*p*-value
Ertapenem	2 (10.0%)	0 (0%)	2 (4.4%)	0.37
Meropenem	2 (10.0%)	0 (0%)	2 (4.4%)	0.37
Imipenem	2 (10.0%)	0 (0%)	2 (4.4%)	0.37
Aminoglycosides	13 (14.13)	9 (6.12)	22 (9.21)	
Amikacin	2 (10.0%)	0 (0%)	2 (4.4%)	0.37
Gentamicin	11 (55.0%)	9 (36.0%)	20 (44.4%)	0.33
Fluoroquinolones	20 (21.74)	36 (24.49)	56 (23.43)	
Ciprofloxacin	10 (50.0%)	18 (72.0%)	28 (62.2%)	0.23
Norfloxacin	10 (50.0%)	18 (72.0%)	28 (62.2%)	0.23
Other classes	17 (18.48)	19 (12.93)	36 (15.06)	
Fosfomycin	0 (0%)	1 (4.0%)	1 (2.2%)	1.00
Nitrofurantoin	0	0	0	
Sulfamethoxazole/Trimethoprim	17 (85.0%)	18 (72.0%)	35 (77.8%)	0.50
Total	92 (100)	147 (100)	239 (100)	

4. DISCUSSION

Antibiotic resistance is currently one of the most significant public health problems, causing high mortality rates. The overuse and misuse of antibiotics cause an increase the antibiotic resistance and lead to the emergence of multidrug-resistant bacterial strains. This could lead to requiring the use of the last line of antibiotics to treat infected patients [4]. *E. coli* is one of the most common pathogens causing a diverse range of diseases affecting all age groups [5].

People with cancer may have a higher risk of infection because of changes in the immune system. *E. coli* is a normal member of the intestinal microbiota. Immunocompromised cancer patients are easily colonized by the bacteria, thus infection of cancer patients by *E. coli* is inevitable. We found that the prevalence of *E. coli* was 15.9%, which is lower than that in other reported (21.4%) [3], but lower than that in the previous reported (14.71%) [6].

The variation in prevalence might be explained by the differences in geographical location and the method to identify bacteria that might increase/or decrease culture positivity/negative rate. Besides the difference in the study population. This finding poses the need for frequent surveillance of the epidemiology of *E. coli* infection among cancer patients in Vietnam.

In this study, the highest proportion of resistance was found in β-lactam which is consistent with previously studied [2]. Among the β-lactam antibiotics, the highest resistance rate was found in ampicillin (95.56%), which is in line with the previous studies [3]. These results can be explained by the cephalosporins (β-lactam class) are

the most commonly used to treat Gram-negative bacilli infection. Besides, *E. coli* can become resistant to β-lactam by producing ESBL. About 23.43% of *E. coli* were resistant to fluoroquinolone, which is lower than the results reported elsewhere [3]. The prevalence of fluoroquinolone resistance in Gram-negative bacteria > 20%, indicates the widespread use of fluoroquinolone that would encourage multiclass drug resistance [7].

The rate of resistance to carbapenems and aminoglycosides was 2.51% and 9.21%, respectively. These resistance rates are much lower than that in other studies (15.6% resistance to carbapenems, and 37.3% resistance to aminoglycosides) [6]. These results suggested that these antibiotics are a good choice for cancer patients infected with *E. coli*.

In this study, all isolates are not resistant to nitrofurantoin, which makes this drug reasonable to treat *E. coli* infection in cancer patients. Fosfomycin, ertapenem, imipenem, meropenem, and amikacin showed a low level of resistance, suggesting that these antibiotics are considered appropriate for the empirical treatment of *E. coli* in the study area.

The development of MDR is a natural phenomenon, the number of MDR raise in immunocompromised conditions, contributing to a further spread of MDR *E. coli* [8].

The rate of MDR in the current study was 80%. This finding is higher than that in the previous reported (66.7%) [3]. MDR *E. coli* infections in cancer patients are a concern because of the restricted therapeutic antibiotic options available. We found that the rate of ESBL positive was 55.6%.

This finding is in line with previous reports [6]. MDR and ESBL-producing *E. coli* are becoming a critical global issue [5].

The ESBL-producing *E. coli* among cancer patients increases the risk of bacteremia and created important reservoirs to spread between cancer patients. MDR and ESBL bacterial infections were thus significantly associated with mortality in cancer patients. Thus, it is important to restrict the use of antibiotics in the hospital, using narrow-spectrum antibiotics based on culture reports wherever possible to reduce the rate of MDR and ESBL-producing *E. coli*, especially in cancer patients.

Our study has one limitation it was performed in a single center, which may not reflect the epidemiology of geographical areas.

5. CONCLUSION

We reported a high rate of antimicrobial resistance, ESBL positive, and MDR *E. coli* isolates from cancer patients in Vietnam. *E. coli* isolates showed high rates of resistance to Ampicillin, Sulfamethoxazole/Trimethoprim, and ceftazidime. Fosfomycin, Ertapenem, Imipenem, Meropenem, Amikacin, and Nitrofurantoin are considered appropriate for the empirical treatment of *E. coli* in the study area. These data are helpful for local antibiotics prescription practice. Further studies are needed to monitor the antibiotic-resistant *E. coli* isolated from cancer patients to help inform clinical evaluation and decision-making.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author Contributions

NQD designed the study. NTT collected the data. NTV analyzed the data and wrote the first draft of the manuscript.

NTKO edited the language. All authors read and approved the final manuscript.

Conflict of Interest:

We have no conflicts of interest to disclose.

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