

## Research Article

# Antimicrobial Susceptibility Pattern of *Escherichia Coli* (E-Coli) and Association of Infections in Immune-Compromised Cancer Patients

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**Abstract: Background:** Incidents of infections in immune-compromised patients are the cause of increased morbidity and mortality, this study aims to determine the microbial spectrum of Cancer patients with urinary tract infections, respiratory tract infections, and gastrointestinal tract infections.

**Materials and Methods:** This is a cross-sectional study conducted at a Layari General Hospital, in Karachi from March 2022 till May 2023. Patients from the oncology department were recruited in the study, Sputum, urine (mid-stream), or stool samples were collected for analysis. SPSS 22 was used to analyze the data. Effect modifiers were controlled through stratification. To assess the association between two variable mean values, a chi-square test was performed keeping the p-value  $\leq 0.05$  as significant.

**Result:** A total of 170 patients were included in the study, with a mean age of  $36.8 \pm 12.9$  years and, a mean weight of  $66.8 \pm 14.2$  kgs. Gender distribution indicated higher incidents in male patients with 95 (%) while 80 (%) females were included in the study. *Escherichia Coli* (E-Coli) was the most frequently reported organism 133 (78.2%) in Urinary tract infection, similarly *Staphylococcus aureus* was most frequently reported in Respiratory tract infection with 86 (50.4%), and *Salmonella* spp. and *Shigella* Spp. were reported with equal frequency in Gastrointestinal infection with 26 (15.6%) and 26 (15.6%) respectively.

**Conclusion:** According to this study's findings, urinary tract infections are the most frequently reported illness in immune-compromised patients, with *Escherichia Coli* (E-Coli) being the most widely reported microorganism. Broad-spectrum antibiotic overuse causes antibiotic resistance and increases illness rates.

**Keywords:** Urinary tract infection, Respiratory infection, Gastrointestinal infection, Micro-organisms, Antibiotic resistance, Gender distribution.

## INTRODUCTION

According to the World Health Organization (WHO), cancer is defined as an uncontrolled and unchecked proliferation of cells. Cancer cells can arise in any organ system and form a group of cells leading to the formation of tumors. The tumor can invade the surrounding structures as well as travel to distant sites termed metastasis. It can invade and metastasize to bone marrow which causes profound abnormality in the production of blood cells especially immune cells resulting in an immunocompromised state primarily [1, 2].

In addition to this, with the advent of the latest oncological treatment options that include chemotherapy, radiotherapy and immunotherapy, which work on inhibition of uncontrolled proliferation of cancer cells have a large number of cure rates and increased cancer-free survival among the cancer population [3]. However, the antineoplastic treatment also has adverse effects on the organ systems that include toxicity to the drugs, and allergic

reactions but most importantly they interfere with the production and function of immune cells in the bone marrow causing hematological abnormalities on peripheral blood films, especially in the neutrophils which are the frontline in the body's defense mechanism [4].

Oncological patients are highly susceptible to nosocomial and opportunistic infections due to underlying disease processes, antineoplastic therapies, and surgical interventions that lead to dysfunction in the innate and adaptive immunity which renders the immune response against pathogens [5]. Such patients develop exaggerated infections that require frequent hospital admissions, long hospital stays, and secondary treatments which cause substantial morbidity and mortality during illness. As cancer patients usually have long-term indwelling catheters, they are more prone to pathogen exposure and develop overt bloodstream infections - BSIs (which are defined as the presence of bacteria, virus, or fungal organisms in the blood culture), urinary tract infections, respiratory tract infections, and gastrointestinal infections [6]. Neutropenia defined as decreased neutrophil count in blood is highly associated with infections with death rates up to 24% in developed countries and 33% in underprivi-

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leged countries. Urgent and appropriate treatment of infection in cancer patients is the mainstay to avoid adverse events [7].

Various studies describe the risk factors, variety of pathogens, environmental factors, antimicrobial susceptibility, antibiotics selection, and range of morbidity among the patients [8]. During the past decades, the microbial pattern has profoundly varied among the oncological patients, Gram-negative bacteria were the major culprit in 1970, but gram-positive bacteria were found predominantly in 1980 [9]. Now during the last 2 decades Gram-negative bacteria again became more prevalent in adult oncological patients and Gram-positive bacteria were seen in pediatric oncological patients [10]. Some countries in Asia for example Malaysia and Pakistan witnessed the same microbial pattern among the cancer patients. Iran observed a similar pattern with gram-negative pathogens being the most common organisms in adults and gram-positive in children [5]. Similarly, many fungal pathogens especially yeasts (*Aspergillus*) and molds *Candida albicans* species are responsible for recurrent hospital admissions and cause invasive fungal infections (IFI) in cancer patients [11]. In a similar fashion, *Escherichia Coli* (E-Coli) has been cultured from the Urine samples of the patient approximately 70-95% of the time [12].

Understanding the variation in the microbial spectrum of different countries is essential to plan better management strategies for the patient as well as a selection of antibiotics to target the specific organisms. However, frequent usage of antibiotics has created antimicrobial resistance against the pathogens. Recent data from WHO has revealed that in the 20<sup>th</sup> century, antimicrobial resistance (AMR) is a substantial global health threat that requires extraordinary measures. Patients with common infections are untreatable due to the narrow spectrum of antimicrobial agents. Death rates exceed more than 700,000 per year due to drug resistance and the figure is more likely to reach ten million by 2050 [6, 9, 13].

30% of antibiotic prescriptions in the Western world are reviewed as unnecessary. In EU and EEA countries antibiotic-resistant bacteria are responsible for more than 33,000 deaths per year and 900,000 disability-adjusted years. The latest data concludes the increased incidence of resistance among the UTI pathogens particularly *Escherichia Coli* (E-Coli) due to inappropriate uses of antibiotics [9-11].

The increased risk of treatment failures emphasizes the growing role of Antimicrobial Susceptibility Testing (AST). It aims to perform rapid diagnostic investigations that identify the pathogen and test the antimicrobial resistance [4]. The ultimate goal would be the availability of the pathogen's susceptibility profile at the time of initiation of therapy so that appropriate antibiotics can be chosen from the very beginning, which aids the health-care provider in better management strategies [6, 12]. According to the latest guidelines, pure and uncontaminated samples of culture extracts are used to test the antimicrobial susceptibility. The sample matrix includes blood culture, urine culture, and sputum culture. For better and more effective antimicrobial sus-

ceptibility testing multiple cultivation rounds are done such as enrichment cultivation and plate cultivation [7].

This study aims to determine the microbial spectrum of cancer patients with urinary tract infections, respiratory tract infections, and gastrointestinal tract infections and to determine the antimicrobial susceptibility pattern of *Escherichia Coli* (E-Coli) isolated from urine samples.

## MATERIALS AND METHODS

This is a cross-sectional study conducted at a Liyari general, a public sector hospital, in Karachi from March 2022 till May 2023, with due permission from Research Ethical Committee (REC NO. LGH/REC/164). Patients from the oncology department were recruited in the study after signing informed consent in the language of understanding. The sample size was calculated with the help of the WHO sample size calculator, keeping the total registered patients in the oncology department as a population (n= 310) confidence interval of 90% and a margin of error of 10% the minimum required sample size was 170. A pre-structured questionnaire was used to collect data, demographic details, medical history, and characteristics of disease including type of cancer were documented. Sputum, urine (mid-stream), or stool samples were collected for analysis. For urine physical analysis, microscopic examination and bacteriological analysis were performed with MacConkey agar and/or cysteine lactose electrolyte deficient (CLED) and sabouraud agar. Isolated organisms were identified with the help of colony morphology, gram staining, and test for biochemical. Similarly, sputum was analyzed for physical appearance and biochemical composition, while stool specimen was analyzed for the presence of protozoa and helminths. Detection of *Cryptosporidium* was performed with the help of the modified Kinyoun method.

## STATISTICAL ANALYSIS

Statistical package for social sciences version 22 was used to enter, sort, and analyze the data. The normality of data was ensured with the help of the Shapiro Wilk Test, as the data was normally distributed the median (IQR) was not performed. Demographic details were analyzed as mean and standard deviation, while continuous variables were analyzed as frequency, percentages, and mean values. Effect modifiers were controlled through stratification. To assess the association between two variable mean values, a chi-square test was performed keeping the p-value  $\leq 0.05$  as significant.

## RESULT

A total of 170 patients were included in the study, with a mean age of  $36.8 \pm 12.9$  years and, a mean weight of  $66.8 \pm 14.2$  kgs. Gender distribution indicated higher incidents in male patients with 95 (%) while 80 (%) females were included in the study. Distribution of patients according to type of cancer indicated highest incident rate of Oral cavity cancer 53(30%), followed by breast cancer 38 (22%), Colon cancer 17 (10%), Ovarian cancer

14 (8%), Rectal cancer 11 (6%), Esophagus cancer 11 (6%), stomach cancer 8 (4%), lung cancer 6 (3%), Gallbladder cancer 5 (2%), Liver, cervix and urinary bladder cancer in 2 (1%), 2 (1%) and 2(1%) patients respectively while pancreatic cancer was identified in 1 (0.5%) patient. The highest frequency of Oral cavity cancer was identified in GI patients with 21 (12.4%) (Table 1).

**Table 1.** Distribution of Cancer within Different Infections of the Study Population.

Type of Cancer	Type of Infection			P-Value
	UTI n(%)	GI n(%)	RTI n(%)	
Oral cavity	19 (15.8)	21 (12.4)	13 (7.6)	0.821
Breast	15 (8.8)	18 (10.5)	5 (2.9)	0.095
Colon	11 (6.4)	2 (1.1)	4 (2.3)	0.536
Rectum	2 (1.1)	4 (2.3)	5 (2.9)	0.797
Ovary	6 (3.5)	7 (4.1)	1 (0.5)	0.082
Esophagus	2 (1.1)	4 (2.3)	5 (2.9)	0.412
Stomach	4 (2.3)	4 (2.3)	0(0)	0.191
Lungs	0(0)	0(0)	6 (3.5)	0.004
Gallbladder	4 (2.3)	1 (0.5)	0(0)	0.034
Liver	0(0)	0(0)	2 (1.1)	0.024
Cervix	1 (0.5)	1 (0.5)	0(0)	0.026
Pancreas	0(0)	0(0)	1 (0.5)	0.007
Urinary Bladder	1 (0.5)	1 (0.5)	0(0)	0.005

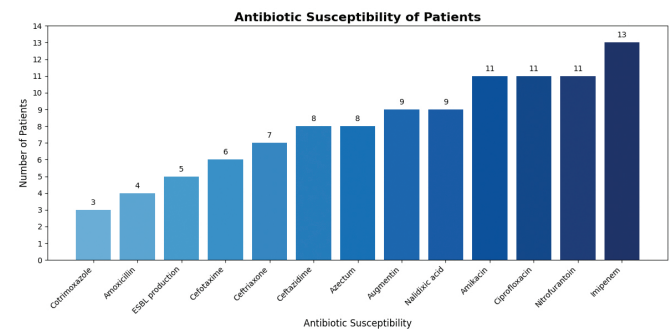
The reported organisms within different infections were distributed in three categories, *Escherichia Coli (E-Coli)* was the most frequently reported organism 133 (78.2%) in Urinary tract infection, similarly *Staphylococcus aureus* was most frequently reported in Respiratory tract infection with 86 (50.4%), and *Salmonella spp.* and *Shigella Spp.* were reported with equal frequency in Gastrointestinal infection with 26 (15.6%) and 26 (15.6%) respectively (Table 2).

**Table 2.** Frequency of Reported Organism in the Study Population.

Variables		n (%)
UTI	<i>Escherichia Coli (E-Coli)</i>	133 (78.2)
	<i>Enterococcus Faecalis</i>	5 (2.7)
	Insignificant Bacteriuria	32 (19.1)
RTI	<i>Pseudomonas Spp.</i>	21 (12.4)
	<i>Serratia Spp.</i>	21 (12.4)
	<i>Staphylococcus epidermidis</i>	21 (12.4)
	<i>Staphylococcus aureus</i>	86 (50.4)
	<i>Klebsiella Spp.</i>	21 (12.4)

GI	<i>Salmonella Spp.</i>	26 (15.6)
	<i>Shigella Spp.</i>	26 (15.6)
	No Growth	118 (68.8)

Antibiotic susceptibility identified the highest frequency of Imipenem 13 (7.6%), followed by Nitrofurantoin, Ciprofloxacin, and Amikacin with 11 (6.4%) each respectively. Cotimoxazole was the only antibiotic with the least reported resistance 3 (1.7%) (Fig. 1).



**Fig. (1).** Frequency of Antibiotic Susceptibility in the Study Population.

Assessment of Bacteria, Fungi, and parasite frequency was reported within infections reported in cancer patients of study, in urinary tract infection gram-positive and gram-negative bacteria were reported in 15(8.8%) patients, *Candida albicans* was reported in 10 (5.8%) patients and *Cryptosporidium* was not reported in UTI. Respiratory tract infection patients reported gram-positive and gram-negative bacteria prevalence in 40 (23.5%) patients, while *Candida albicans* was reported in 20 (11.7%) and no parasite was detected. The gastrointestinal infection had 10 (5.8%) *Cryptosporidium* with 20 (11.7%) gram-negative and gram-positive bacteria (Table 3).

**Table 3.** Frequency of Reported Pathogens in Infections.

Pathogens		Type of Infection			P-Value
		UTI n(%)	RTI n(%)	GI n(%)	
Bacteria	Gram -ve & +ve	15 (8.8)	40 (23.5)	20 (11.7)	0.071
Fungi	<i>Candida albicans</i>	10 (5.8)	20 (11.7)	0(0)	0.195
Parasite	<i>Cryptosporidium</i>	0(0)	0(0)	10 (5.8)	0.016

**DISCUSSION**

Infections among cancer patients pose a considerable challenge to both the healthcare provider and the patients leading to an effect on the quality of life and decreased life expectancy of patients. According to this cross-sectional study, Oral cavity malignancies are the most commonly encountered cancers consistent with a history of tobacco use, alcohol intake, betelnut

exposure, and genetic alterations. It sustains the 16th position among the malignancy worldwide. Oral cavity cancer is the most prevalent cancer in South East Asia (Pakistan, India, Bangladesh, and Sri Lanka) [11]. At the same time, breast cancer, esophageal cancer, and colorectal cancers are frequently diagnosed in the low socioeconomic population due to lack of screening and late diagnosis. Cancer-associated mortalities rise to 8% in Pakistan due to lack of timely interventions, inaccessibility of health care, inappropriate management, and superadded complications such as infections [12].

Various factors elevate the likelihood of infections among the oncological population. The predominant cause is immunosuppression which can be caused by the cancer itself or due to the adverse effects of cancer drugs. The immunosuppression induces derangement in the cellular lineage in the bone marrow and leads to a decrease in Neutrophil counts, which makes the whole body vulnerable to microbial invasion. The whole phenomenon of neutropenia is most common in hematological malignancies. Infection in the presence of a neutropenic state is called Febrile Neutropenia. In solid tumors such as oral cavity cancers, colon cancers, lung cancers, Stomach cancers, or ovarian cancers patients are not significantly immunocompromised and do not encounter prolonged periods of neutropenia. Instead, various other factors increase the risk of infections for instance Injuries and impairment to normal anatomical barriers such as mucosal surfaces and skin, Obstructive mechanism (Stasis of fluids in a closed space resulting in the proliferation of microbial pathogens) which is common in lung cancer, pancreatic cancer, colon cancers, Radiotherapy, chemotherapy, indwelling long term lines or catheters and malnutrition [13].

Typical infection sites depend upon the location of the tumor, the size of the tumor, and indwelling catheter sites. Common sites of infections include Respiratory tract infections, gastrointestinal tract infections, and surgical site infections. The epidemiological pattern of nosocomial infections has evolved, and the microorganisms responsible for these infections have transitioned from gram-positive to gram-negative pathogens over the last two decades [14].

It is imperative to formulate new strategies to counter the challenge by drawing insight from fresh epidemiological data and susceptibility patterns of organisms. The human body hosts over 100 trillion symbiotic micro-organisms which persistently inhabit various areas including skin, oral cavity, and aerodigestive tracts creating an ecosystem. There might exist a unique relationship between the microorganisms when considering the disease pathogenesis, as a growing body of evidence shows that oral bacteria can translocate to the Gastrointestinal tract via a hematogenous route or digestive pathway and can cause a variety of gastrointestinal conditions such as gastroenteritis in immunocompromised patients [15].

We encountered gastrointestinal infections being most common in patients with oral cavity cancers, breast cancers, and ovarian cancer. *Salmonella* species and *Shigella* species were the most common organisms cultured and responsible for gastrointestinal

infections. *Salmonella* are gram-negative, mobile, capable of producing hydrogen sulfide are facultative intracellular microorganisms, they are known for food poisoning around the globe and facilitate cross-infection between animal and human beings [16]. After the initial invasion, it can disseminate throughout the body via hematogenous spread and cause detrimental results in immunocompromised hosts [17]. *Salmonella typhimurium*, *Salmonella dublin*, and *Salmonella enteritidis* accounted for 75% of infections [18]. *Shigella* species are also gram-negative bacteria common in developing countries, poor sanitation and direct person-to-person contact. The high-risk group includes extreme-age populations with weakened immune responses [19].

The infectious complications in respiratory cancers are caused mainly by bacterial pathogens making up to 70% of the overall cases. Usually, there is more than one infectious agent in the course of illness, making it difficult for the physician to manage effectively. However, *Staph aureus* species are the predominant opportunistic organism [20]. Previously, *Staph aureus* was known to be an extracellular organism but it has unique properties to survive intracellularly in the tumor tissues and replicating as well. The resistant intracellular bacteria lead to secondary infections such as Pneumonia and obstructive pulmonary pathologies which result in organ dysfunction and ultimately morbidity and mortality [21]. Similarly, *Pseudomonas aeruginosa* was found to be the second most common pathogen in the immunocompromised individual consistent with the international study [22]. *Klebsiella pneumoniae* is well known for its virulence against individuals with hematological malignancies. It is also viewed as the predominant pathogen to cause serious epidemic and endemic hospital-acquired infections among the oncological population specifically in the lung cancer population [23]. Based on the result of this study, *Serratia* species are also responsible for respiratory tract infections. It gives rise to multiple different clinical presentations; pulmonary infections are rare but mainly occur in patients with weak immunological response. A correlation exists between various strains of *Serratia* and malignancy. For example; Serotype 014:H12 has been identified with upper respiratory tract samples such as sputum and nasal swabs, while serotype 013:H17 is frequently found in samples from the genitourinary tract mainly urine samples [24].

Urinary tract Infections (UTIs) are the most common presentation of sepsis in the hospital. They have a diverse variety of clinical manifestations. It can be mild and treated on an outpatient basis but some turn out to be complicated and need hospital admissions. The complicated UTIs are common in immunocompromised individuals require recurrent hospital admissions and have poor prognosis. It is crucial to define complicated UTIs, Infections that have a high risk of treatment failure due to resistant organisms that require additional workup and different antibiotics with long-term duration [23]. As per the findings of the study, there are a variety of organisms responsible for UTIs, *Escherichia Coli* (E-Coli) being the most common pathogen followed by *Enterococcus faecalis* and other gram-negative organisms. The result is consistent and by the international studies [24, 25].

In today's era of high antibiotic resistance rates, understanding the epidemiology of UTIs and antibiotic susceptibility is of paramount importance. Multiple commercial antibiotics such as imipenem, Nitrofurantoin, Ciprofloxacin, Amikacin, and Co-Trimoxazole were tested against *Escherichia Coli (E-Coli)* to check the efficacy of the drugs. We noticed resistance rates of *Escherichia Coli (E-Coli)* to amoxicillin and co-trimoxazole as also supported by the results of another study [26]. Ampicillin and Co-trimoxazole are widely used medications used for UTI and in the treatment of Respiratory and digestive tract infections. The resistance pattern is higher in developing countries, this can be explained by the inappropriate and misuse of antibiotics without proper medical prescriptions [27, 28]. The current investigation through this study reveals that Imipenem remains an effective drug against *Escherichia Coli (E-Coli)*. The low resistance against *Escherichia Coli (E-Coli)* could be secondary to the infrequent use in our population. Our results are consistent with the study done in Iran very low resistance for Imipenem, Gentamycin, and tetracycline [29]. In developed nations where more stringent policies have been implemented to oversee the sale of antimicrobial drugs, there have been significant reductions in antibiotic consumption and resistance rates [26].

## CONCLUSION

Immune-compromised patients are comparatively more susceptible to encountering respiratory tract infection, with the higher frequency of *Staph Aureus* followed by urinary tract infections and the highest frequency of *Escherichia Coli (E-Coli)*. Broad-spectrum antibiotic overuse causes antibiotic resistance and increases illness rates.

## AUTHORS' CONTRIBUTION

- **Amber Yasmeen Alvi:** Objective, Write-up.
- **Hina Faisal:** Data Collection, Data entry.
- **Azra Idris:** Data Analysis, Laboratory work-up.
- **Maliha Yasmeen:** Write-up, Ethical considerations.
- **Naseha Mushtaq:** Write-up, Results interpretation.
- **Hira Zafar Siddiqui:** Data entry, Analysis, Write-up.

## CONFLICT OF INTEREST

Declared none.

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