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The cause of antimicrobial resistant in enterobacterales pathogens displacement from patients of gastrointestinal cancer

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ABSTRACT

Background: Bacterial infections associated with multidrug resistance have been implicated in high mortality and morbidity reported among cancer patients.

Aim: The purpose of this research was to determine the function that beta-lactam played in the colonization of specific Enterobacterales strains of bacterial infection associated with MDR.

Material and Methods: Patients diagnosed with colon cancer each provided a sample of their feces, totaling forty, while the remaining fifty samples served as a control. These specimens were cultivated on MacConkey agar and kept in an incubator at 37 degrees Celsius for a period of 24 hours. Following this, antimicrobial susceptibility testing utilizing the disc diffusion technique was carried out.

Results: The analysis revealed that 40 out of the 50 samples had a positive outcome. It appear that Escherichia coli and Klebsiella pneumonia were the most common bacteria that were isolated, and the results revealed that the most of bacterial isolates exhibited resistance to Beta –lactam antibiotics.

Conclusion: All of the bacteria that were isolated and analyzed were MDR (Multiple drug resistance). Consequently, these organisms constitute a difficult treatment challenge for those who have Gastrointestinal cancer.

Key words: colorectal cancer, specific enterobacterales, multi drug resistance, beta-lactamase

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INTRODUCTION

Cancer of Gastrointestinal tract is sometimes referred to as colon cancer, rectal cancer, and colorectal cancer. Bowel cancer is another name for this kind of cancer. There is a broad variety of possible signs and symptoms, some of which include blood in the stool, changes in bowel motions, a loss of weight, and exhaustion. Other possible signs and symptoms include. Patients who come from families where colorectal cancer has been diagnosed in the past have a greater likelihood of having the illness themselves. It is imperative that you undergo testing to establish whether or not you have inflammatory bowel disease, a group of conditions that includes Crohn's disease and ulcerative colitis in addition to other conditions that exhibit similar symptoms [1]. It has been established that there is a connection between the three variables, which results in an increased chance of getting colorectal cancer. This increased risk is connected with both hereditary non-polyposis colon cancer and familial adenomatous polyposis colon cancer [2].

The increasing prevalence of antibiotic resistance in disease-causing organisms has become a worldwide problem that has significant ramifications for the treatment of infectious diseases. These repercussions have the potential to significantly impact the healthcare industry. This issue is a direct consequence of the proliferation of superbugs, which are bacteria that are responsible for the transmission of infectious illnesses [3]. It is possible that a significant portion of the issue may be traced back to an increase in the inappropriate use of antibiotics in human health care, agricultural operations, and veterinary care. This resistance is the result of bacteria not responding to treatment with antibiotics [4]. This has resulted in the dynamic and persistent creation and mutation of lactamases, which has resulted in an increase in their activity even against freshly developed-lactam antibiotics. This is because bacterial strains are continually exposed to a broad range of lactam antibiotics [5, 6]. In addition to this, this has led to a rise in the number of bacterial strains that are resistant to lactam antibiotics, which has caused an increase in the prevalence of resistant infections. The proper terminology for these particular enzymes calls for them to be referred to as Extended-Spectrum -Lactamases (ESBLs) [7]. Cancer s' patients persistent Enterobacterales stains continue to be a source of inflammation ,there has been a rise in the number of bacteria that are resistant to the drug [8, 9].

The production of Extended-Spectrum Beta-Lactamases (ESBLs) is a prominent resistance mechanism that hinders antimicrobial

therapy of infections caused by Enterobacterales and poses a severe threat to the antibiotic arsenal that is currently available [10]. There is a considerable correlation between inflammatory bowel disease of the colon and chronic inflammation, which is associated to a number of diseases that are considered to be cancerous. Currently thought to be the most effective medications for treating infections caused by these bacteria [11, 12].

MATERIALS AND METHODS

Samples collection

It was forty stool samples from patients who had colon cancer most of them got chemotherapy and 50 stool samples from healthy controls, in a period from October 2020 to October 2022 Table 1. Samples stored in portable containers, labile and transport to the laboratory. The healthy controls would serve as a comparison group. After arriving at the site, the samples were insulated on Blood agar, SS agar, and MacConkey and specify before being put into an incubator with the temperature set to 37 degrees Celsius for a period of twenty-four hours. In order to identify the species of bacteria that were isolated from the different samples, traditional morphological and biochemical diagnostic tests were used [13]. Escherichia coli ATCC 25922, and Klebsiella Pneumonia ATCC 700603 were used as quality control strains

Isolation and Identification

Isolates were then retained on specific media until additional tests, such as urease and ONPG test; these tests include Sion citrate, SI citrate, Indole. Kligler iron agar, and urease and Biochemical test .It was confirmed via morphological and biochemical investigation that all five of the bacterial kinds belong to the group of bacteria known as Gram-negative bacteria (Escherichia coli, Klebsiella spp., Proteus spp., Enterobacter spp., Pseudomonas aeruginosa [14]. Before determining whether or not an organism was sensitive to a certain antimicrobial agent, the colonies were first suspended in 4-5 milliliters of brain heart infusion. The agar disc diffusion technique that Bauer et al. published was used in the testing that was carried out [15].

Colonies obtained from a young bacterial culture that had been developed on Blood agar and MacConkey agar were treated with 1;100 of penicillin G for bacterial growth inhibition [16].

Disc diffusion using 30 micrograms of cefotaxime, ceftazidime, ceftriaxone, and aztreonam of each antibiotic was originally used to test for the generation of extended range beta-lactamase resistant isolates. In accordance with the guidelines established by the CLSI, these antibiotics were spread over plates that already contained Muller-Hinton agar before being inoculated. After an incubation period of 18 hours at 37 degrees Celsius, the sizes of the inhibition zones around the antibiotics were measured using a ruler. Isolates that displayed an inhibitory zone of less than 26 millimetres for cefotaxime, less than 20 millimetres for ceftazidime, less than 24 millimetres for ceftriaxone, and less than 25 millimetres for aztreonam. This was the working hypothesis [17].

Statistical analysis

The statistical analysis was performed using the Chi-square (X2) test, and the point at which the p-value was considered to be significant was decided to be when it was less than ($p>0.01$) [18].

RESULTS AND DISCUSSION

On MacConkey agar, (77.8%) of 40 stool samples were positive for culture, while (22.2%) were negative. The statistical analysis showed that there were differences that were statistically significant.

According to Table 2, the results of this inquiry, a total of 22 out of the 36 *E. coli* isolates studied showed resistance to both the antibiotic Amikacin and the antibiotic Augmentin. This conclusion was based on the findings of the investigation [19].

All thirteen Klebsiella spp. isolates tested positive for resistance to the antibiotics amikacin and Augmentin, as shown by the findings that have been provided in this study. A success of one hundred percent is represented by this value [20]. The statistical analysis showed that there were discernable differences ($p>0.01$ for each of the isolates that were researched and tested) between samples was collected. This relatively high ratio is comparable to some local studies, which revealed that (100%) Klebsiella isolates were resistant to both amikacin and amoxicillin, and Al-Muhannal, who reported that 93.7% of Klebsiella isolates were resistant to both antibiotics, and AL-Hilli, who said that 89.4% of Klebsiella isolates had-lactam resistance [21, 22]. All of These three researchers came to the same conclusion. The aggregation of the findings from these investigations indicates that the collection of

Tab. 1. Distribution of Isolated bacteria from Colon cancer Patient

	Bacterial Isolates	N0. (%)
1	*Escherichia coli*	23 (50.0%)
2	*Klebsiella pneumonia*	5 (19.2%)
3	*Klebsiella oxytocic*	1 (3,85%)
4	*Proteus Spp.*	5 (15.4%)
5	*Enterobacter spp*	4 (0.0%)
6	*Pseudomonas aerogenosa*	12 (100%)
Total		**50**

Tab. 2. β -lactamase resistance of *E.coli* and *Klebsiella* spp. isolated from Colon Cancer

Bacterial Isolate	N0. of isolates	N0.(%)of isolated resistances
Escherichia Coli	23	19(85.6%)
KLEBSIELLA Spp.	13	13 (92.8 %)
Total	36	32(88.8 %)

Cal $X^2 = 0.365$
Tab.$X^2 = 0.004$
df=1
p-value=0.0949

data that has accumulated as a result of these studies demonstrates that each and every one of these academics, when considered together [23].

According to the results of this particular study, the Klebsiella isolates exhibited a degree of resistance to cephalosporin of the third generation that was between low and moderate, table 3 reveals that 46.1% of the isolates were resistant to ceftazidime, 61.5% of these isolates were resistant to ceftriaxone, and 53.8% of these isolates were resistant to cefotaxime. Additionally, the table 3 shows that out of 19 *E. coli* isolates, only 11 (57.9%) generated. Using the raped test, we found that only eight out of the thirteen Klebsiella spp. isolates were positive (representing 61.3% of the total). The results of a statistical comparison showed that there was difference ($p>0.01$) among the isolates that were tested.

Table 3 shows the high-level resistance against many antibiotics in the present study may be as a result of both intrinsic and acquired mechanisms. This resistance is widespread and constitutes serious clinical threats.

Table 4 shows that the majority of tested Klebsiella isolates were resistant to Augmentin. It was also clear from this table that all Klebsiella isolates were sensitive ciprofloxacin.

Because chemotherapy treatment to a patient's of lowers immune system, infection is a major concern for cancer patients who are immunocompromised. There has been a recent rise in the number of diseases that are caused by organisms that are resistant to beta-lactam antibiotics that are widely used to treat them. This resistance is a direct consequence of the discovery of new enzymes, which have been the cause of the enzymes' development. This resistance has arisen as a direct result of the fact that the organisms in question have been able to avoid the antibiotics' curative effects. Stool samples taken from cancer patients virtually usually include *E. coli* and Klebsiella bacteria that have been. Additionally, all of the *E. coli* and Klebsiella isolate which were examined shown resistance to more than one antibiotic; As a result, such germs pose a significant barrier to the treatment of cancer patients. In Iraq, research initiatives are now being carried out in an effort to isolating and establishing the identification of the bacteria that are associated to tumor cells isolates. Plasmids inside bacteria are the carriers of ESBLs, which may then be passed on to other types of bacteria [24]. Several other families of Extended-Spectrum Beta-Lactamases (ESBLs) have been identified in Enterobacterales

Tab. 3. Antibiotics discs used in this study with their Remarks for *E.coli* (n-23) from colon cancer patients

Types of antibiotic	No. (%) of Resistant Isolates	No. (%) of Intermediate Isolates	No. (%) of Sensitive Isolates
Amikacin	1 (5.3 %)	0 (0.0 %)	18 (94.7 %)
Augmenten	16 (84.21 %)	3 (15.79 %)	0 (0.0 %)
Azteronam	13 (68.4	3 (15.79 %)	3 (15.8 %)
Cefotaxime	14 (73.7 %)	1 (5.26 %)	4 (21.0 %)
Cefoxitin	8 (42 %)	1 (5.26 %)	10 (52.6 %)
Ceftazidime	5 (31.6 %)	2 (10.53 %)	12 (63.2 %)
Ceftriaxone	14 (73.7 %)	1 (5.26 %)	4 (21.0 %)
Chloramphenic l	1 (5.26 %)	2 (5.26%)	16 (84.2 %)
Cifixime	10 (52.6 %)	2 (10.53 %)	7(36.8 %)
Cefepime	15(78.9%)	1 (5.26 %)	3 (15.8 %)
Ciprofloxacin	11 (57.9 %)	2 (10.53 %)	6 (31.6 %)
Co-trimoxazole	9 (47.4 %)	0 (0.0 %)	10 (52.6 %)
Gentamycin	9 (47.4 %)	1 (5.26 %)	9 (47.4 %)
Nalidixic	8 (42.1 %)	2 (10.53 %)	9 (47.4 %)
Pipracillin	17(89.5 %)	1 (5.26 %)	2 (10.5 %)
Rifampine	7 (36.8 %)	0 (0.0 %)	12 (63.2 %)
Tetracycline	10 (52.6%)	1 (5.26 %)	8 (42.1 %)
Trimethoprim	8 (42.1%)	2 (10.35 %)	9 (47.4 %)

Tab. 4. Antibiotics discs used in this study with their Remarks for Klebsiella SPP (n=13)

Types of antibiotic	No. (%) of High Resistant Isolates	No. (%) of Intermediate Isolates	No. (%) of Sensitive Isolates
Amikacin	1 (7.69 %)	0 (0.0 %)	12 (92.33 %)
Augmentin	12 (92.3 %)	1 (7.69 %)	0 (0.0 %)
Azteronam	7 (61.0 %)	0 (0.0 %)	5(38.5 %)
Cefotaxime	7 (53.8 %)	0 (0.0 %)	4 (21.0 %)
Cefoxitin	5 (38.5 %)	0 (0.0 %)	6 (46.15 %)
Ceftazidime	6 (46.1 %)	1 (7.69 %)	8 (46.15 %)
Ceftriaxone	8 (61.51 %)	0 (0.0 %)	6 (21.0 %)
Chloramphenicol	1 (7.69 %)	0 (0.0 %)	12 (92.31 %)
Cifixime	9 (69.2 %).	8 (0.0 %)	4 (30. 8 %)
Cefepime	9 (47.4 %)	1 (7.69 %)	3(23.1%)
Ciprofloxacin	0 (0.0 %)	0 (0.0 %)	13 (100 %)
Co-trimoxazole	8 (61.5 %))	0 (0.0 %)	5 (38.46 %
Gentamycin	10 (76.9 %)	0 (0.0 %)	3(23.1%)
Nalidixic	3 (23.1 %)	4 (30.78 %)	6 (46.15 %)
Pipracillin	11 (84.6 %)	2 (15.38 %)	0 (0.0 %)
Rifampine	10 (76.9 %)	0 (0.0 %)	3(23.1%)
Tetracycline	9 (69.2%)	0 (0.0 %)	4 (30.78 %)
Trimethoprim	8 (61.5 %)	0 (0.0 %)	5 (38.46 %)

strains, the most prevalent of which are CTX-M, TEM, and SHV beta-lactamases [25]. Although ESBL-PE bacteria are often resistant to the majority of beta-lactam antibiotics, carbapenems are it is becoming more common for bacterial isolates to demonstrate antibiotic resistance, which is related with significant clinical consequences. This is important since antibiotic resistance is linked with the spread of disease. It is possible that any one of the following fourprocesses-selection, mutation, phage transduction, or transference-could be responsible for the final evolution of antibiotic resistance. It is possible for an organism to acquire resistance to germs either via its genes or by interaction with the bacteria that are present in its environment [26]. The development of TEM-lactamases, which may be genetically situated on the chromosome or on a plasmid, is most likely the origin of -lactam resistance in *E. coli* isolates. This resistance may be passed on from generation to generation. There is some speculation that plasmids play a role in the transmission of this resistance. Depending on whether component is present, the genetic code for this resistance might be found on either the chromosome or the plasmid [27]. It is thought that TEM-1 is responsible for as much as ninety percent of the ampicillin resistance that *E. coli* demonstrates. Beta-lactamase known as TEM-1 is one that has been discovered inside Gram-negative bacteria is the most often.

CONCLUSION

All of the bacteria that were isolated and analyzed were MDR. Consequently, these organisms constitute a difficult treatment challenge for those who have cancer.

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