Egyptian Journal of Medical Microbiology Volume 33 / No.3 / July 2024 87-93 Online ISSN: 2537-0979

ORIGINAL ARTICLE

Evaluation of Manually Prepared Colistin Agar Performance against Gram Negative Organisms of Infected Cancer Patients in Egypt

[1]Dina M. Bassiouny*, [2]Noha K. Mohammed, [1]Nada N.Nawar, [2]Samah M. Radwan
[1]Department of Clinical and Chemical Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt
[2]Department of Clinical and Chemical Pathology, National Cancer Institute, Cairo University, Cairo, Egypt

Key words:
Infection; Cancer; Colistin; Agar Dilution

Corresponding Author:
Dina Mahmoud Bassiouny
1 Al-Saray St., Al-Manial, Clinical and Chemical Pathology Department
Faculty of Medicine, Cairo University, Cairo 11559, Egypt
Egypt
Tel.: +01003818063
dinabassiouny009@gmail.com

ABSTRACT

Introduction: *Cancer patients are more vulnerable to infections because of changes affecting their immune system due to the cancer itself or the cancer treatment modalities, including surgery, radiation therapy, immunotherapy, and chemotherapy, either alone or in combination.* ***Objectives:*** *The study aimed to determine the rate and the type of infections in cancer patients during the cancer treatment journey and to evaluate the performance of the agar dilution method in testing for Colistin sensitivity by comparing automated and manual testing results.* ***Methods:*** *We conducted a cross-sectional study over 6 months, including 193 patients diagnosed with hematological and non-hematological malignancies and admitted to The National Cancer Institute, Cairo University. Collected data included demographic data of enrolled patients, prescribed antibiotics, lab investigations, cancer treatment &/or surgery. Microbiological data were collected and included types of samples, cultures requested, and isolated organisms with antibiotic susceptibility testing results, especially Colistin MIC and resistance pattern. Colistin agar was prepared and used for testing isolates against Colistin using three concentrations of Colistin Sulphate (4ug/L, 2ug/L, and 1ug/L).* ***Results:*** *Testing for Colistin sensitivity by MIC and agar dilution method showed a statistically significant association with a P value (<0.001).****Conclusion:*** *The agar dilution can be used as a manually accepted method to test for Colistin sensitivity.*

INTRODUCTION

People with cancer are often at a higher risk of infection because of immunosuppression caused by cancer treatment modalities. Cancer treatments, including surgery, radiotherapy, and chemotherapy, can cause short-term or long-term immune system damage[1].

Infections with gram-negative organisms are the most commonly seen in cancer patients[2].

Virulence of infecting organisms is getting more vigorous nowadays, leading to the use of advanced antibiotics such as Colistin to overcome the resistance to other antibiotics[3].

Poor diffusion of Colistin disc through Muller Hinton agar has made disc diffusion unreliable for testing Colistin susceptibility, leading to the use of the more expensive methods of testing that measure the minimal inhibitory concentration (MIC) of the drug by E-test or automated analyzers. Such methods carry more financial burden on countries with limited resources and a large population[4].

Manual methods of Colistin sensitivity testing include many ways, with a unique and easy method called Colistin agar dilution[5].

The present study aimed at preparing the Colistin agar manually in the lab and comparing the results of Colistin sensitivity of the tested isolates with the MIC measured by Vitek2 Compact to evaluate the performance of Colistin agar dilution method to be applied in routine daily work providing the best outcome with fewer expenses achieving the best cost-benefit balance[6].

METHODOLOGY

Setting:

National Cancer Institute and Kasr Al Ainy Hospitals, Cairo University.

Ethical approval:

The study was approved by the Ethical Committee of the Faculty of Medicine at Cairo University in 2021 with serial number MS 344-2021

Study population

Our target population was cancer patients clinically suspected to be infected with signs &/or symptoms of infection.

Methodology and Data Collection

Data from the study included patients (n=193) were collected and included demographics, clinical and

investigational data including diagnosis, chronic illnesses, symptoms and signs of infection as core body temperature, laboratory investigations including inflammatory markers, WBCs, absolute neutrophilic count, and hemoglobin. Data about administered antibiotics, type of cancer treatment according to the applied guidelines and type of surgery if any, were collected as well.

Additional data from 110 samples that revealed gram-negative organisms were collected, including the types of samples, cultures requested, isolated organisms, antibiotic susceptibility testing (AST) results, especially Colistin MIC with interpretation, and resistance pattern.

Microbiological Identification

Identification and AST were done on the included isolates.

Gram-negative isolates were identified using standard laboratory methods, including Gram-stain, colony morphology, and automated methods using the **VITEK 2 Compact**, and then stored at -80 degrees preserved on glycerol broth for further testing of Colistin sensitivity using Colistin agar dilution.

The VITEK 2 Compact system was used for identification (ID) and AST of isolated micro-organisms using ID cards (ID-GN) and AST cards (GN222)[7].

Colistin Agar Dilution

Colistin agar was prepared in the lab according to CLSI of 2021 guidelines, which stated the preparation of 3 different concentrations of Colistin Sulphate agar (C1, C2, and C3). Where C1 Concentration is equivalent to 4ug/L, C2 Concentration is equivalent to 2ug/ L and C3 Concentration is equivalent to 1ug/L[8].

Royal Colistin 500 powder, produced by Egypt Med Company, was used in the preparation of Colistin agar. Each 100 gm of the powder contained 20.75 gm of Colistin Sulphate.

All three concentrations, C1, C2, and C3, were poured on Petri dishes and tested for sterility and performance by positive and negative controls in the form of colistin-sensitive and resistant strains, including *Proteus spp*. that is intrinsically resistant to Colistin and Colistin sensitive *Pseudomonas aeruginosa ATCC* strain 28753[8].

A subculture of 110 gram-negative isolates was prepared, and 0.5 Mcfarland suspension was done of each isolate for inoculation on the three different concentrations of Colistin agar, incubated for 24 hours at 37° degrees, and inspected the next day under illumination for any visible growth[8].

Interpretation of results was made taking into consideration CLSI guidelines and EUCAST guidelines to get the best benefit of the two opinions considering that no colony growth on any of three concentrations as Colistin sensitive and one colony growth on the three concentrations is considered resistant with intermediate sensitivity reported in case of C3 growth with no growth on C1and C2 concentrations[8, 9].

Statistical Methods:

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data were summarized using mean and standard deviation in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test[10]. For comparing categorical data, the Chi-square (c2) test was performed. The exact test was applied as an alternative when the expected frequency was less than 5[11]. P-values less than 0.05 were considered statistically significant.

RESULTS

The study conducted on 193 cancer patients with signs and symptoms of infection at the National Cancer Institute, Cairo University, revealed 110 gram negative organisms. The isolated gram negative organisms were further tested for Colistin sensitivity by Vitek2 Compact and compared to lab-made Colistin agar testing.

Our study included 122 males (63.21%) and 71 females (36.78%), with an adult percentage of 43.52% and a pediatric percentage of 56.47%

Chemotherapy was administered in 79.79 % (n= 154/ 193), and surgery was done in 26.42% (n= 51/193) of included patients.

Infections caused by gram-negative bacteria were 56.9% of included patients (n=110/193).

Fever was documented in 95.85% (n= 185/193) of included patients, while TLC showed variations with a normal range in 18.6 %, leukocytosis in 15.02 %, and leucopenia in 66.32 % of total infected patients. Anemia was reported in 89.6 % of the total included patients (n= 173/193) and thrombocytopenia was found in 47.2 % of total enrolled patients (n=91/193)

Both Patients with hematological and non-hematological tumors suffered from infections with a percentage of 68% (n=131/193) in patients with hematological tumors (wound infections 4.58%, bloodstream infections 83.96 %, and respiratory tract infections 9.16 %, urinary tract infections 1.526%) and 32% (n=62/193) in patients with non-hematological tumors with infections percentage (wound infections 19.35%, bloodstream infections 62.9, respiratory tract infections 6.45%, urinary tract infections 11.29, GIT infections 0.76 %).

The most common type of infection was bloodstream infection, with a percentage of 77.2% of all enrolled patients.

The most common isolated gram-negative organisms were *E-coli*: 24.35% (n=47/193), followed by *Klebsiella spp* with a percentage of 14.5% (n=28/193). Other considerable organisms included *Pseudomonas spp*: 7.77 % (n=15/193), *Acinetobacter spp*: 4.66% (n=9/193), *Enterobacter cloacae spp*: 2.5 % (n=5/193),

Enterobacter aerogenes: 1.03% (n=2/193), *Morganella morganii*:1.5 % (n=3/193), *Salmonella*:0.51% (n=1/193)

The most common isolated gram-positive organism was *Staphylococcus aureus*, with a percentage of 30.56% (n=59/193)

The association between infection and age was statistically significant, with a p-value <0.001, showing the highest mean age of 48 years for patients who suffered from urinary tract infections and the lowest mean age of 18 years for patients who suffered from bloodstream infections. Table (1)

Table 1: Association between Infection and Age (n=193)

		Age (years)					
		Mean	**Standard Deviation**	**Median**	**Minimum**	**Maximum**	**P value**
Infection	**Blood stream infection** 77.2% (n=149/193)	18.25	19.29	11.00	0.25	73.00	< 0.001
	GIT infection 0.5% (n=1/193)	33.00	.	33.00	33.00	33.00	
	respiratory tract infection 8.3% (n=16/193)	37.44	12.56	37.50	18.00	64.00	
	urinary tract infection 4.7% (n=9/193)	48.33	25.49	59.00	3.00	73.00	
	wound infection 9.3% (n=18/193)	39.56	22.93	43.50	2.00	68.00	

Colistin sensitivity testing was done for all gram-negative organisms (n=110) by both MIC measurement using Vitek2 Compact and Colistin agar dilution. Automated testing showed sensitivity to Colistin with a percentage of 96.36 % (n= 106/110), while the agar dilution method showed sensitivity with a percentage of 92.72% (n= 102/110).

MIC for other antibiotics detected by Vitek2 Compact showed the following results: Carbapenem resistance with a percentage of 66.839% in total patients included in the study (n=129/193) and 63.63% in patients with gram-negative infections validation (n=70/110), Aminoglycosides resistance percentage: 30.05 % of total number of patients included in the study (n=58/193) and 34.54% among gram-negative infections (n=38/110), Cephalosporin resistance percentage: 85.49 % in total number of patients included in the study (n=165/193) and 90% among gram-negative infections (n=99/110), Colistin agar sensitivity according to the site of gram-negative infection (n=110) was: 96 % in bloodstream infections, 100 % in GIT infections, 85.7 % in respiratory infections, 88.9 % in Urinary tract infections and 85 % in wound infections.

Organisms that showed 100% sensitivity to Colistin, detected by the Colistin agar dilution method, were *E-coli spp*, *Enterobacter aerogenes*, *Acinetobacter spp*, *and Pseudomonas spp*, *Salmonella*, followed by *Klebsiella spp* that showed sensitivity with a percentage of 88.9 %. Organisms that showed lesser Sensitivity to Colsitin included *Enterobacter cloacae spp* with a sensitivity percentage of 80 %, while *Proteus app was* resistant to Colistin due to intrinsic resistance to Polymixins (Figure 1).

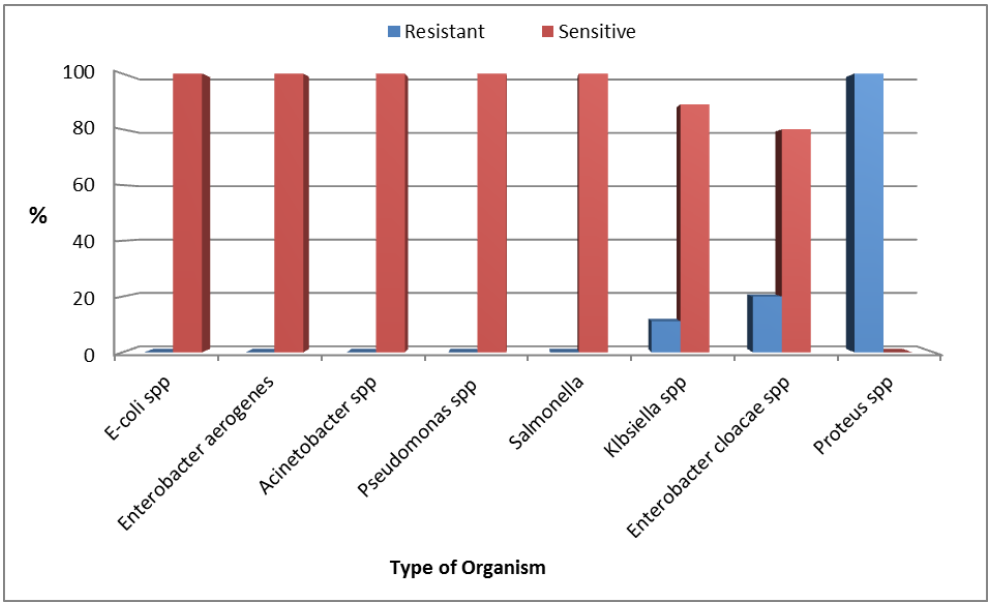

Fig. 1: Result of Colistin sensitivity by Agar Dilution Method (n=110)

The most common gram-negative isolated organism from patients with hematological and non-hematological malignancies was *E-coli*, with a percentage of 26.7 % in hematological malignancies and 19.4 % in non-hematological malignancies.

Bloodstream infections were more common in hematological cancers than non-hematological cancers, with percentages of 84% and 62.9 %, respectively.

Respiratory tract infections were more common in hematological cancers than non-hematological cancers, with percentages of 9.6% and 6.5%, respectively.

On the other hand, urinary tract infections were more common in non-hematological malignancies than hematological malignancies, with percentages of 11.3% and 1.5 %, while wound infections were more common in non-hematological malignancies than hematological malignancies, with percentages of 19.4% and 4.6 %.

Resistance to Colistin was detected the most in wound infections, with a percentage of 16.7% of the total number of wound infections (n=3/18), followed by urinary tract infections at 11.1 % (n=1/9), then respiratory tract infections at 6.3 % (n=1/16), and Bloodstream infections with a percentage of 2 %(n=3/149), resulting in a significant relation between infection and Colistin resistance with P value 0.025. (Figure (2)

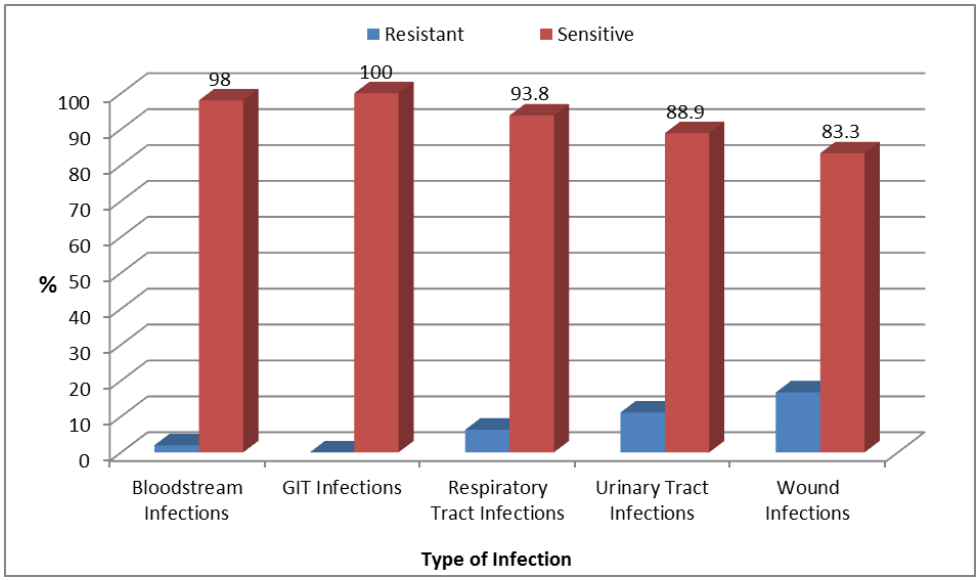

Fig. 2: Relation between Type of Infection and Colistin Resistance/Sensitivity (n=193)

Patients with gram-negative infections showed outcomes of improvement with a percentage of (63.6%) (n=70/110) and worsened outcomes with a percentage of (36.4%) (n=40/110).

Cases whose infections showed sensitivity to Colistin tested by agar dilution method were improved with a percentage of 67.6 % (n=69/102) and a percentage of 62.7 of the total number of patients with gram-negative infections (n=69/110), while Colistin sensitive cases that showed worsened outcome were 32.4 % (n=33/102) and 30% (n=33/110) of the total number of patients with gram-negative infections.

On the other hand, cases whose infections showed Colistin resistance tested by agar dilution method, had an improved outcome with a percentage of 12.5 % (n=1/8) and 1% of the total number of patients with gram-negative infections (n=1/110), while worsened outcome was reported in 87.5 % of Colistin resistant cases (n=7/8) and a percentage of 6.3% of the total number of patients with gram-negative infections (n=7/110).

The association between Colistin testing detected by agar dilution method and patients' outcome was statistically significant with a P value of 0.003.

Testing for Colistin sensitivity by MIC and agar dilution method showed a statistically significant Association with a P value (<0.001).Table (2)

Table 2: Association between Colistin MIC and Colistin Agar Result

		Result of Colistin Sulphate Agar Sensitivity				
		Sensitive		Resistant		P value
		Count	%	Count	%	
Result of Colistin Sensitivity by Vitek2 Compact	**S (MIC < or equal 1)**	102	100.0%	4	50.0%	< 0.001
	R (MIC > 4)	0	0.0%	4	50.0%	

According to the infection type, BSI showed improvement in 64.1 % of total BSI cases, 100% of GIT infection cases improved, respiratory tract infections showed improvement in 28.6 % of total cases of respiratory infections, urinary tract infections showed improvement in 66.7 % of the total urinary tract infection cases, and wound infections showed improvement in 73.3 % of total cases of wound infections.

The association between type of infection and patients' outcome was statistically insignificant (P value 0.308).

DISCUSSION

Infection is considered one of the main factors leading to morbidity and mortality. Cancer patients are more vulnerable to infections due to immunosuppression as a result of cancer itself or its treatment[1].

Bacterial BSI has a higher incidence in cancer patients with hematological and non-hematological malignancies due to chemotherapy-induced neutropenia[1].

Infection with gram-negative bacteria has been considered a worldwide phenomenon, increasing mortality rate and narrowing treatment options[2].

Our study was conducted on 193 cancer patients with signs and symptoms of infection at the National Cancer Institute Cairo University.

Our study included 122 males (63.21%) and 71 females (36.78%). The age of patients ranged from (3 months to 73 years) with a median age of 16 years, which was similar to a study conducted between January 2016 and June 2017 at the National Cancer Institute, Cairo University, Egypt, which discussed colistin resistance in klebsiella in cancer patients, 56% were males and 44% were females with age ranges from 1 to < 18 years, (pediatrics) were 37%, ≤ 55 years were 35% and > 55 years was 28%[12].

In our study, patients with hematological malignancies represented 68 %, and patients with solid tumors represented 32 % of included patients. These percentages were different from those of a study conducted at Chiang Mai University Hospital (CMUH) in Thailand that discussed Colistin treatment in Carbapenem-resistant *Acinetobacter baumannii* (CRAB) in cancer patients, where hematological malignancies constituted 13.09 % and solid malignancies constituted 86.9 % of the study included patients[13], and this contrast can be explained that the NCI branch, where our study was conducted, was dedicated mainly for hematological cancers.

Patients included in our study suffered mainly from infections caused by gram-negative bacteria with a percentage of (56.9%) which was near to a similar study conducted in the Department of Oncology of Kasturba Medical College Hospital (KMCHA), Mangalore that reported a percentage of 69.9% of cancer patients with gram-negative infections[14].

In our study the most common type of infection was blood stream infection, which was 77.2% of total infections, which is similar to a study conducted at the National Cancer Institute, Cairo University, Egypt

which discussed colistin resistance in *klebsiella spp* among cancer patients where blood stream infections were the most common with percentage 58% [12].

In our study the most common type of infection was blood stream infection which was 77.2% of total infections, which is similar to a study conducted at the National Cancer Institute, Cairo University, Egypt which discussed colistin resistance in *klebsiella spp* among cancer patients where blood stream infections were the most common with percentage 58%[12].

In our study the most common isolated gram-negative organisms were *E-coli*: 24.35%, followed by *Klebsiella spp* with a percentage of 14.5% that were near to a similar study done in Children's Cancer Hospital Egypt 57357, that discussed safety of Colistin therapy in pediatric cancer patients and showed *Escherichia coli*, being the most common, with a percentage of 60.2% followed by *Klebsiella Spp* with a percentage of 26.3% [15]. Another similar study done at NCI, Cairo University discussed Gram negative pathogens in febrile neutropenic patients revealed E. coli in 38.6% and *Klebsiella pneumoniae* in 34.3% of cases [16].

In our study Colistin sensitivity testing by MIC measurements using vitek2 Compact revealed a sensitivity rate of 96.36 % while Colistin sensitivity by Colistin agar was 92.72% and that was similar to a study conducted in Tata Medical center (TMC) in Kolkata in 2017 in which Vitek2 Compact MIC results showed a higher sensitivity rate to Colistin than the E test Strip with agreement with broth micro dilution method in percentages of 94 % and 93% respectively [17].

Colistin sensitive strains tested by both Vitek2 Compact and agar dilution method reported percentages 96.36 % and 92.72% with more reliable results of agar dilution method according to patients' condition and that was similar to a study conducted in Amsterdam between 2013 and 2017 that showed Very major error (VME) rate for VITEK® 2 alone that was 30.6% and was reduced to 10.2% using the VITEK® 2/Agar Dilution (AD) combined testing. The combined testing had agreement with BMD of 97 % [18].

Other antibiotics' MIC was detected using Vitek2 Compact and showed the following results: Carbapenem resistance in a percentage of 63.63% that was lower than a study conducted in Tata medical center (TMC) in Kolkata that detected Meropenem resistance in 79.7% of tested isolates [17].

Aminoglycosides resistance percentage: 30.05 % (n=58/193) (but in 110 cancer patients with gram negative infections it was 34.54%). (n= 38/110), Cephalosporin resistance percentage: 85.49 % (n=165/193) (but in 110 cancer patients with gram negative infections it was 90%). (n=99/110), Quinolones resistance percentage: 63.21% (n=122/193) (but in 110 cancer patients with gram negative infections it was 74.54%). (n= 82/110). In similar study conducted at NCI, Cairo university discuss Colistin resistance in cancer patients also showed antibiotic sensitivity by Vitek and showed the following results resistance to Carbapenems (meropenem 53.5%), resistance to Aminoglycosides (Gentamycin 45 % and Amikan 35 %), resistance to Quinolones (Levofloxacin 73.5 %, Ciprofloxacin 71 .5 %), resistance to Cephalosporins (Cefazolin 92 % , ceftriaxone 91 %, Ceftazidime 89 %, Cefepime 86.5%), As tested by broth micro dilution resistance to colistin (8.8%) , E-tests showed that 8% were Colistin-resistant [12].

The most common gram positive isolated organism was *Staphylococcus aureus* in a percentage of 27.5 % in hematological malignancies and 37.1 % in non-hematological malignancies and most common gram negative organism was *E-coli* with percentage 26.7 % in hematological malignancies and 19.4 % in non-hematological malignancies. That was near to a study conducted at University of Gondar comprehensive specialized hospital, Ethiopia where regardless to type of cancer S. *aureus* was the predominant gram-positive isolate, (51.5.6%) [19].

CONCLUSIONS

At the end of our study, we can say that infections in cancer patients can be very challenging due to several factors.

Colistin as an advanced antibiotic, used in the treatment of such infections, should have more attention to use, dosage, and testing methods.

Comparison between MIC testing using automated systems and the agar dilution method showed significant results with promising outcomes of the agar dilution testing method.

The agar dilution method for testing Colistin sensitivity is considered a reliable and affordable testing method that can be applied on a wider scale.

To conclude our study, we recommend the following:

- Application of Comparative study between agar dilutions, automated MIC testing, and broth micro-dilution on a wider scale with a bigger sample size and different clinical diagnoses of involved patients to get a clearer image of all testing methods.
- Scheduling regular reviews of antibiotic policy and routine auditing of antibiotic usage to decrease Colistin resistance

This original manuscript is not published, in press, or submitted elsewhere in English or any other language, and is not currently being considered for publication elsewhere. I have contributed significantly to the research as an author in all steps of concept and design, analysis, and data interpretation, manuscript drafting, revising, and submitting to the journal. All authors declare that they have seen and approved the manuscript's content and contributed significantly to the work.

Potential conflicts of interest: There are no conflicts of interest, financial or otherwise to declare.
Financial support: Cairo University fund for MSc students.

REFERENCES

1. Kubeček O, Paterová P, Novosadová M. Risk Factors for Infections, Antibiotic Therapy, and Its Impact on Cancer Therapy Outcomes for Patients with Solid Tumors. Life (Basel). 2021 Dec 11;11(12):1387.
2. Bhat S, Muthunatarajan S, Mulki SS, Archana Bhat K, Kotian KH. Bacterial Infection among Cancer Patients: Analysis of Isolates and Antibiotic Sensitivity Pattern. Int J Microbiol. 2021 Jan 7:8883700.
3. Miethke, M.; Pieroni, M.; Weber, T.; Brönstrup, M.; Hammann, P.; Halby, L.; Arimondo, P.B.; Glaser, P.; Aigle, B.; Bode, H.B.; et al. Towards the sustainable discovery and development of new antibiotics. Nat. Rev. Chem. 2021(5): 726–749.
4. Uwizeyimana JD, Kim D, Lee H, Byun JH, Yong D. Determination of Colistin Resistance by Simple Disk Diffusion Test Using Modified Mueller-Hinton Agar. Ann Lab Med. 2020 Jul; 40(4):306-311.
5. Satlin MJ. The Search for a Practical Method for Colistin Susceptibility Testing: Have We Found It by Going Back to the Future? J Clin Microbiol. 2019 Jan 30;57(2):e01608-18.
6. Poornima Ramanan, Nicolynn Cole, Peggy Kohner, James Uhl, Robin Patel, Audrey Schuetz, Colistin Susceptibility Testing of *Enterobacteriaceae* by Agar Dilution (AD), Broth Microdilution (BMD) and Polymyxin NP, *Open Forum Infectious Diseases*, Volume 4, Issue suppl_1, Fall 2017, Page S596
7. Surbhi Khurana, Rajesh Malhotra, Purva Mathur, Evaluation of Vitek®2 performance for colistin susceptibility testing for Gram-negative isolates, *JAC-Antimicrobial Resistance*, Volume 2, Issue 4, December 2020, dlaa101.
8. CLSI, Wayne, PA and USA. (2021). Clinical and Laboratory Standards Institute. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing: Tween-seventh Informational Supplement M100-S27.
9. Colistin Breakpoints, EUCAST general consultation (6 Oct - 15 Nov, 2021).
10. Chan YH (2003a): Biostatistics102: Quantitative Data – Parametric & Non-parametric Tests. Singapore Med J.;44(8): 391-396.
11. Chan YH (2003b): Biostatistics 104: Correlational Analysis.Singapore Med J.;44(12) : 614-619.
12. Zafer MM, El-Mahallawy HA, Abdulhak A, et al. (2019) Emergence of colistin resistance in multidrug-resistant *Klebsiella pneumoniae* and *Escherichia coli* strains isolated from cancer patients. *Ann Clin Microbiol Antimicrob* 18: 1-8.
13. Katip W, Uitrakul S, Oberdorfer P. Short-Course Versus Long-Course Colistin for Treatment of Carbapenem-Resistant *A.baumannii* in Cancer Patient. Antibiotics (Basel). 2021 Apr 22;10(5):484.
14. Bhat S, Muthunatarajan S, Mulki SS, Archana Bhat K, Kotian KH. Bacterial Infection among Cancer Patients: Analysis of Isolates and Antibiotic Sensitivity Pattern. Int J Microbiol. 2021 Jan 7;2021:8883700.
15. Adel N, Khedr R, Elanany M, Zaki HF, Hafez H, El-Abhar H. Outcome and safety of colistin usage in pediatric cancer patients with carbapenem-resistant enterobacteriaceae bacteremia at children cancer hospital Egypt. Ann Afr Med. 2023 Jan-Mar;22(1):82-87.
16. Tohamy ST, Aboshanab KM, El-Mahallawy HA, El-Ansary MR, Afifi SS. Prevalence of multidrug-resistant Gram-negative pathogens isolated from febrile neutropenic cancer patients with bloodstream infections in Egypt and new synergistic antibiotic combinations. Infect Drug Resist. 2018 May 25;11:791-803.
17. Das S, Roy S, Roy S, Goelv G, Sinha S, Mathur P, Walia K, Bhattacharya S. Colistin susceptibility testing of gram-negative bacilli: Better performance of vitek2 system than E-test compared to broth microdilution method as the gold standard test. Indian J Med Microbiol. 2020 Jan-Mar;38(1):58-65.
18. Lellouche J, Schwartz D, Elmalech N, Ben Dalak MA, Temkin E, Paul M, Geffen Y, Yahav D, Eliakim-Raz N, Durante-Mangoni E, Iossa D, Bernardo M, Daikos GL, Skiada A, Pantazatou A, Antoniadou A, Mouton JW, Carmeli Y; AIDA study group. Combining VITEK® 2 with colistin agar dilution screening assist timely reporting of colistin susceptibility. Clin Microbiol Infect. 2019 Jun;25(6):711-716.
19. Worku M, Belay G, Tigabu A. Bacterial profile and antimicrobial susceptibility patterns in cancer patients. Plos one. 2022; 17(4):e0266919.