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# The microbial spectrum and antimicrobial resistance pattern in pediatric cancer patients with febrile neutropenia at King Abdullah University Hospital, Jordan

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## Abstract

**Background** Febrile neutropenia (FN) is a life-threatening complication of cancer therapy. Appropriate antibiotic treatment improves the clinical outcome in these patients; however, the increasing rate of anti-microbial resistance makes its therapy particularly challenging.

**Aim** This study aims to investigate the microbial spectrum and antimicrobial resistance pattern in cancer patients with FN at King Abdullah University Hospital, Jordan.

**Method** Blood cultures of 261 FN patients pre-diagnosed with malignancy (age 1–18 years) were enrolled in this study.

**Results** The most common isolated microorganisms were gram-positive bacteria (50.2%). Gram-infections with *coagulase-negative Staphylococcus* (CONS) are the most prevalent pathogens, followed by gram-negative infections with *Klebsiella pneumonia* and fungal infections with nonalbicans strains. All CONS, *Methicillin-resistant Staphylococcus aureus* (MRSA), and *enterococcus species* were sensitive to Vancomycin and Teicoplanin. Ten percent of the gram-negative organisms were *Extended-spectrum beta-lactamase* (ESBL) and all were sensitive to carbapenems. 66.7% of *pseudomonas aeruginosa* blood cultures were sensitive to Piperacillin-Tazobactam and 83.4% were sensitive to carbapenems. All Enterobacter species were sensitive to Carbapenems.

**Conclusion** Isolates showed various antibiotic sensitivity and resistance patterns; therefore, a judicious management plan is essential to establish an appropriate and effective institutional policy for the use of empirical antibiotics in patients of FN.

**Keywords** Febrile neutropenia, Microbial spectrum, Antimicrobial resistance, Infection, Cancer

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## Background

Febrile neutropenia (FN) is known as the most common serious complication of cancer therapy [10]. It is encountered in the majority of pediatric patients undergoing chemotherapy [13, 27]. Previous studies reported that the mortality rate of febrile neutropenic pediatric patients is approximately 1–6% ([13, 17, 22]; María E [33]) and can be as high as 11–12% in some groups [27, 34]. Documented infections include mostly bacterial infections, but fungal and viral infections are also recognized. The management of FN is considered an oncologic emergency. Prompt antibiotic therapy greatly influences and improves the clinical outcome; however, the increasing rate of anti-microbial resistance makes FN particularly challenging with subsequent increases in morbidity and mortality rates ([10]; M E [32]).

FN is defined as a single oral temperature greater than or equal to 38.3 °C (101 F) or a temperature greater than 38 °C (100.4 F) persisting for at least an hour in a patient who has an absolute neutrophil count (ANC) < 1500 cells/mm<sup>3</sup> [39]. The Common Toxicity Criteria established by the US National Cancer Institute grades neutropenia based on ANC include grade 0:  $\geq 2000$  cells/mm<sup>3</sup>; grade 1:  $\geq 1500 - < 2000$  cells/mm<sup>3</sup>; grade 2:  $\geq 1000 - < 1500$  cells/mm<sup>3</sup>; grade 3:  $\geq 500 - < 1000$  cells/mm<sup>3</sup>; grade 4: < 500 cells/mm<sup>3</sup>. However, the term neutropenia is clinically used for ANC < 1500 cells/mm<sup>3</sup> (grades 2 or greater) [7].

Despite the substantial decline in infection-related mortality in recent years, infections are still the main reason for morbidity and mortality in cancer patients with fever and neutropenia [38]. The appropriate strategy of clinical vigilance and immediate treatment is considered a key factor in managing febrile neutropenic patients [10, 15]. Several guidelines of empiric antibiotic therapy were developed in specific sites and regions in the world; however, some recommendations may not be as applicable in other areas where there are considerable differences in the microbial spectrum, the incidence of resistant organisms, availability of antibiotics, and/or healthcare-associated economic conditions [10].

While the pattern of bacterial pathogens causing infection in neutropenic patients has shown a significant shift from gram-negative to gram-positive bacteria over the past decades [21, 38, 41], there are still remarkable sites and region-specific differences in the microbial spectrum and resistance patterns of the pathogen [10]. In addition, despite bacteria being the most common pathogens in febrile neutropenic pediatric patients, fungal infections are an emerging concern and deserve early intervention [15]. Therefore, the need for ongoing updates on the initial choice of empiric antibiotic therapy is becoming essential. The aim of this study

is to investigate the microbial spectrum and antimicrobial resistance pattern in cancer patients with FN at King Abdullah University Hospital (KAUH), a tertiary hospital in the north of Jordan that offers advanced health care for patients in the Middle East region.

## Methods

This study aims to investigate the microbial spectrum and antimicrobial resistance pattern in cancer patients. This is a hospital-based retrospective study conducted at King Abdullah University Hospital (KAUH), a tertiary hospital in the north of Jordan that offers advanced health care for patients in Jordan. This study included all episodes of chemotherapy-induced FN with positive blood culture in children admitted to the hospital from January 2008 to December 2021. The study included patients with ages ranging from 1 to 18 years old, at diagnosis, and followed for hematological malignancies or solid tumors who were admitted for chemotherapy-induced FN and positive blood culture. Patients who have received cancer treatment other than chemotherapy were excluded from this study.

The standard practice at KAUH for microbiological testing is to obtain at least two sets of blood cultures at the time of admission before starting antibiotic treatment. Samples were cultured (inoculated onto Chocolate agar, 5% sheep Blood agar, MacConkey agar, and Sabouraud dextrose agar plates) and bacterial identification and antibiotic susceptibility were determined by using the Vitek 2 Compact system (Automated instrument for ID/AST testing) (bioMérieux, Marcy l'Etoile, France). VITEK-2 identification cards were used for gram-positive, and gram-negative bacteria and yeast. VITEK-2 AST-cards were used for performing antimicrobial susceptibility (antibiotics and antifungal susceptibility).

The standard approaches for FN in KAUH are to manage the infection with empiric therapy, initiated immediately after blood culture sampling and before conducting any other investigations. Empirical therapy choices are based on patients' history availability and updated information regarding the local antimicrobial susceptibility pattern. The efficient laboratory diagnoses and workflows are of great importance in narrowing the antimicrobial spectrum as definitive therapy as soon as possible to match the antimicrobial stewardship program principles.

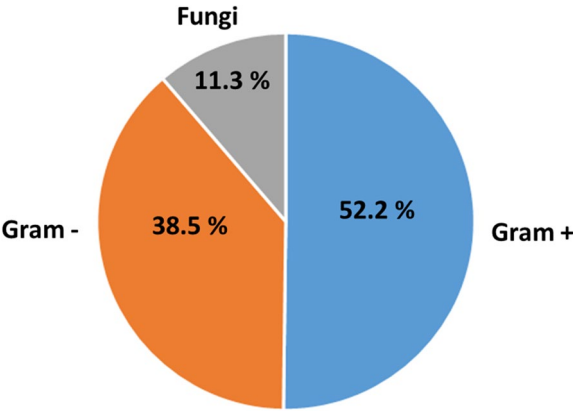
The study was approved by the Institutional Review Board at Jordan University of Science and Technology (IRB 893-2020). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS, version 16.0) software.

**Table 1** Comparative distribution of the characteristics of patients with hematological malignancies and solid tumors

	Hematological tumors (N:158; 60.5%) N (%)	Solid tumors (N:103; 39.5%) N (%)	Total tumors (N:261; 100%) N (%)
Gender			
Male	91 (62.3%)	55 (37.7%)	146
Female	67 (58.2%)	48 (41.8%)	115
ANC grading			
Grade 1	16 (72.7%)	6 (27.3%)	22
Grade 2	13 (72.2%)	5 (27.8%)	18
Grade 3	15 (65.2%)	8 (34.8%)	23
Grade 4	62 (73.8%)	22 (26.2%)	84
Non-neutropenic	52 (45.6%)	62 (54.4%)	114
Type of organism			
Gram-positive	83 (59.3%)	59 (40.7%)	142
Gram-negative	74 (67.9%)	35 (32.1%)	109
Fungi	14 (43.7%)	18 (56.3%)	32

**Results**

As shown in Table 1, this study analyzed the blood culture results of 261 patients pre-diagnosed with malignancy (146 male and 115 female patients). The majority of underlying malignancies were hematological malignancies, in 158 patients (60.5%) compared to solid tumors in 103 patients (39.5%). Acute lymphoblastic leukemia was the most common underlying hematological diagnosis (104 of 158; 65.8%), followed by lymphomas (33 of 158; 20.8%; Non-Hodgkin lymphoma 17; 10.7%, Hodgkin lymphoma 16;10.1%), and acute myeloid leukemia (AML) (21 of 158; 13.4%). The number of patients classified with low ANC (grades 2, 3, and 4) was 125 patients, the average ANC during admission for these patients was 830 cells/microliter. The percentage of patients with ANC less than 500 cells/microliter (grade 4) at the time of admission was 39.2% in hematological malignancy, compared to 21.3% seen in solid tumors. The most common isolated microorganisms from FN cancer patients were gram-positive bacteria (142/283; 50.2%), followed by gram-negative bacteria (109/283; 38.5%), and fungal infection (32/283; 11.3%) (Fig. 1). Blood cultures with gram-positive organisms were higher in hematological malignancy (83; 59.3%) compared to solid tumors (59; 40.7%). Similarly, blood cultures with gram-negative organisms were also higher in hematological vs. solid tumors (74; 67.9% vs 35; 32.1%). Conversely, fungal infections were shown to be higher in solid tumors (18; 56.3%) compared to hematological malignancies (14; 43.7%). It should be noted that 10.3% of all patients had polymicrobial bacteremia (gram-positive and gram-negative).



**Fig. 1** Pathogens involved in the microbologically documented infections

*CONS* was the most frequently isolated pathogen from gram-positive cultures (75 %), followed by *MRSA* (7.7%), *Enterococcus fecalis* and *Methicillin-sensitive Staphylococcus aureus* (*MSSA*) (5.6 %) (Table 2). *ESBL-negative Klebsella pneumonia* was the most common gram-negative organism (21%), followed by *ESBL-positive Escherichia coli* (15 %) and *Acinetobacter baumannii* (12%) (Table 3). It should be mentioned that 107 patients had *CONS* sepsis, 60% were seen in hematological malignancy and 40% were seen in solid tumors. Twenty-six of 107 patients were on prophylactic antibiotics (24 patients on Bactrim and 2 patients on Ciprofloxacin) with 4 of 26 patients coexisting gram-negative organisms. As seen in Table 4, candida species represent 90% of fungal blood cultures, mostly *Candida parapsilosis* (47%) followed by *candida albicans* (19%). 11 of 261 patients were on a prophylactic antifungal (fluconazole or voriconazole) where only 1 patient developed *fungus fusarium* positive culture.

All *CONS*, *MRSA*, and *enterococcus species* were sensitive to vancomycin and teicoplanin. One blood culture of *streptococcus viridians* was resistant to vancomycin and teicoplanin and sensitive to rifampicin (Table 5). Ten percent of the gram-negative organisms were *ESBL* and all were sensitive to carbapenems. 66.7% of *pseudomonas aeruginosa* blood cultures were sensitive to Piperacillin-Tazobactam and 83.4% were sensitive to carbapenems. Two patients with extensively drug-resistant (*XDR*) *pseudomonas aeruginosa* were resistant to all antibiotics (shown in Table 6); therefore, so they were treated with colistin. Fifty percent of *Acinetobacter calcoaceticus baumannii* organisms showed sensitivity to Cefepime, Piperacillin-Tazobactam, Carbapenems, and Aminoglycosides. Two patients with multidrug-resistant (*MDR*) *acinetobacter baumannii* were resistant to all antibiotics (shown in Table 6) and were treated with colistin. All

**Table 2** Bacterial gram-positive culture results, classified by grade of neutropenia

	Neutropenia grade					Total *
	Grade 1	Grade 2	Grade 3	Grade 4	ANC > 2000	
	(n = 8)	(n = 11)	(n = 11)	(n = 51)	(n = 61)	
<i>Methicillin-resistant staphylococcus aureus</i>	0	0	2	5	4	11
<i>Methicillin-sensitive staphylococcus aureus</i>	1	0	0	4	3	8
<i>Enterococcus faecalis</i>	0	2	2	0	4	8
<i>Alpha hemolytic streptococcus other pneumoniae</i>	0	0	0	2	1	3
<i>Coagulase-negative staphylococcus</i>	7	9	6	37	48	107
<i>Micrococcus luteus</i>	0	0	1	0	0	1
<i>Streptococcus pneumoniae</i>	0	0	0	1	1	2
<i>Streptococcus sanguinis</i>	0	0	0	1	0	1
<i>Streptococcus viridians</i>	0	0	0	1	0	1

**Table 3** Bacterial gram-negative culture results, classified by grade of neutropenia

	Neutropenia grade					Total *
	Grade 1	Grade 2	Grade 3	Grade 4	ANC >2000	
	(n = 14)	(n = 4)	(n = 13)	(n = 33)	(n = 45)	
<i>Acinetobacter baumannii</i>	0	2	2	4	5	13
<i>MDR Acinetobacter baumannii</i>	0	0	0	0	2	2
<i>Acinetobacter junii</i>	0	0	0	0	1	1
<i>Acinetobacter lwoffii</i>	0	0	0	2	1	3
<i>Aeromonas salmonicida</i>	0	0	0	0	1	1
<i>Cronobacter sakazakii</i>	0	0	0	0	1	1
<i>Enterobacter cloacae</i>	4	0	0	3	3	10
<i>Enterobacter intermedius</i>	0	0	1	0	0	1
<i>Enterobacter sakazakii</i>	1	0	0	0	0	1
<i>ESBL negative Escherichia coli</i>	1	0	0	4	3	8
<i>ESBL negative Klebsiella pneumoniae</i>	3	2	4	5	9	23
<i>ESBL positive Escherichia coli</i>	3	0	1	7	5	16
<i>ESBL positive Klebsiella pneumoniae</i>	1	0	0	1	2	4
<i>XDR Pseudomonas aeruginosa (extensively drug-resistant)</i>	1	0	1	0	0	2
<i>Pseudomonas aeruginosa</i>	0	0	2	3	1	6
<i>Pseudomonas putida</i>	0	0	1	0	0	1
<i>Klebsiella oxytica</i>	0	0	0	1	0	1
<i>Moraxella catarrhalis</i>	0	0	0	0	1	1
<i>Pantoea agglomerans</i>	0	0	0	0	3	3
<i>Proteus mirabilis</i>	0	0	0	0	1	1
<i>Salmonella spp.</i>	0	0	0	0	1	1
<i>Sphingomonas paucimobilis</i>	0	0	1	1	3	5
<i>Stenotrophomonas maltophilia</i>	0	0	0	2	2	4

*Enterobacter species* were sensitive to Carbapenems, 70% to Aminoglycosides, and 80% 4th generation Cephalosporin (Table 6). Finally, All *Candida parapsilosis* cultures were sensitive to voriconazole and amphotericin B, 50% to Echinocandins and 64% to fluconazole (Table 7).

## Discussion

FN is a life-threatening complication associated with chemo/radiotherapy-treated cancer in pediatric patients (M E [32]). More than half of pediatric cancer patients undergoing chemotherapy have been shown to develop

**Table 4** Fungi culture results, stratified by grade of neutropenia

	Neutropenia grade					Total *
	Grade 1	Grade 2	Grade 3	Grade 4	ANC >2000	
	(n = 0)	(n = 3)	(n = 3)	(n = 7)	(n = 18)	(n = 32)
<i>Candida albicans</i>	0	0	0	1	5	6
<i>Candida dubilensis</i>	0	0	1	0	1	2
<i>Candida haemulonii</i>	0	0	0	0	1	1
<i>Candida lusitanae</i>	0	0	0	0	1	1
<i>Candida parapsilosis</i>	0	3	2	3	7	15
<i>Candida pelliculosa</i>	0	0	0	1	0	1
<i>Candida tropicalis</i>	0	0	0	1	1	3
<i>Fungus fusarium</i>	0	0	0	0	1	1
<i>Rhodotorula glutinis</i>	0	0	0	1	1	2

**Table 5** Gram-positive bacteria sensitivity

	Vancomycin	Rifampicin	Tiecoplanin	Clindamycin	Oxicillin	Cephazolin/ Cephalexine
<i>Methicillin-resistant staphylococcus aureus</i> (n = 12)	100 %	100%	100%	80 %	0	8%
<i>Methicillin-sensitive staphylococcus aureus</i> (n = 8)	100%	100%	100%	100%	100%	75%
<i>Enterococcus faecalis</i> (n = 8)	100%	12%	100%	12%	NA	NA
<i>Coagulase-negative staphylococcus</i> (n = 106)	100%	NA	100%	NA	NA	NA
<i>Micrococcus luteus</i> (n = 1)	100%	100%	100%	100%	100%	100%
<i>Streptococcus pneumoniae</i> (n = 2)	100%	50%	50%	50%	NA	NA
<i>Streptococcus sanguinis</i> (n = 1)	100%	NA	100%	NA	NA	NA
<i>Streptococcus viridans</i> (n = 1)	0	100%	0	0	NA	100%

**Table 6** Gram-negative bacteria sensitivity

	Cephalosporin	Tazocin	Amikacin	Gentamycin	Cefipiem	Carbapenems	Levofloxacin
<i>E. Coli</i> (ESBL –ve) (n = 8)	100%	87 %	87%	50 %	100%	100%	37.5 %
<i>K. pneumonia</i> (ESBL –ve) (n = 23)	100%	52%	87%	74%	82 %	100%	56%
<i>Acinetobacter baumannii</i> (n = 13)	30%	50%	50%	50 %	50%	50 %	15%
<i>Enterobacter cloacae</i> (n = 10)	50 %	50%	70%	60%	80%	100%	70%
MDR <i>Acinetobacter baumannii</i> (n = 2)	0	0	0	0	0	0	0
<i>Acinetobacter junii</i> (n = 1)	100%	100%	100%	100%	100%	100%	NA
<i>Acinetobacter lowffii</i> (n = 3)	100%	100%	100%	100%	100%	100%	Na
<i>Aeromonas salmonicidia</i> (n = 1)	100%	100%	100%	100%	100%	100%	100%
<i>Cornobacter sakazaki</i> (n = 1)	100%	100%	100%	100%	100%	100%	0
<i>K. pneumonia</i> (ESBL +ve) (n = 4)	0	50%	75%	25%	0%	100%	100%
<i>Pantoea agglomerans</i> (n = 4)	100%	100%	100%	100%	100%	100%	100%
<i>Proteus mirabilis</i> (n = 1)	0	100%	100%	100%	0	100%	NA
<i>E. Coli</i> (ESBL +ve) (n = 16)	0	37.5%	37.5%	37.5 %	12.5 %	100%	32%
XDR <i>Pseudomonas aeruginosa</i> (n = 2)	0	0	0	0	0	0	0
<i>Pseudomonas putida</i> (n = 1)	NA	NA	100%	NA	100%	100%	0
<i>Pseudomonas aeruginosa</i> (n = 6)	16.60%	66.6%	100%	66.6%	83.3%	83.3%	50%
<i>Salmonella</i> spp (n = 1)	100%	NA	NA	NA	100%	100%	100%
<i>stenotrophomonas maltophilia</i> (n = 4)	25%	0	25%	0	0	0	25%
<i>Sphingomonas paucimobilis</i> (n = 5)	80%	100%	100%	100%	100%	100%	60%

**Table 7** Fungal sensitivity

	Echinocandins	Fluconazole	Voriconazole	Amphotericin B
<i>Candida albicans</i> (n = 6)	16%	100%	16%	100%
<i>Candida parapsilosis</i> (n = 14)	50%	64%	100%	100%
<i>Candida dubilensis</i> (n = 2)	NA	50%	100%	100%
<i>Candida tropicalis</i> (n = 3)	33%	100%	100%	100%
<i>Rhodotourla glutinis</i> (n= 2)	0	0	50%	50%

infection [7, 39]. Delayed management of these neutropenic patients can increase morbidity and mortality rates [20, 23]. Although the risk assessment and management criteria of patients with FN have been widely carried out in adults, these models of assessment have shown that they are not consistent/compatible with pediatric patients ([4]; María E [33]). In addition, the prevalence and evolution of antimicrobial resistance, due to the empirically unjustified use of broad-spectrum antibiotics, have shown to be variable among different care centers in the world [9, 37]. Therefore, it is essential to continuously check the prevalence and sensitivity patterns of different microorganisms to be able to carefully revise the institutional policies for the use of appropriate empirical antibiotics in patients of FN. The present study represents the second report of the microbial spectrum and antimicrobial susceptibility profile from febrile neutropenic cancer patients in King Abdullah University Hospital (KAUH), a tertiary-care center in northern Jordan, Irbid.

In this study, we found that gram-positive bacteria were the most prevalent pathogens (50.2 %) followed by gram-negative bacteria (38.5%). Our results are consistent with previous data analysis on febrile neutropenic pediatric patients conducted in the same care center (KAUH) where gram-positive bacteria were the most prevalent pathogens [2]. This shift in the microbiological pattern of infection from gram-negative to gram-positive has been reported by previous studies performed in developing and developed countries [3, 5, 11, 17, 25, 26, 29, 41]. However, while other studies reported an increasing proportion of gram-positive bacterial infection, gram-negative bacteria were still the most prevalent pathogens [16, 18, 24, 35, 37]. In consistent with earlier studies [30, 31] *Staphylococcus* species were found as the most prevalent gram-positive pathogen in this study, but in contrast to a recent report from Palestine reported that *Enterococcus* spp. was the most prevalent gram-positive pathogen [17]. 50% of *Staphylococcus aureus* (MRSA and MSSA) cultures were found in patients who developed Grade 4 ANC. In agreement with previous reports [12, 35, 37] *Klebsiella pneumonia* and *Escherichia coli* were found to be the most common isolated gram-negative organisms in this study. Twenty-five percent of *Klebsiella*

*pneumonia* and 50% of *Escherichia coli* and *pseudomonas aeruginosa* cultures were found in patients who developed grade 4 ANC.

The shift in the microbiological pattern of infection from gram-negative to gram-positive can be attributed to secondary factors; for instance, the potential oro-intestinal mucosa damage, caused by the intensive courses of chemotherapy, which can be considered a predisposing factor for the infection with gram-positive pathogens. In addition, the use of prophylactic oral antibiotics during the course of chemotherapy might selectively diminish the intestinal infection with gram-negative pathogens. Finally, the frequent use of indwelling catheters in cancer patients can lead to the development of skin-derived gram-positive infections as previously stated in former studies [2, 26, 28]. This shift in the bacterial spectrum emphasizes the need to alter treatment schedules for proper patient care. Even though gram-positive bacteria have become more prevalent pathogens, gram-negative bacteria still make up 40% of the pathogens found in patients with FN. In addition, gram-negative bacteria are associated with higher morbidity and mortality compared to gram-positive bacteria [40]. Therefore, guidelines for the empirical treatment should also cover these organisms specifically. However, it should be noted that other factors such as the local resistance patterns, previous culture data, patient's symptoms, and grade neutropenia should be considered when selecting empirical antibiotic treatments, as the most appropriate treatment approach may vary in various local settings.

In the present study, fungal infections were shown to be the third most commonly isolated pathogen (11.3%) in the blood cultures of febrile neutropenic patients. Unlike gram-positive and gram-negative microorganisms, fungal infections are shown to be higher in solid tumors (56.3%) compared to hematological malignancies (43.7%). The nonalbicans strains have shown to be the most frequently isolated pathogen from the blood cultures of fungal infections, results that are consistent with previous reports [2, 3, 19]. Forty-three percent of fungal infections were in grades 3 and 4 neutropenia. The infection rate and severity were inversely related to the ANC [6, 8].



The antimicrobial susceptibility profile of micro-organisms was also evaluated in this study in order to select the appropriate antimicrobial agent [1]. All *staphylococcus aureus* isolates were sensitive to vancomycin (100%) and teicoplanin (100%). MSSA was 100% sensitive to clindamycin, whereas MRSA was 80% sensitive to clindamycin. These findings also match with previous studies reporting that 100% *staphylococcus aureus* strains were sensitive to vancomycin [26, 35]. On the other hand, our findings contradict findings from a study conducted in Iran [37], where all *staphylococcus aureus* isolates were resistant to vancomycin, however, the results of the same study were similar to our findings regarding the majority of *staphylococcus aureus* strains that were sensitive to clindamycin. In our study, all *Klebsiella pneumoniae* isolates were highly sensitive (100%) to carbapenems. In addition, the majority of isolated *Klebsiella pneumoniae* was ESBL negative and all were sensitive to cephalosporin. These results are also consistent with other studies that reported susceptibility ranging from 90 to 100% for carbapenems and cephalosporins [36, 37]. *E. coli* resistance to fluoroquinolones is known as a common phenomenon in many care centers around the world [14] which was also found to be the case in our study where only 30–40% of *E. coli* isolates were sensitive to fluoroquinolones. The majority of *E. coli* were ESBL positive (65%) and all were resistant to cephalosporins, which is contrary to other studies that reported the majority *E. coli* were susceptible to cephalosporins [37]. Regarding the susceptibility to carbapenems, we found that *E. coli* isolates were 100% sensitive to carbapenems, compared to only 65% susceptibility reported in other studies [35, 37]. *Pseudomonas aeruginosa* showed 66% sensitivity to tazocin and 100% to amikacin, which comes in partially agreement with previous study reporting 100% sensitivity to both tazocin and amikacin [35]. Therefore, based on the results of antimicrobial susceptibility profile in this study, the implementation of multidisciplinary antimicrobial stewardship policies for patients with high-risk FN in our center was feasible and well accepted. For example, the significant decrease in the carbapenem and glycopeptide consumptions based our local guidelines has been reflected on antimicrobial sensitivity profile as shown above.

The results of this study provided valuable information about the microbial spectrum and antimicrobial susceptibility profile to develop treatment guidelines in febrile neutropenic cancer patients. However, this study has some limitations. First, our data were collected from a single care center. The pattern of causative pathogens and their

antibiotic susceptibilities are influenced by the antibiotic resistance status which can be varied between each care center and community. Second, there were some limitations in data collection since our study is retrospective. Finally, the sample size was relatively small.

## Conclusion

Gram-positive infections with *coagulase-negative Staphylococci* are the most prevalent pathogens in febrile neutropenic pediatric patients, followed by gram-negative infections with *Klebsiella pneumoniae* and fungal infections with nonalbicans strains. Pathogen isolates show various antibiotic sensitivity and resistance patterns; therefore, a judicious management plan is essential to establish an appropriate and effective institutional policy for the use of empirical antibiotics in patients of FN.

## Abbreviations

FN	Febrile neutropenia
ANC	Absolute neutrophilic count
KAUH	King Abdullah University Hospital
CLSI	Clinical and Laboratory Standard Institute

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Not applicable

## Authors' contributions

DA, HO, DG, OA, and OM performed data collection, DA, DS, and BD performed the statistical analysis. DA, GTA, and SA analyzed and interpreted the data. DA and SA prepared the manuscript. All authors read and approved the final manuscript.

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## Availability of data and materials

The data supporting the findings listed are available from the corresponding author upon request.

## Declarations

## Ethics approval and consent to participate

This study was conducted after receiving approval from the Ethics Review Committee of the Institutional Review Board at Jordan University of Science and Technology (IRB 893-2020).

## Consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

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