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by Budi Utomo .

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RESEARCH REPORT: Microbiologically documented infection and antimicrobial sensitivities in pediatric malignancy patients with febrile neutropenia at Dr Saiful Anwar Hospital, Malang, Indonesia

[1]Savitri Laksmi Winaputri, [1*]Dominicus Husada, [2]Budi Utomo, [3]Irene Ratridewi, [3]Susanto Nugroho, [1]I Dewa Gede Ugrasena, [1]Parwati Setiono Basuki, [1]Ismoedijanto

[1)] Department of Child Health, Faculty of Medicine, Universitas Airlangga– Dr. Soetomo Hospital, Surabaya
[2)]Department of Public Health & Preventive Medicine, Faculty of Medicine, Universitas Airlangga, Surabaya
[3)]Department of Child Health, Faculty of Medicine, Universitas Brawijaya– Dr. Saiful Anwar Hospital, Malang
[*]Corresponding author: Dominicus Husada (dominicushusada@yahoo.com)

Abstract. Background: Febrile neutropenia in malignancy children increase the risk of infection, morbidity and mortality. Microbiologically documented infection in pediatric malignancy has not been studied in Saiful Anwar Hospital. **Purpose**: determine profile of blood, urine, sputum, and wound bed culture and antimicrobial sensitivities pattern in pediatric malignancy patients with febrile neutropenia. **Methods**: Pediatric malignancy patients with febrile neutropenia and microbiologically documented infection admitted to dr Saiful Anwar General Hospital Malang, were studied from 2016 to 2019. Bacterial and fungal etiology were identified, along with antimicrobial sensitivities patterns. **Results**: 53 (17%) of 307 pediatric malignancy patients with febrile neutropenia experienced 75 episodes of microbiologically documented infection. 40 (53,3%) gram-negative and 34 (45,3%) gram-positive isolated from 75 isolated pathogens. The most common gram-negative were *Klebsiella pneumonia* (n=15) and *Escherichia coli* (n=8). The most common gram-positive were *Coagulase-negative Staphylococci* (n=14) and *Enterococcus faecalis* (n=7). *Escherichia coli, Coagulase-negative Staphylococci*, *Enterococcus faecalis*, and *Staphylococcus aureus* were 100% sensitive to all tested antimicrobials. *Klebsiella pneumonia* and *Acinetobacter baumanni* were 100% sensitive to almost all tested antimicrobials. *Pseudomonas aeruginosa* was found less sensitive (0-80%) to all tested antimicrobials. **Conclusion**: Investigation of antimicrobial sensitivities of these organisms may guide successful antimicrobial therapy and improve quality of pediatric malignancy care.

Keywords: Microbiologically Documented Infection; Febrile Neutropenia; Pediatric Malignancy; Culture; Antimicrobial Sensitivities.

Abstrak. Latar Belakang: Demam neutropenia pada keganasan anak meningkatkan risiko infeksi, morbiditas dan mortalitas. *Microbiologically Documented Infection* merupakan masalah utama di dunia, namun belum dilakukan penelitian di RSUD Dr. Saiful Anwar. **Tujuan:** Melihat gambaran kultur darah, urine, sputum, dan dasar luka dan pola sensitivitas antimikroba pada keganasan anak dengan demam neutropenia. **Metode:** Pasien keganasan anak dengan demam neutropenia di bangsal Hemato-onkologi Departemen Ilmu Kesehatan Anak RSUD Dr. Saiful Anwar Malang dan terdiagnosis *Microbiologically Documented Infection* pada tahun 2016-2019, ditentukan etiologi, serta pola sensitivitas antimikroba. **Hasil:** Dari 307 pasien keganasan anak dengan demam neutropenia, 53(17%) pasien mengalami 75 episode *microbiologically documented infection*. Didapatkan 40(53,3%) bakteri gram negatif dan 34(45,3%) gram positif dari 75 hasil kultur. Bakteri gram negatif yang paling banyak ditemukan adalah *Klebsiella pneumonia* (n=15) dan *Escherichia coli* (n=8), serta *Coagulase-negative Staphylococci* (n=14) dan *Enterococcus faecalis* (n=7) pada gram positif. *Escherichia coli, Coagulase-negative Staphylococci, Enterococcus faecalis, dan Staphylococcus aureus* 100% sensitif terhadap semua antimikroba yang diuji. *Klebsiella pneumonia* dan *Acinetobacter baumanni* 100% sensitif terhadap hampir semua anitmikroba yang diuji. *Pseudomonas aeruginosa* memiliki sensitivitas rendah (0-80%) terhadap semua antimikroba yang diuji. **Kesimpulan:** Penelitian tentang sensitivitas antimikroba pada organisme tersebut dapat menjadi panduan untuk keberhasilan terapi dan meningkatkan kualitas pelayanan pada keganasan anak.

Keywords: *Microbiologically Documented Infection*; Demam Neutropenia; Keganasan Anak; Hasil Kultur; Sensitivitas Antimikroba.

Introduction

Febrile neutropenia is a common complication in pediatric patients with malignancy and increases the risk of infection, morbidity, and mortality.[1,2] Blood-stream infections are among the most serious infections and a major cause of mortality. Pediatric malignancy patients are known to have an increased risk of infections, especially blood-stream infections, due to immunosuppression caused by the malignant disease and the antineoplastic treatment cause.[2] The common risk factors reported for infection are younger age, absolute neutrophil count <500/mm^3, intravascular catheters, high temperature, and immunosuppressive antineoplastic regimens.[3]

In this retrospective descriptive study, we characterize the Microbiologically Documented Infection, their association with different types of cancer, and the pattern of antimicrobial sensitivities among pediatric malignancy patients with febrile neutropenia. This study aimed to determine the profile of blood, urine, sputum and wound bed culture and antimicrobial sensitivities in pediatric malignancy patients with febrile neutropenia and microbiologically documented infection.

Materials and Methods

A retrospective descriptive study was conducted of all pediatric malignancy patients (age ≤18 years) with febrile neutropenia admitted to the hemato-oncology ward at Pediatrics Department of dr Saiful Anwar General Hospital Malang who had positive blood, urine, sputum and wound bed culture from January 2016 to December 2019. Pediatric patients with hematological malignancies (ALL, AML, Non-Hodgkin Lymphoma, and Hodgkin Lymphoma) and solid tumors (Medulloblastoma, Retinoblastoma, Neuroblastoma, Nephroblastoma, Hepatocellular carcinoma, Osteosarcoma, and other solid tumors) were studied using medical records.

Fever was defined as a single oral measurement temperature is ≥38.5°C or ≥38.0°C for 2 hours according to European Society of Medical Oncology (ESMO) Clinical Practice Guideline. Febrile neutropenia is a fever with an oral temperature ≥38.5°C on single measurement or an axillary temperature ≥38°C (100 ° F) for 2 hours with ANC less than 500 cells/mm^3 or ANC <1000/mm^3 and is predicted will decrease to <500/mm^3 within 48 hours. Meanwhile, ANC <100/mm^3 described as profound neutropenia which has higher risk of infection.[4,5]

Nutritional status was determined by WHO weight-for-length/height growth chart for patients aged <5 years old and CDC stature-for-age and weight-for-age growth chart for patients ≥5 years old. Nutritional status was divided into obesity, overweight, normal, wasted, and severely wasted.[6] Chemotherapy was divided into patients who underwent chemotherapy and not. Cytotoxic compunds used as chemotherapy were cyclophosphamide, cisplatin, carboplatin, cytarabine, 5-fluorouracil, vincristine, etoposide, daunorubicin, doxorubicin, bleomycin, dactinomycin, and L-asparaginase.[7] Relapse was divided into patient had relapsed and not. According to the National Cancer Institute, relapse is the re-emergence of a malignant disease after a disease-free period, relapse can be interpreted as the return of disease or signs and symptoms of the disease after a period of improvement.[8]

The inclusion criteria for this study were all pediatric malignancy patients with febrile neutropenia and episodes of clinically and microbiologically proven infection. Exclusion criteria for this study were pediatric patients with

congenital neutropenia and other severe diseases which are also characterized by neutropenia, such as HIV AIDS.

Microbiologically documented infection (MDI) was determined as the patient suffered infection clinically and was found pathogenic bacteria/fungi on blood, urine, sputum and wound bed in microbiological culture.[9]

This study was approved by the Research Ethics Committee of Dr. Saiful Anwar General Hospital Malang (No: 400/265/K.3/302/2019, date December 2nd 2019).

Descriptive analytics were performed in this study using Statistical Package for Social Sciences (SPSS) for Windows version 25 to analyze the frequency distribution of microbiologically proven bacterial and fungal infection and antimicrobial sensitivities in pediatric malignancy patients with febrile neutropenia. No statistical analytics were conducted in this study.

Results

During the study period, January 2016 to December 2019, a total of 307 pediatric patients with malignancy and febrile neutropenia were admitted to the hemato-oncology ward at Pediatrics Department of dr Saiful Anwar General Hospital Malang. Microbiologically documented infection was detected in 75 episodes, in 53 (17%) pediatric patients with malignancy and febrile neutropenia.

Of the 53 patients studied, leukemia (n=37) was the most common malignancy with microbiologically documented infection, followed by solid tumors (n=14) and lymphoma (n=2). Duration of fever ≤5 days, leucocytes <4000/mm^3, platelet <20.000/mm^3, neutrophil <100/mm^3, monocytes <100/mm^3, procalcitonin >0,5 ng/mL and underwent chemotherapy were the common parameters found in pediatric malignancy patients with microbiologically documented infection and febrile neutropenia (Table 1).

Table 1. Demographic, clinical and laboratory results of pediatric malignancy patients with febrile neutropenia and microbiological documented infection

Parameters	Leukemia		Lymphoma		Solid tumors		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Total number of malignancy patients with febrile neutropenia	219		31		57		307	
Total number of malignancy patients with febrile neutropenia and microbiologically documented infection	37	(16)	2	(6)	14	(24)	53	(17)
Age								
>10 years	7	(19)	0		4	(28.6)	11	(20.8)
>5-10 years	12	(32.4)	1	(50)	6	(42.9)	19	(35.8)
1-5 years	16	(43.2)	1	(50)	3	(21.4)	20	(37.7)
<1 years	2	(5.4)	0		1	(7.1)	3	(5.7)
Sex								
Male	16	(43.2)	2	(100)	7	(50)	25	(47.2)
Female	21	(56.8)	0		7	(50)	28	(52.8)
Nutritional Status								
Normal	18	(48.7)	1	(50)	6	(42.9)	25	(47.2)
Severely wasted	5	(13.5)	1	(50)	6	(42.9)	12	(22.6)
Wasted	10	(27)	0		2	(14.2)	12	(22.6)
Overweight	1	(2.7)	0		0		1	(1.9)
Obese	3	(8.1)	0		0		3	(5.7)
Duration of fever								

≤5 days	28	(75.7)	1	(50)	12	(85.7)	41	(77.4)
>5 days	9	(24.3)	1	(50)	2	(14.3)	12	(22.6)
Hemoglobin								
≥7 -10g/dL	30	(81.1)	1	(50)	9	(64.3)	40	(75.5)
<7 g/dL	7	(18.9)	1	(50)	5	(35.7)	13	(24.5)
Leucocytes								
≥4000/mm^3	10	(27.0)	0		1	(7.1)	11	(20.8)
<4000/mm^3	27	(73.0)	2	(100)	13	(92.9)	42	(79.2)
Platelet								
≥50.000/mm^3	7	(18.9)	2	(100)	4	(28.6)	13	(24.5)
20.000-<50.000/mm^3	10	(27.0)	0		1	(7.1)	11	(20.8)
<20.000/mm^3	20	(54.1)	0		9	(64.3)	29	(54.7)
Neutrophils								
<500/mm^3 (severe neutropenia)	15	(40.5)	0		7	(50)	22	(41.5)
<100/mm^3(profound neutropenia)	22	(59.5)	2	(100)	7	(50)	31	(58.5)
Monocytes								
>100/mm^3	17	(45.9)	1	(50)	5	(35.7)	23	(43.4)
≤100/mm^3	20	(54.1)	1	(50)	9	(64.3)	30	(56.6)
CRP								
<0,3 mg/dL	0		0		0		0	
≥0,3 mg/dL	3	(8.1)	0		0		3	(5.7)
Not examined	34	(91.9)	2	(100)	14	(100)	50	(94.3)
Procalcitonin								
<0,5 ng/mL	3	(8.1)	0		3	(21.4)	6	(11.3)
≥0,5 ng/mL	27	(73.0)	2	(100)	9	(64.3)	38	(71.7)
Not examined	7	(18.9)	0		2	(14.3)	9	(17.0)
Central Venous Catheter								
No	26	(70.3)	2	(100)	12	(85.7)	40	(75.5)
Yes	11	(29.7)	0		2	(14.3)	13	(24.5)
Relapse								
No	28	(75.7)	1	(50)	13	(92.9)	42	(79.2)
Yes	9	(24.3)	1	(50)	1	(7.1)	11	(20.8)
Chemotherapy								
No	13	(35.1)	1	(50)	1	(7.1)	15	(28.3)
Yes	24	(64.9)	1	(50)	13	(92.9)	38	(71.7)

Figure 1 presented an increasing number of positive cultures in pediatric malignancy patients with febrile neutropenia from 2016 to 2019. A total of 75 episodes of microbiologically documented infection, detected 9 positive cultures in 2016 and 26 positive cultures in 2019. Gram-positive bacteria were also increasing from 2016 to 2019, with 3 positive cultures in 2016 and 15 positive cultures in 2019. Meanwhile, Gram-negative bacteria detected were relatively constant from 2016 to 2019. The ratio of Gram-positive bacteria to Gram-negative bacteria among the study period of microbiologically documented infection was 0.5 in 2016 and increased to 1.36 in 2019.

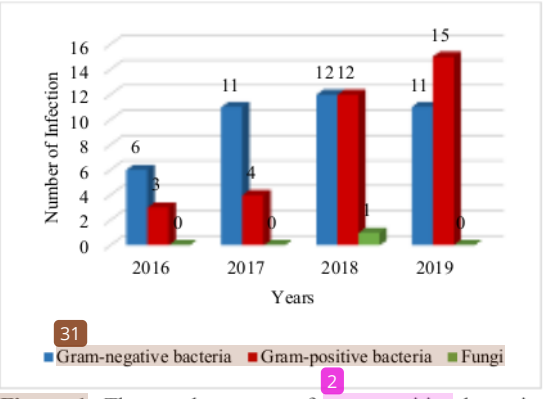

Figure 1. The yearly pattern of gram-positive bacteria, gram-negative bacteria, and fungal in pediatric malignancy patients with febrile neutropenia and microbiologically documented infection (2016-2019)

In this study, detected 19 positive blood cultures, 30 positive urine cultures, 21 positive sputum culture, 4 positive wound bed culture, and 1 positive fungal cultures (Table 2). Positive urine culture with significant count (≥10^5 CFU of bacteria/mL) was considered urinary tract infection.

Table 2. The pattern of isolated pathogens from blood, urine, sputum and wound bed cultures in pediatric malignancy patients with febrile neutropenia and microbiological documented infection

Species	Number of Episodes					
	Blood	Urine	Sputum		Wound bed	Total
			Bacteria	Fungi		
Gram-negative bacteria						
Acinetobacter baumanii		1	2			3
Acinetobacter haemolyticus			1			1
Acinobacter jejunii		2				2
Burkholderia cepacia	1					1
Escherichia coli (ESBL)	1	6	1			8
Enterobacter cloacae			2			2
Klebsiella oxycita			1			1
Klebsiella pneumoniae (ESBL)	6	5	4			15
Pseudomonas aeruginosa	2	1	2			5
Serratia liquefaciens		1				1
Stenotrophomonas maltophilia			1			1
Total Gram-negative bacteria	**10**	**16**	**14**			**40**
Gram-positive bacteria						
Corynebacterium striatum					1	1
Enterococcus faecalis		6			1	7
Enterococcus faecium		1				1
Enterococcus casseliflavus		1				1
Streptococcus pneumoniae			1			1
Staphylococcus aureus			1		1	2
Staphylococcus haemolyticus		2				2
Coagulase-Negative Staphylococci	9	3	1		1	34
Staphylococcus sciuri		1				1
Streptococcus mitis			2			2
Streptococcus sp. (NF)			2			2
Total Gram-positive bacteria	**9**	**14**	**7**		**4**	**34**
Fungi						
Candida albicans				1		1
Total Fungi				**1**		**1**
Total	19	30	21	**1**	**4**	**75**

Table 3 showed a total of 40 (53,3%) of 75 recovered isolates were Gram-negative organisms and 34 (45,3%) of 75 were Gram-positive organisms. *Klebsiella pneumonia* was the most common Gram-negative pathogen, it was identified in 15 (20%) of 75 isolates, followed by *E coli* (8 [10,6%]), *Pseudomonas aeruginosa* (5 [6,66%]) and *Acinetobacter baumanni* (3 [4%]). *Coagulase-negative Staphylococci* was the most common Gram-positive pathogen, it was identified in 14 (18,6%) of 75, followed by *Enterococcus faecalis* (7 [9,3%]). *Staphylococcus aureus* was found only in 2 (2.6%) and *Streptococcus* in 5 (6,6%) cases. Gram-negative and Gram-positive bacteria are more common in hematological malignancy (leukemia) than in solid tumors or lymphoma.

Table 3. The pattern of isolated pathogen in pediatric patients with febrile neutropenia based on type of malignancy

Species	Number of Episodes			Total
	Leukemia	Lymphoma	Tumor solid	
Gram-negative bacteria				
Acinetobacter baumanii	3			3
Acinetobacter haemolyticus	1			1
Acinobacter jejunii	1		1	2
Burkholderia cepacia			1	1
Escherichia coli (ESBL)	6	1	1	8
Enterobacter cloacae	2			2
Klebsiella oxycita	1			1
Klebsiella pneumoniae (ESBL)	12		3	15
Pseudomonas aeruginosa	5			5
Serratia liquefaciens		1		1
Stenotrophomonas maltophilia			1	1
Total Gram-negative bacteria	**31**	**2**	**7**	**40**
Gram-positive bacteria				
Corynebacterium striatum			1	1
Enterococcus faecalis	4	2	1	7
Enterococcus faecium			1	1
Enterococcus casseliflavus	1			1
Sreptococcus pneumoniae	1			1
Staphylococcus aureus			2	2
Staphylococcus haemolyticus	2			2
Coagulase-negative Staphylococci	10		4	14
Staphylococcus sciuri	1			1
Streptococcus mitis	1		1	2
Streptococcus sp. (NF)	2			2
Total Gram-positive bacteria	**22**	**2**	**10**	**34**
Fungi				
Candida albicans	1			1
Total Fungi	**1**			**1**
Total				**75**

Tables 4 and 5 showed the results of in vitro antimicrobial sensitivities test of the 75 isolated strains of Gram-positive and Gram-negative bacteria. The number of isolates tested was different for each antimicrobial. *Klebsiella pneumonia* revealed high sensitivity (100%) to gentamycin, cefepime, amikacin, levofloxacin, amoxiclav, ciprofloxacin, fosfomycin, linezolid, tigecycline, and nitrofurantoin, but resistance to piperacillin-tazobactam, and was less sensitive to meropenem (91%). *Escherichia coli* isolates were 100% sensitive to all tested antimicrobials. *Pseudomonas aeruginosa* revealed less sensitivity to gentamycin (80%), meropenem (75%), ceftizoxime (50%) and ceftazidime (33%), and was found resistant to cefepime, piperacillin-tazobactam, ampicillin and ampicillin-sulbactam. *Acinetobacter baumanii* isolates were 100% sensitive to all tested antimicrobial, except ceftriaxone. *Coagulase-negative staphylococcus* and *Staphylococcus aureus* revealed high sensitivity to erythromycin, clindamycin, vancomycin, trimethoprim-sulfamethoxazole, and gentamycin. *Coagulase-negative staphylococcus* and *Enterococcus faecalis* isolates were 100% sensitive to linezolid. *Enterococcus faecalis* was high sensitivity to ampicillin, ciprofloxacin, amoxiclav and benzylpenicillin. *Streptomycin sp* isolates was sensitive to Erythromycin. Ampicillin, cefepime, and ceftriaxone was found less sensitive for Other Gram-positive bacteria.

Table 4. The Antimicrobial sensitivities pattern of gram-negative bacteria

Antimicrobials	**Gram-negative bacteria (n=40)**									
	***Klebsiella pneumoniae* (n=15)**		***Escherichia coli* (n=8)**		***Pseudomonas aeruginosa* (n=5)**		***Acinetobacter baumanii* (n=3)**		**Other Gram-negative bacteria (n=9)**	
	n	**(%sensitivity)**	**n**	**(%sensitivity)**	**n**	**(%sensitivity)**	**n**	**(%sensitivity)**	**n**	**(%sensitivity)**
Gentamicin	5	(100)	3	(100)	5	(80)	3	(100)	5	(100)
Meropenem	11	(91)	6	(100)	4	(75)	1	(100)	4	(100)
Cefepime	1	(100)	1	(100)	2	(0)	1	(100)	1	(100)
Piperacillin-Tazobactam	1	(0)	2	(100)	2	(0)			1	(100)
Amikacin	11	(100)	5	(100)					2	(100)
Levofloxacin	4	(100)	1	(100)			1	(100)	2	(100)
Amoxicillin-clavulanic acid	1	(100)					1	(100)	1	(100)
Ampicillin			1	(100)	2	(0)	1	(100)	1	(0)
Ampicillin-Sulbactam					2	(0)	1	(100)	3	(67)
TMP-SMX			2	(100)			1	(100)	5	(100)
Ceftazidime					3	(33)	1	(100)	1	(100)
Ceftizoxime					2	(50)				
Ceftriaxone			1	(100)			1	(0)	1	(0)
Ciprofloxacin	3	(100)	1	(100)			2	(100)	1	(100)
Fosfomycin	2	(100)	2	(100)						
Linezolid	2	(100)								
Tigecyclin	4	(100)	1	(100)						
Nitrofurantoin	1	(100)								

TMP-SMX: Trimethoprim/sulfamethoxazole

Table 5. The Antimicrobial sensitivities pattern of gram-positive bacteria

Antimicrobials	Gram-positive bacteria (n=34)									
	Coagulase-negative staphylococci (n=14)		*Enterococcus faecalis* (n=7)		*Staphylococcus aureus* (n=2)		*Streptococcus* (n=5)		Other Gram-positive bacteria (n=6)	
	n	(%sensitivity)	n	(%sensitivity)	n	(%sensitivity)	n	(%sensitivity)	n	(%sensitivity)
Linezolid	2	(100)	2	(100)					1	(100)
Nitrofurantoin	3	(100)	3	(100)					3	(100)
Ampicillin			6	(100)					2	(50)
Erythromycin	4	(100)			1	(100)	1	(100)		
Clindamycin	2	(100)			1	(100)				
Gentamicin	5	(100)			1	(100)			4	(100)
Vancomycin	4	(100)			1	(100)			2	(100)
TMP-SMX	7	(100)			2	(100)			2	(100)
Doxycyclin	1	(100)								
Tetracyclin	2	(100)								
Ciprofloxacin			1	(100)						
Amoxicillin-clavulanic acid			1	(100)						
Benzylpenicillin			1	(100)						
Cloxacillin					1	(100)				
Cefepime									2	(50)
Cefotaxime									1	(100)
Ceftriaxone									2	(50)
Tigecyclin									1	(100)
Oxacillin									1	(100)

TMP-SMX: Trimethoprim/sulfamethoxazole

Discussion

Gram-negative bacteria are the most common cause of infection in pediatric malignancy patients with febrile neutropenia, especially *Escherichia coli, Pseudomonas aeruginosa* and *Klebsiella pneumonia*. The causative agents of infection in febrile neutropenia has shifted from Gram-negative to Gram-positive bacteria. Gram-negative bacteria still account for 40–50% of pathogens identified in febrile neutropenia patients.[10] The cause of the shift is presumed to be caused by years of empirical antibiotic treatment, which are more directed to Gram-negative than Gram-positive bacteria. Treatment often fails due to an increase of methicillin resistance to *staphylococcus*.[10,11]

The most common Gram-negative bacteria found in blood cultures in this study were *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. Das et al stated that the bacteria found consisted of *E. Coli* (17.9%), *Staphyloccoccus aureus* (13.4%) and *Klebsiella Pneumonia* (10.4%) in pediatric malignancy patients with febrile neutropenia.[12] A previous study by Al-Mulla et al stated that *Klebsiella pneumoniae* was the most common Gram-negative bacteria found in blood cultures of pediatric patients with malignancy.[3] Prasad et al stated in their research that Gram-negative bacteria, namely *Pseudomonas species*, *E coli* and *Klebsiella sp*, were more commonly identified in pediatric malignancy patients with febrile neutropenia.[13] Reyes et al in their study stated that 65% of Gram-negative bacteria were found in blood cultures, which consisted of *Pseudomonas sp*, *Escherichia coli*, and *Klebsiella pneumonia*.[14] A study by Gudiol et al stated that Gram-negative bacteria, namely *E. Coli, Pseudomonas aeruginosa, and Klebsiella sp* were more common in malignancy patients

with febrile neutropenia than gram-positive bacteria.[15]

In this study, *Coagulase-negative Staphylococci* was the most common Gram-positive bacteria identified in culture. Hakim et al in their research stated that *Viridans streptococci, Escherichia coli*, and *Pseudomonas aeruginosa* were the most common bacteria found in patients with malignancy.[16] A study by Agyeman et al stated that 46 of 73 isolated pathogens were gram-positive bacteria (*Staphylococcus aureus, Staphylococcus coagulase-negative, and streptococcus mitis*), while gram-negative was 27/73 (*E.coli and Pseudomonas aeruginosa*).[17] Carvalho et al stated that the most common gram-positive bacteria isolated in malignancy patients were streptococci group (*Viridans streptococci*) and enterococci group (*Enterococcus faecium*).[18] A study by Budiana et al stated that the organisms that often cause bacteremia in patients with malignancy are gram-negative bacteria (*Escherichia coli, Klebsiella pneumonia*, and *Pseudomonas aeruginosa*), followed by gram-positive aerobic cocci bacteria (*Staphylococcus sp, Streptococcus sp* and *Enterococcus*).[19] Patients with a quantitative or qualitative deficiency of PMN may develop infections caused by bacteria (*Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa,* and recently an increasing number of resistant gram-negative organisms) and fungi (especially *Candida species, Aspergillus species, species Fusarium*, and *Zygomycetes*).[20,21,22]

In this study, the most common bacteria on urine culture identified were *Enterococcus faecalis, Escherichia coli*, and *Klebsiella pneumoniae*. A study by Parikh et al stated patients with malignancies with suspected urinary tract infection, urine culture results detected most of the isolates were Gram-negative bacteria, *Escherichia coli* and *Klebsiella pneumoniae*.[23] Fungal culture identified positive results for *Candida albicans* on sputum culture. Fungal infections in malignant children have increased, mostly caused by *Candida albicans, Candida tropicalis, Candida krusei,* and filamentous fungi (*Aspergillus, Mucor,* and Fusarium).[24]

Tang et al stated that the most common drug resistance gram-positive bacteria isolated in pediatric malignancy patients were methicillin-resistant coagulase-negative staphylococcus (85.6%), methicillin-resistant S. aureus (12.5%) and vancomycin-resistant enterococci (12.5%).[11] Prabhash et al stated that ceftazidime and piperacillin-tazobactam as empirical agents for infection in cancer is alarming and the strict regulation of vancomycin use should be considered in low prevalence area of methicillin-resistant *Staphylococcus aureus*.[25] The number of *Staphylococcus aureus* and *streptococcus spp* infections in this study were small, thus any comment on the antimicrobial sensitivity patterns of these organisms would be invalid.

This study only observed patients who had developed febrile neutropenia in pediatric malignancy patients, to determine profile bacterial from blood, urine, sputum, wound bed culture and antimicrobial sensitivities in our hospital. This may not represent the reality of all patients who have febrile neutropenia in pediatric malignancy patients. It is important to realize the limitations of this study. Our study is the first published study from dr Saiful Anwar General Hospital to report the bacterial and fungal etiology of pediatric hematology/oncology patients with febrile neutropenia and to identify antimicrobial susceptibility of these organisms to guide empirical antimicrobial therapy and improve the quality of pediatric malignancy care.

Conclusion

To effectively treat infection in the pediatric malignancy patients with febrile neutropenia, knowledge of the pathogens and the antimicrobial sensitivity patterns in individual centers is crucial. The etiology of microbiologically documented infection in pediatric malignancy patients with febrile neutropenia in this study was predominantly gram negative, with *Klebsiella pneumonia, E Coli, Pseudomonas aeruginosa* and *Acinetobacter baummani* the most frequently isolated organisms. Therefore, the initial choice of empirical therapy at our center must have adequate Gram-negative and antipseudomonal coverage. Our susceptibility results suggest that therapy with ampicillin and gentamycin was a viable treatment strategy.

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Conflict of Interest

The authors declare that there is no conflict of interest for this research.

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