Zagazig University Medical Journal
www.zumj.journals.ekb.eg

Volume 28, Issue 6, November 2022(311-317) Supplement Issue

Manuscript ID ZUMJ-2001-1701 (R1)
DOI **10.21608/zumj.2020.22639.1701**

ORIGINAL ARTICLE

Evaluation of Infection Risk and Antibiotics Exposure at a Pediatric Oncology Unit: Single Center Study

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Submit Date 2020-02-05

Revise Date 2020-06-17

Accept Date 2020-06-23

ABSTRACT

Background: Pediatric cancer patients are at greater risk of infection due to their impaired immunity and intense anticancer therapy. So, the use of antibiotics in these patients is common to reduce the incidence of infection. This study aimed to evaluate infection risk and antibiotic exposure for patients admitted to the pediatric oncology unit.

Methods: The study was carried out in the Pediatric Hematology and Oncology unit, Zagazig University Hospitals, over a period of one year from September 2018 to September 2019. The study included 80 patients attending to the unit. All patients were subjected to full history taking, clinical examination, routine laboratory investigations and assessment of risk factors for infection. Culture and sensitivity tests were done to evaluate the antibiotic exposure, guide the antibiotic choice and revise prescription orders.

Results: According to the distribution of risk factors of infection among the studied group, we found that all groups were immuno-compromised with peripheral intravenous catheters and took immunosuppressive drugs, 53.8% had increased length of stay and 50% did personal hygiene. No one had surgery or urinary devices. The blood culture results distribution revealed that (81.25%) had no growth and (18.75%) were infected. The majority were *Staphylococcus aureus and E coli* (5%) and (3.75%) respectively. Regarding the results of the cultures, the antibiotic that had the highest percentage of sensitivity among the bacterial organisms discovered was Tigecycline (71.4%).

Conclusion: Avoiding the risk factors of infection helps in decreasing the incidence of infection among cancer patients. The prescription of antibiotics must be according to the culture results.

Keywords: Pediatrics; Oncology; Infection; Antibiotics.

INTRODUCTION

Childhood cancer patients have an increased risk of infections and complications acquired from hospitals as many defects in their immune response to infection arise from a variety of factors acting simultaneously or sequentially. The underlying disease and the medications used to treat it play important roles in this problem **[1]**. In pediatric oncology patients, there are many risk factors for infection. Many of them are related to the patient, while others are related to the units in which they are treated. Avoiding these risk factors with the implementation of fundamental procedures such as hand hygiene, transmission-based measures, environmental hygiene, bundles of HAI prevention and antimicrobial stewardship are key elements of any successful infection prevention program **[2]**. Modern medicine is powered by antibiotics. Their use decreases deaths in children and improves their lifespan. Furthermore, the number of infections by multidrug resistant bacteria is growing worldwide, and untreatable infections are becoming a reality. There is a lack of production of new antibiotics besides increased resistance to current agents [3]. The increasing frequency of antibiotic-resistant bacteria is mainly because of antibiotic overuse and poor adherence to recommended infection control measures. Healthcare units must minimize overuse and misuse of antibiotics to control the spread of these pathogens, and new strict programs must be implemented to improve health workers' hand hygiene habits and other recommended infection control procedures [4]. Antimicrobial Stewardship program (ASP) is one of the main strategies to surmount the resistance. It includes the accurate and responsible management of antibiotic use. The antimicrobial is chosen in a timely and appropriate

manner for the optimum clinical results for the management or prevention of infection with scant toxicity to the patient and minimal affection on resistance [5].The aim of our work is to evaluate infection risk and antibiotic exposure for patients admitted to the pediatric oncology unit to guide the antibiotic choice depending on the results of culture and sensitivity tests.

METHODS

The study was carried out in the Pediatric Hematology and Oncology unit, Zagazig University Hospitals over a year from September 2018 to September 2019. The study included 80 patients attending the Pediatric Hematology and Oncology unit and having the inclusion and exclusion criteria. The sample was obtained by a simple random sample technique until the needed sample size was fulfilled. The age ranged from 2 years to 15 years. Both sexes who were diagnosed with solid and hematological malignancies were involved in the study, considering each admission of the same patient as a new case. Patients with chronic infections and patients who were outside the age group mentioned were excluded from the study. Written informed consent was obtained from first degree relatives of the patients and the study was approved by the research ethical committee and the institutional review board (IRB) of the Faculty of Medicine, Zagazig University. The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. All patients were subjected to full **history taking,** including personal history such as name, age, sex, residency, etc. All patients were asked about their present history and the complaint. Past history was taken, including general health status, past illnesses, hospitalizations, surgical interventions, medications, allergies, immunizations, diet and finally growth and development evaluation. All patients were also asked for their family history of hereditary diseases. General and local examinations were done for all patients to detect any medical problems or infections. The routine laboratory work-up was done as complete blood count, ESR, and blood cultures. All positive data in routine investigations of infection were documented in relation to the presence of neutropenia. All risk factors threatening the process of infection prevention that are related to the patient were assessed. For example, immunity status, increased length of stay, self-cleaning and personal hygiene, taking immunosuppressive drugs, having surgical interventions, presence of long-term venous catheters, presence of urinary or ventilator devices. [6] The effect of antibiotic exposure was assessed by collecting information to clear some details on each patient's antibiotics such as their names, doses, exposure times, switching, the outcome on each individual case's health status and prescription either was according to a written policy or not and also according to culture and sensitivity results or not. The level of healthcare workers' adherence to Stewardship antibiotic program was also assessed. The elements assessed were: early detection of sepsis; localization of source of sepsis; doing workup and markers of sepsis; presence of indication for prophylactic antibiotics; de-escalation of antibiotics according to cultures; starting empirical antibiotics according to the localization; obtaining cultures according to localization; following up the response of antibiotics; analysis of causes of negative response; presence of a final plan and decision to stop antibiotics. **[5] Isolation, identification, and antimicrobial susceptibility of organisms were performed as follows:** Blood cultures: 5 ml of blood were obtained from each patient under complete aseptic conditions because modern blood culture systems are highly accurate in detecting bacteremia. The cultures were done for aerobic, and anaerobic bacteria and fungi. All culture and sensitivity tests were done for all children before starting the empirical antibiotics to avoid blurring of the results. All cultures were done by VITEK MS which is an automated mass spectrometry microbial identification system. Isolation and identification were carried out and available sensitivity to antibiotics was done. **[7] *Statistical analysis:*** Data collected during history, basic clinical examination, laboratory investigations and results were coded, entered, and analyzed using Microsoft Excel software. Data were then entered into the Statistical Package for the Social Sciences (SPSS) version 20.0 software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by (mean ± SD).

RESULTS

The total number of patients was 80. 50 patients (62.5%) were male and 30 patients (37.5.5%) were female. Age of patients was distributed as 6.32±3.45 with minimum 2 years and maximum 14 years Table (1). The infection pattern presentation among the studied patients is demonstrated in Table (2). Fever was observed in about 36.25% of patients. Table (3) shows the detailed distribution of risk factors of hospital acquired infections among the studied group. Regarding the distribution of the blood culture results, 18.75% showed growth and the type and distribution of the isolated organisms are shown in Table (4). Table (5). shows the antibiotics susceptibility results for bacterial organisms. Each case had a single type isolated organism. The most antibiotic that had the

highest percentage of sensitivity among the bacterial organisms discovered was Tigecycline in 10 cases with percentage of (71.4 %). In the second grade, we found Moxifloxacin with percentage of (57.1 %) while in the third grade we find Ciprofloxacin and Gentamicin with percentage of (50 %). On the other side, the most antibiotic that has the highest percentage of resistance among the bacterial organisms discovered is Cefepime and Trimethoprim – Sulfamethazine with percentage of (42.8 %) Table (6) shows the antifungal susceptibility results for the only detected case of *Candida species*. However, it was not a routine to do antifungal sensitivity testing. The level of healthcare workers' adherence to Stewardship antibiotic program is detailed in Table (7).

Table (1): Demographic data of the studied group. Age and sex distribution for the studied patients:

Variant	Number	Percentage%
Sex		
Male	50	62.5
Female	30	37.5
Total	80	100.00
Age/ years		
Mean± SD	6.32±3.45	
Median (Range)	5.0 (2-14)	

Table (2): Infection pattern presentation among the studied patients: (Total N=80)

The presentation	N. of cases	Percentage
Fever	29	36.25%
Diarrhea (Gastroenteritis)	18	22.5%
Bed sores	2	2.5%
Upper respiratory tract infections	17	21.25%
Lower respiratory tract infections	13	16.25%
Urinary tract infections	9	11.25%

Table (3): Distribution of risk factors of hospital acquired infections among the studied group: (Total N=80)

Risk factors	Patients number	Total N.	Percentage %
Immuno-compromised	-VE	0	0.0
	+VE	80	100.0
Peripheral intravenous catheters	-VE	0	0.0
	+VE	80	100.0
Increased length stay	-VE	37	46.3
	+VE	43	53.8
Immunosuppressive drugs	-VE	0	0.0
	+VE	80	100.0
Surgery	-VE	80	100.0
	+VE	0	0.0
Urinary devices	-VE	80	100.0
	+VE	0	0.0
Personal hygiene	-VE	40	50.0
	+VE	40	50.0
	Total	80	100.0

Table (4): Distribution of the blood culture results:

Organisms Patients number	Total N.	Percentage %	Total number (%)
No Growth	65	81.25	65 (81.25%)
Acinetobacter Baumannii complex	1	1.25	15 (18.75%)
Candida species	1	1.25	
E. coli	3	3.75	
Enterococcus faecium	1	1.25	
Klebsiella pneumoniae	2	2.5	
Staphylococcus aureus	4	5	
Staphylococcus haemolyticus	1	1.25	
Staphylococcus hominis	2	2.5	

Table (5): Antibiotics susceptibility results for bacterial organisms:

Organisms	Gram positive organisms													Gram negative organisms								
	Staph. aureus			Staph. haemo-lyticus			Staph. hominis			Entero. faecium				E. coli			Kleb. Pneumo-niae			Acinet. Bauma-nnii c.		
Antibiotics	S	I	R	S	I	R	S	I	R	S	I	R		S	I	R	S	I	R	S	I	R
Penicillins																						
Penicillin	1	-	-	-	-	1	-	-	2	1	-	-		-	-	-	-	-	-	-	-	-
Ampicillin	-	-	-	-	-	-	-	-	-	1	-	-		-	-	3	-	-	1	-	-	1
Oxacillin	1	-	1	-	-	1	-		2	-	-	-		-	-	-	-	-	-	-	-	-
Penicillin – Tazobactam	-	-	-	-	-	-	-	-	1	-	-	-		1	-	-	-	-	1	-	-	-
Ampicillin – Sulbactam	-	1	-	-	-	-	-	-	-	-	-	1		-	-	2	-	-	1	-	-	1
Amoxicillin – Clavulinic acid	-	1	-	-	-	-	-	-	-	-	-	-		1	-	-	-	-	-	-	-	-
Carbapenems																						
Imipenem	-	1	-	-	-	-	-	-	-	-	-	-		2	-	1	1	-	1	-	1	-
Meropenem	-	-	-	-	-	-	-	-	-	-	-	-		2	-	1	1	-	1	-	-	-
Ertapenem	-	-	-	-	-	-	-	-	-	-	-	-		2	-	1	1	-	-	-	-	-
Aztreonam	-	-	-	-	-	-	-	-	-	-	-	-		-	-	2	-	-	2	-	-	1
Cephalosporins																						
Cefazolin	-	-	1	-	-	-	-	-	-	-	-	-		-	-	-	-	-	1	-	-	-
Ceftazedin	-	-	1	-	-	-	-	-	-	-	-	-		-	-	1	-	-	1	-	-	-
Ceftriaxone	-	-	-	-	-	-	-	-	-	-	-	-		-	-	2	-	-	-	-	-	1
Cefepime	-	-	-	-	-	-	-	-	-	-	-	-		-	-	3	-	-	2	-	-	1
Cefotaxime	-	1	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-
Quinolones																						
Ciprofloxacin	3	-	-	1	-	-	-	2	-	1	-	-		2	-	1	-	-	1	-	-	1
Levofloxacin	3	-	-	1	-	-	-	2	-	1	-	-		-	-	-	-	-	-	-	-	-
Moxifloxacin	2	-	-	1	-	-	2	-	-	1	-	-		1	-	1	1	-	-	-	-	1
Ofloxacin	1	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-
Norfloxacin	1	-	-	-	-	-	-	-	-	-	-	-		1	-	-	-	-	-	-	-	-
Sulfonamides																						
Trimethoprim – Sulfamethazine	1	-	2	1	-	-	2	-	-	-	-	-		2	-	1	-	-	2	-	-	1

Organisms	Gram positive organisms													Gram negative organisms								
	Staph. aureus			Staph. haemo-lyticus			Staph. hominis			Entero. faecium				E. coli			Kleb. Pneumo-niae			Acinet. Bauma-nnii c.		
Amikin	2	1	-	-	-	-	-	-	-	-	-	-		2	-	-	2	-	-	-	-	-
Gentamicin	2	-	-	-	1	-	2	-	-	-	-	-		3	-	-	-	-	2	-	-	1
Tobramycin	-	1	-	-	-	-	-	-	-	-	-	-		1	-	1	-	2	-	-	-	1
Macrolides																						
Azithromycin	-	-	1	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-
Erythromycin	1	-	2	1	-	-	-	1	1	1	-	-		-	-	-	-	-	-	-	-	-
Tetracyclines																						
Tetracycline	1	-	-	-	-	1	1	-	1	-	-	1		-	-		-	-	-	-	-	-
Minocycline	-	-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	1	-	-	-
Others																						
Tigecycline	3	-	-	1	-	-	2	-	-	1	-	-		2	-	-	1	-	-	-	-	1
Vancomycin	-	-	1	1	-	-	2	-	-	1	-	-		-	-	-	-	-	-	-	-	-
Linezolid	1	-	-	1	-	-	2	-	-	1	-	-		-	-	-	-	-	-	-	-	-
Clindamycin	1	-	-	1	-	-	-	-	2	-	-	1		-	-	-	-	-	-	-	-	-
Quinupristin & Dalfopristin	1	-	-	1	-	-	2	-	-	1	-	-		-	-	-	-	-	-	-	-	-
Fosfomycin	-	-	-	-	-	-	-	-	-	-	-	-		1	-	-	-	-	-	-	-	-

Table (6): Antifungal susceptibility results:

Antifungals	Sensitive	Intermediate	Resistant
Amphotericin B	**1**	-	-
Flucytosine	-	**1**	-
Fluconazole	**1**	-	-
Itraconazole	-	**1**	-
Ketoconazole	-	-	**1**
Nystatin	-	-	**1**

Table (7): Level of healthcare workers (HCWs) adherence to Stewardship antibiotic program:

Elements	Adherent	Not adherent
Early detection of sepsis	✓	-
Localization of source of sepsis	✓	-
Workup and markers of sepsis	✓	-
Indication for prophylactic antibiotics	✓	-
Starting empirical antibiotics according to the localization	-	✓
Obtaining cultures according to localization	-	✓
De-escalation of antibiotics according to cultures	✓	-
Follow up the response of antibiotics and analysis of causes of negative response	-	✓
Final plan and decision to stop antibiotics	-	✓
Total percentage	55.5%	44.5%

DISCUSSION

Children with cancer are at an increased risk for health-associated infections (HAI) due to their diagnosis and immunosuppressive medication. Repeated visits to healthcare settings also increase the risk of exposure to resistant organisms [8].

The aim of this study was to evaluate the infection risk and estimate of antibiotic exposure for patients admitted to the pediatric oncology unit to guide the antibiotic choice depending on the results of culture and sensitivity tests.During the study period, we checked for multiple risk factors of infection in pediatric oncology. The study revealed that all patients were immuno-compromised with

inserted peripheral intravenous catheters and took immunosuppressive drugs. In addition, our study demonstrated that 53.8% had an increased length of stay and 50% did personal hygiene.In order to implement an effective infection control program, the previously identified risk factors should be considered by the higher authorities to plan for appropriate corrective action.The percentage of infected patients reported in the study reached (18.75%) among all patients included in the study. This percentage is lower than the percentage found in Da Silva Gama and colleagues' study, which found that 20% of infected people developed hospital acquired infection [9].It was found in the present study that out of all infected patients, the highest number (4 cases, with a percentage of 26.67%) were affected by *Staphylococcus aureus*. The second highest number (3 cases with a percentage of 20%) of patients were affected by *E. coli*. *Klebsiella pneumonia and Staphylococcus hominis* were responsible for infecting (2 cases with percentage 13.33 %), (2 cases with percentage 13.33%) of patients, respectively. Only (4 cases with percentage 26.67 %) of patients were being infected by other types of microorganisms.

A total of 42 bacterial pathogens were identified in a study in Ethiopia conducted by W Mulu and colleagues, including *S. Aureus*, which was the main isolate, accounting for 26.2 percent, followed by *E. Coli* and Coagulase negative *Staphylococcus* species with 21.4 percent each [7].

In a study in Morocco, Razine found that *Staphylococcus* spp was the most isolated organism (18.7%) among patients with hospital-acquired infections [10].Fungal infection is one of the most significant causes of morbidity and mortality in immunologically disordered patients. Over the past few decades, the rate of these infections may have increased due to reduced immunity in such patients or progress in chemotherapy regimens. Our study revealed that the incidence of fungal infection among all infected cases was (one case with a percentage of 6.67 %). On the other side, Parisa Badiee and colleagues found that the incidence of invasive fungal infections in pediatric patients with hematologic neoplasms was (16.3 per cent) [11].

Antibiotics are strong medicines that cure many infections and, when correctly used, can save lives. They either stop reproducing bacteria or kill them. They are recognized as the most important therapeutic breakthrough in medical history. Moreover, 20 to 50 per cent of all antibiotics used in U.S. acute care hospitals are either superfluous or disadvantageous [12].This misuse and overuse of antibiotics, as well as poor infection prevention and control has led to rising antibiotic resistance, which has been one of the most dangerous and increasing threats to public health. New resistance mechanisms are emerging and spreading globally [13].In our study, cultures from all patients were done to detect the organism and determine the sensitivity to antibiotics. 81.25% of all cultures done were negative cultures. This may be due to the real absence of infection in some patients and the presence of atypical microorganisms.

Regarding the results of the cultures, the most antibiotic that has the highest percentage of sensitivity among the bacterial organisms discovered is Tigecycline with a percentage of (71.4 %). In second grade, we found Moxifloxacin with a percentage of (57.1 %) while in third grade we found Ciprofloxacin and Gentamicin with a percentage of (50 %). On the other side, the most antibiotic that has the highest percentage of resistance among the organisms discovered is Cefepime and Trimethoprim – Sulfamethazine with percentage of (42.8 %).Strong evidence shows that hospital-based programs focused on improving prescriptions for antibiotics, usually referred to as "Antibiotic Stewardship Programs"(ASPs). It is capable of both optimizing infection treatment and reducing antibiotic adverse reactions.The level of HCWS adherence to Stewardship antibiotic program is nearly 55.5%. Starting empirical antibiotics according to the localization, obtaining cultures according to localization, following up the response of antibiotics and analysis of causes of negative response and final plan and decision to stop antibiotics are the deficient elements for achieving an efficient Stewardship antibiotic program.

These programs are designed to help clinicians raise the quality of care for patients and improve patient safety by increasing infection cure rates, reducing treatment failures, and increasing the frequency of proper therapy [14]. It is a must to achieve a successful (ASPs) and to become a unique goal for all hospital departments, not only the oncology department.

CONCLUSIONS

Pediatric oncology patients are at an elevated risk of life-threatening infections and complications due to their existing diseases and the intensive chemotherapy they receive. The easiest and most effective solution to this problem is to identify the risk factors that facilitate the occurrence of that and avoid them. We should pay attention to the use of empirical antibiotics and not to give them without prior cultures. Prescription of antibiotics must be according to a written policy according to the culture results.

Recommendations:

Trying to improve the use of antibiotics is a major concern for patient safety and public health. Also, there is a need to improve antibiotic use as one of

the main key strategies required to solve the problem of antibiotic resistance. Antimicrobial Stewardship program is one of the important strategies to overcome this problem, so it is a must to be implemented through an integrated team of hospital individuals.

Conflict of interest: The authors declare no conflict of interest.

Funding sources: The authors have no funding to report

REFERENCES

1. Viscoli C, Varnier O, Machetti M. Infections in patients with febrile neutropenia: epidemiology, microbiology, and risk stratification. Clin Infect Dis. 2005;40(Supplement_4):S240-5.
2. Thom K, Kleinberg M, Roghmann M. Infection prevention in the cancer center. Clin Infect Dis. 2013;57(4):579-85.
3. Blair J, Webber M, Baylay A, Ogbolu D, Piddock L. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol. 2015;13(1):42-51.
4. Boyce J. Consequences of Inaction: Importance of infection control practices. Clin Infect Dis. 2001;33(s3):S133-7.
5. Nathwani D, Sneddon J, Patton A, Malcolm W. Antimicrobial stewardship in Scotland: impact of a national programme. Antimicrob Resist Infect Control. 2012; 1:2-4.
6. Kim M, Boynton D, Roswell P, Cheryl P. Infection prevention in oncology and other immunocompromised patients. APIC. 2014;(44):202-789.
7. Mulu W, Kibru G, Beyene G, Damtie M. Postoperative nosocomial infections and antimicrobial resistance pattern of bacteria isolates among patients admitted at FelegeHiwot Referral Hospital, Bahirdar, Ethiopia. Ethiop J Health Sci. 2012;22(1):7-18.
8. Dutta A, Flores R. Infection prevention in pediatric oncology and hematopoietic stem cell transplant recipients. HCAI Child. 2018,16:281–99..
9. Silva G, Hernández P, Freitas M, Padoveze M, Oliveira C, Paulino L, et al. Good infection prevention practices in three Brazilian hospitals: Implications for patient safety policies. J Infect Public Health. 2019;12(5):619-24.
10. Razine R, Azzouzi A, Barkat A, Khoudri I, Hassouni F, Chefchaouni A, et al. Prevalence of hospital-acquired infections in the university medical center of Rabat, Morocco. Int Arch Med. 2012;5(1):1-8.
11. Badiee P, Zareifar S, Haddadi P, Jafarian H. Incidence of fungal infections in pediatric patients with hematologic neoplasms. Arch Pediatr Infect Dis. 2017;5(3):0-4.
12. Alshammari T, Larrat E, Morrill H, Caffrey A, Quilliam B, LaPlante K. Risk of hepatotoxicity associated with fluoroquinolones: A national case-control safety study. Am J Heal Pharm. 2014;71(1):37-43.
13. Huttner A, Harbarth S, Carlet J, Cosgrove S, Goossens H, Holmes A, et al. Antimicrobial resistance: A global view from the 2013 World Healthcare-Associated Infections Forum. Antimicrob Resist Infect Control. 2013;2(1):1-13.
14. Nowak M, Nelson R, Breidenbach J, Thompson P, Carson P. Clinical and economic outcomes of a prospective antimicrobial stewardship program. Am J Heal Pharm. 2012;69(17):1500-8.

To Cite:

Said, S., Mohammed, M., Ahmed, A., El-Sokkary, R.., Evaluation of Infection Risk and Antibiotics Exposure at a Pediatric Oncology Unit: Single Center Study. *Zagazig University Medical Journal*, 2022; (311-317): -. 10.21608/zumj.2020.22639.1701