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Original Article (Pages: 18691-18699)

Antibiotic Resistance Pattern in Nosocomial Infections in Children's Hospital

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Abstract

Background: Indiscriminate use of antibiotics in the treatment of Nosocomial Infections (NIs) has led to microbial mutation and drug resistance. Antibiotic resistance is a threat to public health, especially for children. The aim of this study was to investigate NIs and antibiotic resistance in children's hospitals.

Methods: This study was conducted retrospectively and descriptively using paper and electronic files of patients admitted to Dr. Sheikh Children's Hospital of Mashhad, Iran in 2023. The data were categorized in three seasons. Type and frequency of NIs, microbial mass, and antibiotic resistance were investigated based on seasons and hospital departments. Data were analyzed through descriptive statistics by Excel software.

Results: The most common type of NIs in all three seasons of the study was blood system infection (BSI) (64.98 %). Although in ICU, Ventilator-Associated Event Infection (VAEI) was more common. Klebsiella, with an average of 18.97%, was the most common cause of NIs. The most commonly used antibiotics were cephalosporin, and vancomycin. The highest rate of resistance was related to Acinetobacter. In the second and third seasons, this bacterium showed more than 80-100% resistance to cephalosporin, fluoroquinolone, aminoglycoside and carbapenem. The highest rate of Klebsiella antibiotic resistance was seen against carbapenem (83.33%) in the second season of the study. In the third season of the study, Escherichia coli showed more resistance to cephalosporin compared to other antibiotics (66%). In the second season, Pseudomonas showed 100% resistance to carbapenem.

Conclusion: The results showed high antibiotic resistance of common pathogens against commonly used antibiotics. And due to the vulnerability of children, necessary interventions should be made to reduce the rate of NIs and control the use of antibiotics.

Key Words: Antibiotic resistance, Children Hospital, Nosocomial infection.

* Please cite this article as: Jahangiri M, Mosaddegh MR, Sepehri Z, Bahari M, Ghasemi A, Jahangiri S. Antibiotic Resistance Pattern in Nosocomial Infections in Children's Hospital. Int J Pediatr 2024; 12 (03):18691-18699. DOI: **10.22038/ijp.2024.79890.5453**

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Received date: Jan.12,2024; Accepted date: Mar.21,2024

1- INTRODUCTION

NIs include infections acquired through health care providers such as hospitals. The fastest onset of NI is 48 hours after hospital admission, but they can also appear 3 days after discharge or 30 days after surgery. However, in some cases, such as surgery, NIs may occur within 30 days of discharge, such as surgical site infections. In recent decades, NIs have become an alarming health challenge worldwide, and their incidence is increasing rapidly, especially in developing countries (1).

Bacteria are the cause of 90% of NIs, of which Klebsiella pneumonia, Staphylococcus aureus, Pseudomonas and Proteus species are the most important leading factors (2). Most NIs present as pneumonia, Nosocomial Bloodstream Infections (NBSIs), nosocomial Urinary Tract Infections (UTIs), and nosocomial Surgical Site Infections (SSIs) (3). NIs are caused by different routes. For example, in urinary tract infections, which comprise 40-45% of hospital infections, about 80% occur due to catheterization and 20% occur due to urinary tract manipulation (2).

According to the report of the World Health Organization (WHO), the incidence of NIs varies from one region to another, and out of every 100 people, 17 people are suspected of having NI, ten of which are from developing regions (3). NIs are one of the leading and important causes of death, disability, increased length of hospitalization, and increased hospital costs (2). WHO declared 1.7 million per year NIs and 99000 related deaths every year (4). The severity and occurrence rate of NIs are affected by the immunological status of patients. The most vulnerability to NIS is observed in burn, intensive care (ICU), organ transplant, and neonate departments (5).

Treatment of NIs is a long-term process and antibiotics are used in the process of treating patients. However, irrational use of antibiotics has created problems (3). The emergence of antibiotic resistance following hospital infections is one of the health challenges of recent decades. Pathogenic microbes become resistant to medicines by mutation and create new generations that antibiotics have no effect on (6). Some repeated medical interventions, including the widespread use of immunosuppressant drugs and antibiotics, have caused the development of transferable resistance in pathogenic agents. The treatment of NIs is very difficult due to the resistance of most of the microbial strains and is expensive due to the long hospitalization period of the patients (2). Considering the serious threat to the health of patients due to antibiotic resistance in bacterial pathogens, WHO named 2011 as the year of antibiotic resistance (7). In the document of 2019, WHO has also placed antibiotic resistance among the ten factors that threaten health at the global level? In recent years, with the increase in the frequency of bacteria resistant to multiple pharmaceutical agents, the rate of treatment-resistant NIs that can easily lead to death has increased (8). The widespread use of antibiotics in various sectors such as agriculture, animal husbandry, veterinary medicine, and medical practices has led to the spread of multidrug-resistant organisms globally, and children are no exception to this danger (9). According to WHO estimates, every year in the world, infections caused by multidrug-resistant bacteria lead to 700,000 deaths, of which about 200,000 deaths occur in newborns (10).

The prevalence of NIS in Middle Eastern countries is significant. In a study conducted by Nasiri et al., in Iran, 3.3% of patients reported NIs. Bone marrow transplant units were the largest reservoir of NIs transmission. The most common

infections were identified in the bloodstream, urinary tract, surgical site, and lower respiratory tract (11). According to a study in Saudi Arabia, 5 to 10 percent of cases requiring treatment in emergency care were related to NIs. They reported that the NIs rate is increasing day by day, especially in the ICU. Among various pathogens, Staphylococcus aureus was the most common cause of NIs (12).

Due to the diversity of bacteria isolated from culture samples in different geographical regions and the emergence of different types of microbial resistance, timely recognition and diagnosis of antibiotic resistance, as well as the correct use of antibiotics are vital to reduce the development of pharmaceutical resistance. Since the use of antibiotics in various infections has increased, the investigation of antibiotic resistance is considered a research priority in every region. This study was conducted with the aim of determining nosocomial bacterial infections and the pattern of antibiotic resistance in a reference children's hospital.

2- MATERIALS AND METHODS

2-1. Design and population

The current research was conducted through census method retrospectively and descriptively using the information available in the paper and electronic files of patients admitted to Dr. Sheikh Children's Hospital in Mashhad city, Iran, in the last 9 months of 2023.

2-2. Inclusion and exclusion criteria

The inclusion criteria were as follows: All hospitalized children between 1 and 18 years of age who had no previous history of hospitalization and were hospitalized for the first time and were in contact with only one microbial agent were included in the study. Children who had an underlying disease before hospitalization, as well as those who had a history of hospitalization or infection, were excluded from the study.

2-3. Data collection

The tool for data collection was the questionnaire number one (patient diagnosis) of the Ministry of Health, Treatment, and Medical Education of Iran, which included demographic characteristics as well as signs and symptoms of urinary, pulmonary and blood infections along with the culture results. Completing the questionnaires was done under the supervision of the infection control nurse.

Samples were prepared and cultured for each infected person at 3:00 p.m. after the injection of drugs at 2:00 p.m. Based on the investigations, some places and tissues that had the highest prevalence of contamination were selected for sampling. These samples were collected from blood, deep wound, urine, sputum, urinary catheter, trachea, venous catheter and feces of children with NIs who were hospitalized in different departments.

The data were categorized and analyzed in three periods of three months. The information related to the type of hospital infections and their frequency in different departments of the hospital, as well as the type of microbial mass and their frequency in different months were investigated. Finally, antibiotic resistance was investigated based on bacteria and antibiotics. According to the investigations conducted in the studied hospital, the commonly used antibiotics included cephalosporin, ciprofloxacin, clindamycin, caspofungin/voriconazole, carbapenem, vancomycin, ampicillin, linezolid, liposomal ampho trypsin, and colomycin. Considering that no intervention was done on the patients and the patients' information remained confidential, this study did not have any problem in terms of research ethics.

2-4. Data analysis

The data were analyzed descriptively using Excel software version 2016. The Mean value was used to describe quantitative variables; and frequency and percentage were used to describe qualitative variables.

3- RESULTS

In this study, 10,505 patients hospitalized in different departments were examined, and a total of 156 patients were identified with NIs. Based on this, the rate of NIs was 1.4%. Of the total study population, 61% were boys and 39% were girls. The mean age of the studied patients was 5.35 years. The average length of hospitalization of the patients in the present study was 15.35 days per month.

In the current section, we refrain from explaining the items shown in the table, and instead explain the other results that do not exist in the tables. At first, the number of NIs was determined based on the culture preparation location. The relevant results in the three study periods are separately reported in **Table 1**. In the first, second, and third three months of the study, 64.8%, 58.5 %, and 71.66 % of infections were BSI type, respectively. UTI prevalence in the three periods of study was 10.8 %, 29.2 % and 5 % respectively. VAEI was responsible for NIs in 24.32 %, 12.19%, and 23.33% in the three periods of study, respectively.

Table-1: Frequency of NIs based on type, department and time of sampling

Study periods	Department	Type of NIs		
		BSI	UTI	VAEI*
First three months	ICU	11	2	18
	Pediatric 1	8	5	0
	General Pediatric	4	1	0
	Internal	20	0	0
	Hematology	5	0	0
	Total	48	8	18
Second three months	ICU	5	2	5
	Pediatric 1	3	10	0
	General Pediatric	6	0	0
	Internal	6	0	0
	Hematology	4	0	0
	Total	24	12	5
third three months	ICU	10	1	14
	Pediatric 1	4	1	0
	General Pediatric	8	0	0
	Internal	13	1	0
	Hematology	8	0	0
	Total	43	3	14

*VAEI: ventilator assisted events infection

In the data related to the first quarter of the study, the most common cause of BSI was Klebsiella, the most common cause of UTI was Escherichia coli, and the most common cause of VAEI was Acinetobacter. In the next three months,

the most common cause of BSI and VAEI was Klebsiella and the most common cause of UTI was Escherichia coli. In the last quarter, the most common cause of BSI was Klebsiella, and the most common cause of VAEI was Acinetobacter. The number of UTI cases was very low (3 cases), which were caused by Candida, Escherichia coli and Acinetobacter. Microbial masses with the highest frequency in each period are shown in **Table 2**.

Table-2: Microbial masses with the highest frequencies

Variable	Type of microbial mass	Frequency	Frequency percentage
First three months	Staphylococcus	22	19.8
	Pseudomonas	17	15.3
	Klebsiella, E. coli	14	12.6
Second three months	Klebsiella	20	20.83
	Pseudomonas	13	13.5
	Staphylococcus epidermidis	12	12.5
Third three months	Klebsiella	31	23.48
	Staphylococcus epidermidis	25	18.9
	Pseudomonas	14	10.6

In the following, it was investigated which departments of the hospital had the highest frequency of blood culture microbial masses. The results are presented via **Table 3**.

Table-3: Frequency of blood culture microbial mass in various departments in different periods of the study

Departments	First three months	Second three months	Third three months
Emergency	37	-	64
Internal 1	17	19	20
Internal 2	19	14	16
ICU	28	18	26
Nephrology	9	5	1
General	0	2	0
Surgery	1	-	-
Pediatric 1	-	38	5
Total	111	96	132

It should be mentioned that in the first three months, in the emergency department and ICU, the most common microbial mass was staphylococci. In the second three months, Klebsiella was the most common microbial pathogen in pediatric ward 1, Pseudomonas was the most common microbial pathogen in internal ward 1, and Escherichia coli was the most common microbial pathogen in ICU. In the third three months, in the internal parts, Klebsiella and staphylococcus epidermidis had a significant prevalence. In the emergency department, the abundance of Klebsiella, Pseudomonas and Staphylococcus epidermidis was significant. Klebsiella, Acinetobacter and Staphylococci

epidermis were the most common microbial pathogens in ICU during this period.

In all three study periods, the most commonly used antibiotics were cephalosporin, carbapenem and vancomycin, respectively. In this sense, there were no differences between critical departments and other departments. The percentage of antibiotic resistance of the most common microbial masses is shown in **Table 4**.

Table-4: Antibiotic resistance of microbial pathogens with the highest frequencies in the three various periods of the study

Time of study	The most frequent Microbial masses	Antibiotic Microbial Resistance (%)				
		Cephalosporin	Fluoroquinolone	Aminoglycoside	Carbapenem	Beta-lactamase inhibitors
First three months	Klebsiella	60	20	-	55	-
	Escherichia coli	50	50	-	15	-
	Pseudomonas	29	0	25	50	-
	Acinetobacter	50	0	71	60	-
Second three months	Klebsiella	75	0	-	83.33	80
	Escherichia coli	58.33	30	-	11.11	44.44
	Pseudomonas	33.33	0	33.33	100	0
	Acinetobacter	100	100	100	80	-
Third three months	Klebsiella	69	28	-	40	20
	Escherichia coli	66	33	-	0	0
	Pseudomonas	50	16	20	80	-
	Acinetobacter	100	100	83	88.8	-

4- DISCUSSION

The variety of organisms that cause NIs and therapeutic interventions, the indiscriminate use of antibiotics, the importance of speeding up the diagnosis, and treatment of infections all show the importance of investigating the rate of NIs and the antibiotic resistances created which are associated with them (13). According to the studies conducted in Iran, the prevalence of NIs has been different in different hospitals (14). This difference can be caused by the difference in hospitalized patients because the presence of accompanying and underlying diseases and the small age or old age of the patients can affect the rate of Nis (15).

In this study, the three major sites for NIs include BSI (64.98 %), VAEI (19.94 %), and UTI (15%). These results were also reported by Kalanuria et al., in which the prevalence rates of UTI, VAEI and BSI were 31%, 24%, and 16%, respectively (16). Our results also showed that VAEI was the most common NIs in the ICU.

According to the results, Klebsiella, Staphylococcus, Pseudomonas, Escherichia coli, and Acinetobacter were the main causes of NIs. Our results are consistent with the studies by Tolera et al. (17) and Sikka et al. (18), where the most

common gram-negative bacteria causing NIs were Escherichia coli, Klebsiella and Pseudomonas aeruginosa. In the study by Agaba et al., the most gram-negative causes of Nis were Klebsiella, and Acinetobacter (19). In the present study, Staphylococcus aureus was the most important gram-positive bacterium in causing NIs, which is in agreement with the results of the study by Agaba et al. (19), and Wang et al (20).

According to the results, all common gram-negative pathogens in the present study had at least a 50% resistance to one of the investigated antibiotics. In a study performed in Iran, the level of resistance in gram-negative bacilli had been increased while it was lower in the gram positive cocci. The higher rates of antibiotic resistance belonged to ampicillin/sulbactam, piperacillin/tazobactam, and ceftriaxone (21). In a study in a children's hospital in northern Iran, all gram positive and negative bacterial isolates showed significant resistance to antibiotics in which Pseudomonas and Acinetobacter were more common in the isolated samples (22). In parallel with the results of the present study, a study in the United States showed that the antibiotic resistance of the causative pathogens in patients with NIs is increasing, especially for staphylococci and enterobacteriaceae (Pseudomonas aeruginosa) (23). The results of this study and many other studies indicate a high prevalence of antibiotic resistance among children. This could be due to the fact that antibiotics are used more than any other type of medicine in the treatment of children. Because children are frequently exposed to infections of various causes, from the more common infections such as urinary tract infections to the less common meningitis (10).

Increasing resistance to antibiotics and new mechanisms of resistance to treatment have made NIs difficult to manage. Paying attention to risk factors such as poor patient immunity, long-term medical procedures, and invasive techniques, which are known as the most basic ways of infection during treatment, have been considered as effective solutions in the management of NIs (24).

5- CONCLUSION

The results of the present study confirmed the high antibiotic resistance of common pathogens responsible for NIs. To control the spread of NIs, which has become difficult due to the increasing antibiotic resistance, it is recommended that infection control practices in hospitals be monitored and revised. Also, the necessary revisions regarding the dosage of antibiotics based on the age of the patients should also be done by the health policy makers.

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