Original Investigation / *Özgün Araştırma*

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Assessment of Healthcare-Associated Infections in Pediatric Intensive Care Unit

Çocuk Yoğun Bakım Ünitesindeki Sağlık Bakımı İlişkili Enfeksiyonların Değerlendirilmesi

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Abstract

Objective: In this study, it was aimed to determine the incidence and rate of healthcare-associated infections, and to determine the susceptible microorganisms and antibiotic susceptibilities by examining the patients hospitalized in our Pediatric Intensive Care Unit retrospectively.

Material and Methods: Patients who were hospitalized for more than 48 hours between January 2014 and June 2019 at Trakya University Hospital Pediatric Intensive Care Unit were examined retrospectively and criteria and formulas for Centers for Disease Control and Prevention were used in calculations.

Results: A total of 49 healthcare-associated infections were detected in 6825 patient days in a total of 725 patients. Healthcare-associated infection rate was found to be 6.76%. 29 invasive device related infections were detected. Ventilator usage rate was 38%, ventilator associated pneumonia rate was found to be 11.19 per 1000 interventional device days, central venous catheter usage rate was 40%, central venous catheter related hospital infection rate was found to be 0.73 per 1000 interventional device days and urinary catheter usage rate was 26%, catheter related urinary tract infection rate was found to be 0.56 per 1000 interventional device days. The most common agents were *Acinetobacter baumannii* (37%), *Pseudomonas aeruginosa* (16.6%), *Klebsiella pneumoniae* (16.6%), *Escherichia coli* (9.2%), respectively.

Conclusion: The healthcare-associated infection rates of our Pediatric Intensive Care Unit were found at the level of developed countries when compared to other countries. However, our rate of ventilator-associated pneumonia was high. The common problem of pediatric intensive care units is multi-antibiotic resistant microorganisms.

Keywords: Pediatric intensive care unit, healthcare-associated infection, surveillance

Öz

Giriş: Çalışmamızda Çocuk Yoğun Bakım Ünitemizde yatan hastalar geriye dönük incelenerek sağlık bakımı ilişkili enfeksiyonlarının sıklık ve hızlarının saptanması, etken mikroorganizmaların ve antibiyotik duyarlılıklarının belirlenmesi amaçlanmıştır.

Gereç ve Yöntemler: Trakya Üniversitesi Tıp Fakültesi Hastanesi Çocuk Yoğun Bakım Ünitesi'nde Ocak 2014-Haziran 2019 tarihleri arasında 48 saatten uzun süre yatan hastalar geriye dönük incelenmiştir ve hesaplamalarda Hastalıkları Önleme ve Kontrol Merkezi kriterleri ve formülleri kullanılmıştır.

Bulgular: Toplam 725 hastada, 6846 hasta gününde, toplam 49 sağlık bakımı ilişkili enfeksiyon saptanmıştır. Sağlık bakımı ilişkili enfeksiyon hızı %6.76 olarak bulunmuştur. 29 invaziv araç ilişkili enfeksiyon saptanmıştır. Ventilatör kullanım oranı %38, ventilatör ilişkili pnömoni hızı 1000 girişimsel araç gününe 11.19, santral venöz kateter kullanım oranı %40, santral venöz kateter ilişkili hastane enfeksiyonu hızı 1000 girişimsel araç gününe 0.73, üriner kateter kullanım oranı %26, kateter ilişkili üriner sistem enfeksiyonu hızı 1000 girişimsel araç gününe 0.56 olarak bulunmuştur. En sık görülen etkenler sırasıyla *Acinetobacter baumannii* (%37), *Pseudomonas aeruginosa* (%16.6), *Klebsiella pneumoniae* (%16.6), *Escherichia coli* (%9.2) olarak saptanmıştır.

Sonuç: Çocuk Yoğun Bakım Ünitemizin sağlık bakımı ilişkili enfeksiyon hızları diğer ülkelerle kıyaslandığında gelişmiş ülkeler düzeyinde bulunmuştur. Ancak ventilatör ilişkili pnömoni oranımız yüksektir. Çocuk yoğun bakım ünitelerinin ortak sorunu çoklu antibiyotik dirençli mikroorganizmalardır.

Anahtar Kelimeler: Çocuk yoğun bakım ünitesi, sağlık bakımı ilişkili enfeksiyon, sürveyans

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Introduction

Healthcare-associated infections (HAI) are an important cause of morbidity and mortality in children treated as inpatients. Moreover, they are responsible for prolonged length of hospital stay and increased costs (1). Even though healthcare-associated infections are seen worldwide, their incidence varies between countries, regions, and hospitals. These differences are related to microorganisms found commonly in hospitals, to the team that have a role in the transportation of these microorganisms and provide healthcare and patients, and to various interactions between the patients (1,2). Pediatric patients requiring intensive care are more prone to HAIs. Natural defense mechanisms like skin integrity, coughing reflex, and gastric motility are deteriorated in these patients. Such severe diseases repress both natural and acquired immunity. Broad-spectrum antibiotics started with treatment purposes due to suspected sepsis deteriorate the protective flora and lead to the reproduction of pathogen bacteria and fungi (3). Healthcare-associated infections in pediatric inpatients can be seen as intravenous or intraarterial catheter-associated blood flow infections, ventilator-associated pneumonia (VAP), urinary tract infections, surgical wound infections, and infections related to implanted foreign objects. Healthcare-associated infections cause high morbidity and mortality. In addition, they prolong length of hospital stay and raise the cost of treatment (4). Aim of this retrospective study was to examine the incidence of HAI recorded on the hospital infection control and surveillance system of our Pediatric Intensive Care Unit (PICU), location of infection, microorganisms growing in cultures, and antibiotic resistance, and thus, to determine the latest condition of our unit and re-organize our antibiotic policy and protective measures.

Materials and Methods

The study was carried out in the six bed PICU of our hospital. Pediatric intensive care unit is a hospital unit having two isolated rooms which patients aged 1-18 years are admitted. This unit accepts post-operative patients aged 1-18 years cerebral spinal fluid brought to the emergency service or are admitted to wards or epicenters but require advanced life support during follow-up. Active surveillance is constantly carried out by the hospital infection control committee in the PICU. A retrospective investigation was conducted on the records of inpatients admitted to our PICU between January 2014 and June 2019. During this period of time, a total of 725 patients were admitted in the PICU, and of these patients, 38 were diagnosed with HAI. Our study included the data of these 38 patients (49 attacks).

Patients who were admitted to another hospital within the past one month, patients that died within the first two days of admission or that were discharged from the hospital, and patients referred to our hospital from another one with HAI were excluded from the study.

The following definitions and formulas were used in the calculation of the rate of healthcare-associated infection:

Length of hospital stay: The total of days that a patient spends in the hospital as an inpatient. Only the day of admission is counted and the day of discharge is not. It expresses the total number of days of all PICU inpatients for a year.

Days of invasive device: It expresses the total number of days inpatients are exposed to invasive devices in the PICU for a year.

The rate of healthcare-associated infection: (The number of healthcare-associated infections/the number of inpatients) x100

Incidence density of healthcare-associated infection: (The number of healthcare-associated infections/Days of being ill) x1000

The rate of invasive device use: Days of invasive device/ Days of being ill

The rate of invasive device-associated healthcare-associated infection (per 1000 catheter days): the number of invasive device-associated HAI /Days of invasive device) x1000

The rate of invasive device-associated healthcare-associated infection (IDAHAI) % (per each 100 patients): (the number of IDAHAI /the number of inpatients) x100

Healthcare-associated infections were defined on the basis of Centers for Disease Control and Prevention (CDC) criteria (5). The patients were retrospectively reviewed in terms of HAI types, HAI rates, agent microorganisms and antibiotic susceptibility. Characteristics such as age, sex, diagnosis at admission, comorbid diseases, length of hospital stay, day of hospital stay at the time of diagnosis, the presence of infection during admission, presence and type of an underlying disease, presence of a risk factor for infection development, antibiotics used prior to HAI diagnosis, HAI type, microorganism type, and culture growth site were retrospectively evaluated in patients diagnosed with healthcare-associated infection. All patients suspected of HAI in the PICU undergo appropriate laboratory tests and radiologic imaging that support diagnosis. Together with blood culture, urine, sputum, cerebral spinal fluid, wound site, catheter and endotracheal aspirate and tube cultures in those receiving ventilator treatment are taken.

Risk factors that may affect infection development in all patients diagnosed with health care-associated infection were determined. Risk factors were listed as venous/arterial catheter use, nasogastric catheter, urinary catheter, central venous catheter, intubation tube, peritoneum dialysis catheters, ventriculoperitoneal shunt catheter, tracheostomy, percutaneous endoscopic gastrostomy catheter, long term antibiotic use, loss of consciousness, H_2 receptor blocker use, immunosuppression, transfusion, total parenteral nutrition, and having undergone operation.

This study was approved by Trakya University Faculty of Medicine Scientific Research Ethics Committee on November 6, 2019 with the protocol number BAEK 2019/398.

Statistical Analysis

Statistical analyses were performed on SPSS 19.0 (Serial number: 10240642) statistics package program. Descriptive statistics, Mann-Whitney U were used as statistical method. Numerical datawere expressed as mean and standard deviation and categorical data as frequency distribution and percentage. In relation to HAI, HAI rate, HAI incidence density, ratio of invasive device use, central venous catheter-associated bloodstream infection (CVC-ABSI), catheter-associated urinary tract infection (CA-UTI), and epidemiologic data like VAP ratio were calculated.

Results

Between the duration of time of the study, a total of 38 patients (5.24%), 14 (36.8%) girls and 24 (63.2%) boys, diagnosed with HAI and recorded on the infection control and surveillance system were included into our study. Forty-nine HAI attacks that developed in these 38 patients were taken under assessment. Of these patients, 31 had 1 HAI attack, 4 had 2 attacks, 2 had 3 attacks, and 1 had 4 attacks. Rate of HAI was detected as 6.76%, and HAI incidence density in 1000 days of being ill was found as 7.16. Mean age was found as 5.6 ± 6.0 years (minimum 1 month, maximum 16.8 years) and mean body weight as 18.8 ± 19.1 kilograms (minimum 2.6, maximum 75 kg) (Table 1). Table 2 presents invasive device-associated HAI rates in our PICU.

When admission status of the patients was reviewed, it was seen that 22 (57.9%) patients were admitted due to infection and 16 (42.1%) were admitted for reasons other than infection. Mortality rate after hospital admission was found as 50%. When diagnoses at admission were reviewed, it was found that 17 (44.74%) patients were diagnosed with pneumonia, 5 (13.6%) were admitted following resuscitation (referral from an epicenter after resuscitation), and 5 (13.6%) had status epilepticus, respectively. Other diagnoses at admission included 2 (5.26%) acute gastroenteritis (severe dehydratation) cases, 2 (5.26%) hypoxic ischemic encephalopathy sequela cases, and one post-operative case (rhabdomyosarcoma, tumor resection), one transverse myelitis, one thalamic aneurism hemorrhage, one neuroblastoma, one medulloblastoma, one Hodgkin's lymphoma, and one spina bifida case. One and only patient admitted for trauma was hospitalized due to status epilepticus subject to head trauma after motor vehicle accident. At least one underlying disease was present in 33 of the patients diagnosed with HAI, one patient had two chronic diseases, and there were no comorbid diseases in 5. The most common comorbid disease was cerebral palsy.

Out of 49 HAI attacks diagnosed during the study period, the first was VAPs with 53.1% (n= 29), the second was bloodstream infection (BSI) with 20.4% (n= 10) and the third was clinically defined pneumonia with 6.1% (n= 3). Eight of the patients developing ventilator-associated pneumonia has ce-

Table 1. Demographics of the pediatric intensive care unit and HAI rates

Number of inpatients in the PICU	725
Number of patients in whom HAI was detected	38
Number of days being hospitalized	6846
Mean length of PICU stay (day)	9.44
Mean length of stay of patients with HAIs (day)	49.86 (min 7-max 207)
Day of HAI incidence (day)	17.1 (min 6-max 40)
Boys [n (%)]	24 (63.15%)
Girls [n (%)]	14 (36.84%)
Age, year (mean)	5.6
Day of invasive device	Urinary catheter day 1770 CVC day 2730 Ventilator day 2592
HAI rate	6.76%
HAI incidence density	7.16
Ratio of invasion device use	Urinary catheter ratio 26% CVC ratio 40% Ventilator ratio 38%
Invasive device-associated HAI rate-per (1000 invasive device day)	CA-UTI rate 0.56 CVC-ABSI rate 0.73 VAP pneumonia 11.19

HAI: Healthcare-associated infection, CA-UTI: Catheter-associated urinary tract infection, CVC: Central venous catheter, CVC-ABSI: Central venous catheter-associated bloodstream infection VAP: Ventilator-associated pneumonia.

Table 2. Invasive device-associated HAI rates

	n	Total number of in patients	Total number of days being ill	Ratio of device use	Total day of invasive device	Invasive device-associated HAI rates (per 1000 invasive device days)
VAP	26	725	6846	38%	2592	11.19
CVC-ABSI	2	725	6846	40%	2730	0.73
CA-UTI	1	725	6846	26%	1770	0.56

HAI: Healthcare-associated infection, CA-UTI: Catheter-associated urinary tract infection, CVC-ABSI: Central venous catheter-associated bloodstream infection VAP: Ventilator-associated pneumonia.

Table 3. Healthcare-associated infections of the patients

Healthcare-associated infections	n	%
Ventilator-associated pneumonia	26	53.1%
Laboratory-proven bloodstream infection	10	20.4%
Clinically defined pneumonia	3	6.1%
Central venous catheter-associated bloodstream infection	2	4.1%
Meningitis or ventriculitis	1	2.0%
Catheter-associated urinary tract infection	1	2.0%
Meningitis developing postoperatively	1	2.0%
Decubitis ulcer infection	1	2.0%
Primary superficial incisional surgical site infection	1	2.0%
Arterial or venous infection	1	2.0%
Soft tissue infection	1	2.0%
Urinary system infection not associated with catheter	1	2.0%
Total	49	100.0%

Table 4. Distribution of the patients' infection agent

	Agent	n	%
Gram negative bacteria	*Acinetobacter baumannii*	20	37.0%
	Pseudomonas aeruginosa	9	16.6%
	Klebsiella pneumoniae	9	16.6%
	Escherichia coli	5	9.2%
	Serratia marcescens	2	3.7%
	Enterobacter aerogenes	2	3.7%
	Klebsiella oxytoca	1	1.8%
Fungi	*Candida albicans*	3	5.5%
	Candida parapsilosis	1	1.8%
Gram positive bacteria	Koagülaz (-) stafilokok	2	3.7%
*There are patients in whom more than one agent grew.			

rebral palsy, four patients had an underlying malignancy, and two were diagnosed with spinal muscular atrophy. Four patients had tracheostomy. Mean time spent under mechanical ventilator in patients developing VAP was 22.3 days.

Out of the samples taken from patients, 48 (88.8%) gram-negative bacteria, 2, (3.7%) gram-positive bacteria, and 4 (7.4%) fungi were isolated (Table 4).

The primarily isolated infection agents from the samples were found as *Acinetobacter baumannii* in 20 patients (37%), *Pseudomonas aeruginosa* in 9 (16.7%) patients, and *Klebsiella pneumonaiae* in 9 (16.7%) patients, respectively. While one of the coagulase negative staphylococci (CNS) was *Staphylococcus capitis*, the other was *Staphylococcus hominis*. When isolation sites of the primarily isolated agents detected in patient samples were examined, *A. baumannii* was detected in respiratory tract samples with 41.9%, in blood samples with 16.6%, *A. baumannii* and CNS in cerebral spinal fluid samples with 50.0%, *A. baumannii* and *K. pneumoniae* in urine samples with 50%, *A. baumannii* in wound site with 40% and in the tip of the catheter with 100%. Figure 1 shows the ratio of the agents detected according to invasive device-associated HAI types.

While 95% of *A. baumannii* strains in healthcare-associated infections were resistant to carbapenem, colistin resistance was not seen. While 78% of *K. pneumoniae* strains were resistant to carbapenem, this rate was 56% in *P. aeruginosa*. One of the coagulase negative staphylococci (50%) was resistant to methicillin. Multiple drug resistance was found in gram-negative microorganisms. Figure 2 summarizes resistance rates of gram-negative bacteria.

Discussion

While HAI is seen in 5-10% of patients admitted to hospital in developed countries, this rate is two-25 fold more in developing countries and surpasses 25% (6). HAI incidence in children

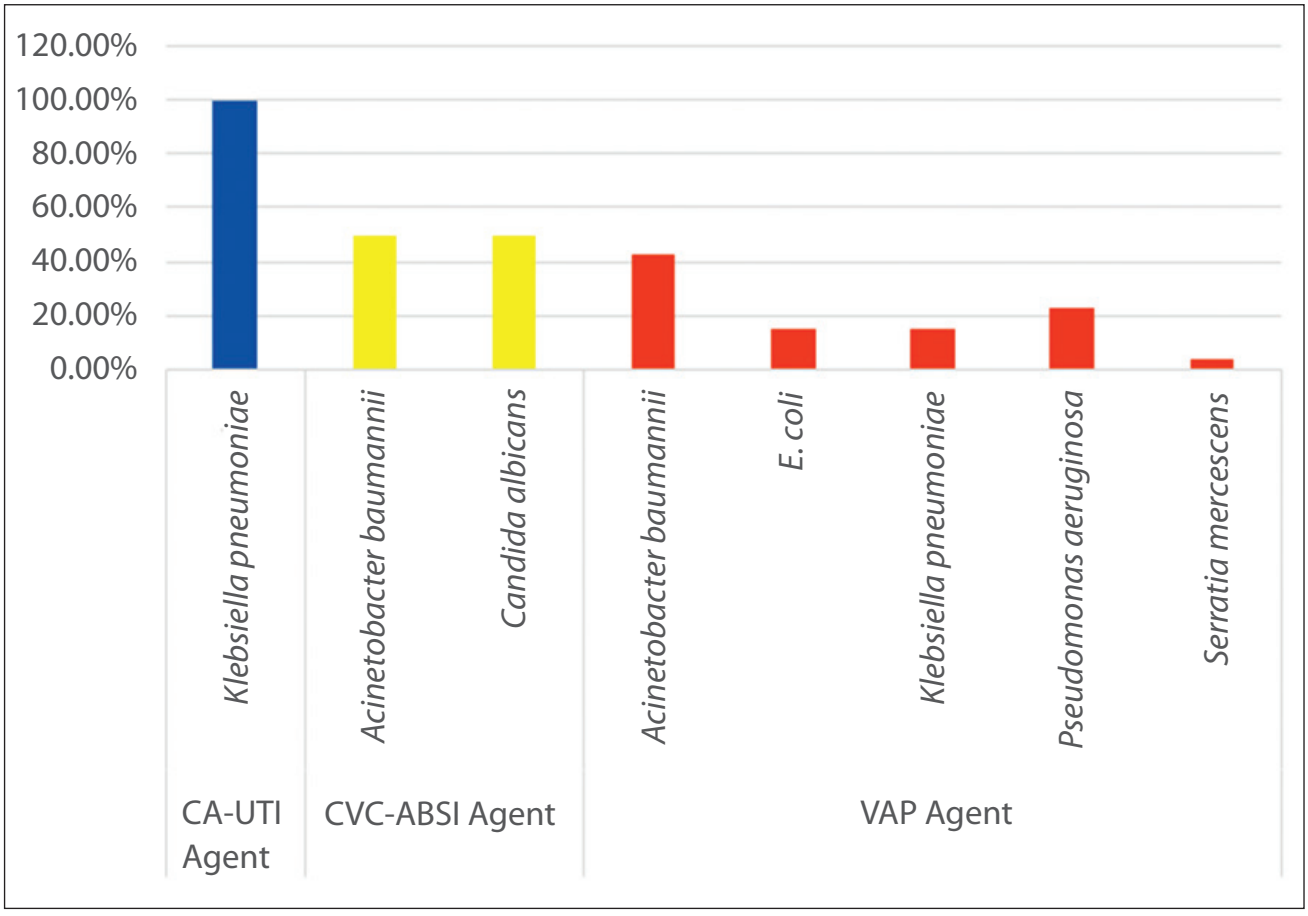

Figure 1. Invasive device-associated HAI and agents.

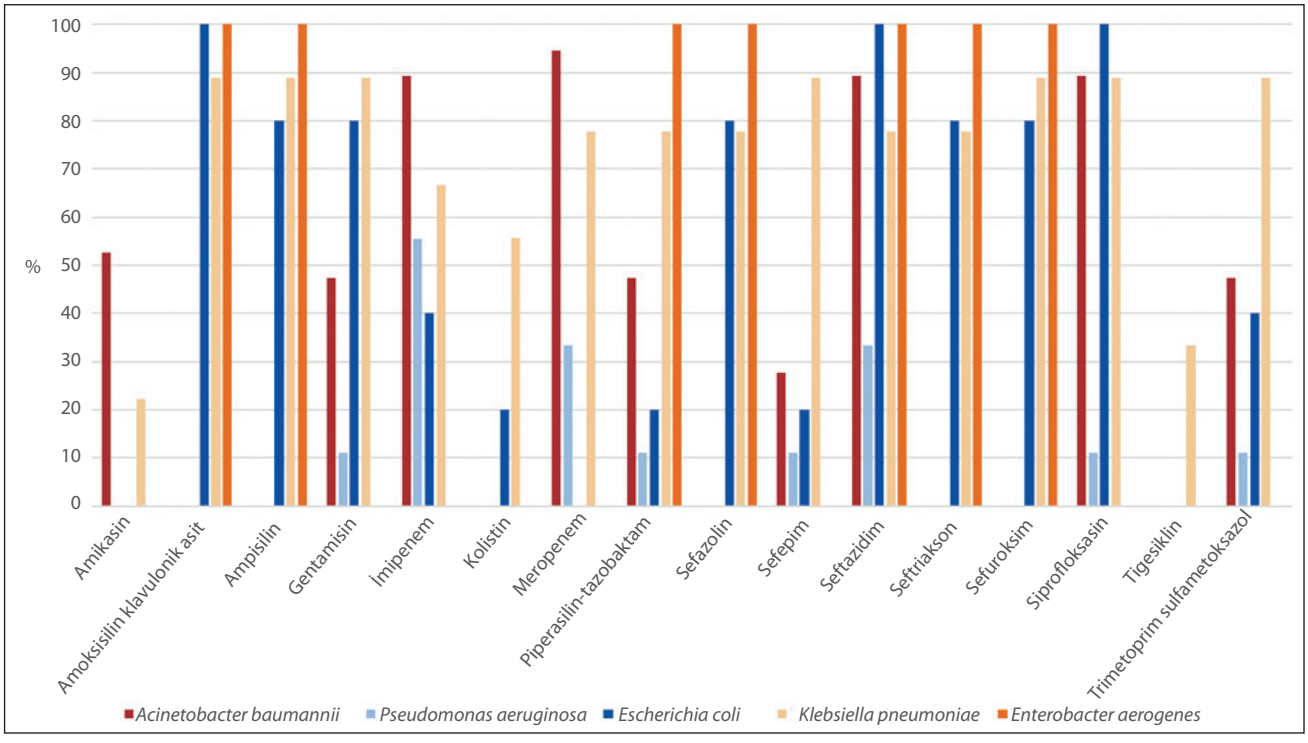

Figure 2. Resistance status of Gram-negative bacteria.

show inverse proportion with age and the country's level of development. Healthcare-associated infections show inverse correlation with age in adult and child patients, and while HAI is between 7-9% in children aged under one year, it is between 1.5-4% in children aged 1-10 years (7). Children are under more risk in terms of HAI compared to adults due to vascular problems, frequent necessities of drug applications, and the need for a more often nurse care in pediatric intensive care units (8). Pediatric HAI rates in several studies have been reported as 6-13.7% in the USA, 18.3% in Brazil, 29.6% in Egypt, and 6.7% in Switzerland (9-12). In a single-center study conducted in Izmir, Turkey, HAI rate has been found as 32.7%, in a study conducted in Pediatric Health and Diseases wards in Istanbul in 2010, the same rate was found as 9.6%, and HAI rate has been determined as 16.3% in a study carried out in the Pediatric Clinic and PICU of Uludag University Medical Faculty (13-15). In a study from Turkey in which 50 PICUs from 27 different cities have participated, HAI rate has been detected as 37% (16). When these data were compared to ours, our pediatric intensive care unit is at the level of developed countries with 6.76% in terms of HAI rate. We are of the opinion that this is because within years, the nurse/patient ratio has been brought to a better level, hand hygiene is of crucial importance, infection control measures are strictly followed, and invasive procedures are terminated in the shortest possible time. The difference detected between the studies can arise from many factors. For instance, the number of HAI increases due to reasons such as short number of staff per patient, surplus number of chronic patients requiring long admission, and insufficiency of physical means.

The most common HAI in PICUs is BSI, followed by pneumonia and UTI (4). The most common HAI in our PICU in the study was pneumonia, 26 of which were VAP and 3 were clinical pneumonia. This was followed respectively by BSI and UTI. Invasive device-associated HAI in our PICU was VAP, which was followed by CVCA-BSI and CA-UTI. Considering infection agents, the first three pathogens in terms of incidence were *A. baumannii*, *P. aeruginosa* and *K. pneumoniae*. In a prospective study from Spain, it has been detected that the most frequent HAI seen in PICU was BSI, followed by respiratory tract infections and UTI. In the same study, it has been established that the most frequent agent in bacteremia was central nervous system (CNS), the most frequent agent of pneumonia was *P. aeruginosa*, and that of UTI was *Escherichia coli*. VAP rate has been found as 23.9 for 1000 invasive device days, CVC-ABSI rate as 12.4 and CA-UTI rate as 10.7 (2). In a study conducted in a PICU in Brazil, it has been reported that the most common HAIs were respectively pneumonia (31.6%) and BSI (17.3%), and the agents were respectively gram-negative bacteria (54.8%), gram-positive bacteria (23.8%), and fungi. The most frequently isolated gram-negative bacteria have been reported as *A. baumannii* and *K. pneumoniae* (10). In a study from our country, the most common HAI has been reported as lower respiratory tract infection (23.5%), and the most frequently isolated agents have been determined as *P. aeruginosa*, *Acinetobacter* spp. and *Candida* spp. (16). In our study, the most common agent in VAP was *A. baumannii*, in BSI, it was *A. baumannii* and *Candida* albicans, in pneumonia, it was *A. baumannii*, and in UTI, it was 50% *A. baumannii* and 50% *K. pneumoniae*. In our hospital, the primary HAI agent is *A. baumannii*. In a study from Japan conducted retrospectively with 426 patients in a PICU, it has been reported that VAP rate per 1000 invasive devise days was 3.5, CVC-ABSI rate was 4.3 and CA-UTI rate was 13.6. In the same study, it has been determined that the most common CVC-ABSI agent was CNS and that of CA-UTI was *E. coli*, *P. aeruginosa* and *K. pneumoniae* (17). In a study from a PICU in Egypt, it has been concluded that CVC-ABSI rate per 1000 invasive device days was 11.9, VAP rate was 31.7, and CA-UTI was 0, and the most common isolated agents related to VAP were *Klebsiella* spp., methicillin-resistant *Staphylococcus aureus*, followed by *P. aeruginosa* (18). HAI has been reported as lower respiratory tract infection in a multicenter study from our country, and the most commonly isolated agents have been found as *P. aeruginosa*, *Acinetobacter* spp. and *Candida* spp. Seventy-one percent Carbapenem resistance has been detected in *P. aeruginosa* and 83% colistin resistance in *Acinetobacter* strains (16). In our PICU, invasive device-associated HAI rates were found as 11.19 for VAP, 0.73 for CVC-ABSI, 0.56 for CA-UTI per 1000 invasive device days, and when compared to other studies, a distinctively lower values were found except for VAP. It has been reported in the studies conducted that the most common agent in CA-UTI was *E. coli*, followed by *Klebsiella* spp., *Enterococcus* spp., *Proteus mirabilis*, *P. aeruginosa*, *Candida* spp. (19). In our 1 CA-UTI case, the agent that was isolated was *K. pneumoniae*. We believe that the reason for low rates of CVC-ABSI and CA-UTI is that we do not have a high rate of catheter insertion and that we remove the catheter at the shortest time possible.

The second most common HAI in pediatric and neonatal intensive care units is ventilator-associated pneumonia. It constitutes 7% to 32% of HAI and 10% of pediatric device-associated infections. There are some mechanisms recommended for VAP development: its progress is considered to start with the colonization of the upper respiratory tract to tracheal colonization, leading to tracheid and eventually to pneumonia. This depends on the number, type and virulence of bacteria, on mechanical factors and on natural host defenses like humoral and cellular immunity, as well. Mechanical defenses like ciliary movement and mucus secretion are deteriorated in intubated patient, which acts as a reservoir for pathogens. It causes proton pump inhibitors that neutralizes stomach pH and is used for stress ulcer prophylaxis, and histamine type 2 receptor antagonists lead to upper gastrointestinal system colonization. Aspiration risk increases in a patient lying on his/her back and whose mental state is probably depressive (secondary two sedation or disease) (20). Of our 21 patients developing VAP,

eight had cerebral palsy, two had spinal muscular atrophy and four had tracheostomy. Length of mechanical ventilator stay for these patients was high. VAP rate in our unit was much higher than that reported in the literature despite caring for hand hygiene, routine mouth care, performing endotracheal aspiration when needed, preferring oral intubation, following asepsis rules for tracheostomy care, trying to shorten length of mechanical aspiration, taking necessary isolation measures, and training our staff. In this retrospective study, the differentiation between tracheitis and VAP was not clearly made, and growth in tracheal aspirate cultures may have been interpreted in favor of surplus infection. It was surmised that not having non-invasive respiratory support technology, high number of patients with chronic diseases, and the fact that intubated patients are more frequently laid on their back may have raised this ratio. Data were included into the study as are recorded on the surveillance system.

As of the 1990s, infections caused by multi-resistant gram-negative microorganisms have increased worldwide and started to become a serious clinical problem (21). Similarly, multi-resistant gram-negative bacteria stand out in our study and are the most common reasons of HAIs.

Active surveillance is performed in our hospital. However, our primary limitation is the retrospective design of the study. Other limitations include insufficiency of file content and the fact that present deficiencies of the surveillance records were detected during the study.

To conclude, along with the fact that every PICU has its own rates, agents and infections, the common problem is multidrug resistant microorganisms. Preparing national guidelines may contribute on this matter.

Ethics Committe Approval: This study approval was obtained from Trakya University Faculty of Medicine Scientific Researches Ethics Commitee (Decision no: 18/28, Date: 06.11.2019).

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- NAÇ; Design- NAÇ, RD; Supervision- NAÇ; Resource- EDÖÇ, NAÇ; Data Collection and/or Processing- EDÖÇ, RD; Analysis and/or Interpretation- NAÇ; Literature Search- NAÇ, EDÖÇ; Writing- EDÖÇ, NAÇ; Critical Review- RD.

Conflict of Interest: Authors declared no conflict of interest.

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