ORIGINAL ARTICLE ÖZGÜN ARAŞTIRMA

# Healthcare-associated Infections in the Department of Pediatric Hematology-oncology; A Single Center Evaluation

## Çocuk Hematoloji-onkoloji Kliniğinde Sağlık Bakımı İlişkili Enfeksiyonlar; Tek Merkez Deneyimi

**Zeynep Gizem Ergün Özdel* (0000-0002-6851-7933), Solmaz Çelebi** (0000-0002-3536-0263), Adalet Meral Güneş*** (0000-0002-0686-7129), Melike Sezgin Evim*** (0000-0002-4792-269X), Betül Berrin Sevinir**** (0000-0002-3232-7652), Birol Baytan*** (0000-0002-9375-2855) Metin Demirkaya***** (0000-0003-2880-0117), Serdal Kenan Köse****** (0000-0002-6734-3847), Benhur Çetin******* (0000-0002-8470-4907), Taylan Çelik******** (0000-0002-7568-035X), Enes Salı********* (0000-0002-8136-1240), Mustafa Hacımustafaoğlu** (0000-0003-4646-660X)**

*Bursa Uludağ University Faculty of Medicine, Department of Pediatrics, Division of Social Pediatrics, Bursa, Turkey
**Bursa Uludağ University Faculty of Medicine, Department of Pediatric Infectious Diseases, Bursa, Turkey
***Bursa Uludağ University Faculty of Medicine, Department of Pediatric Hematology, Bursa, Turkey
****Bursa Uludağ University Faculty of Medicine, Department of Pediatric Oncology, Bursa, Turkey
*****Biruni University Faculty of Medicine, Department of Pediatrics, İstanbul, Turkey
******Ankara University Faculty of Medicine, Department of Biostatistics, Ankara, Turkey
*******Erciyes University Faculty of Medicine, Department of Pediatric Infectious Diseases, Kayseri, Turkey
********Çanakkale Onsekiz Mart University Faculty of Medicine, Department of Pediatric Infectious Diseases, Çanakkale, Turkey
*********Ümraniye Training and Research Hospital, Clinic of Pediatric Infectious Diseases, İstanbul, Turkey

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**Address for Correspondence/Yazışma Adresi:** Zeynep Gizem Ergün Özdel, Bursa Uludağ University Faculty of Medicine, Department of Pediatrics, Division of Social Pediatrics, Bursa, Turkey
**Phone:** zgergun@gmail.com
**E-mail:** +90 532 785 94 69

## Abstract

**Introduction:** With advances in the treatment of Pediatric Hematology-Oncology (PHO) patients, the survival of patients are increasing day by day. However, Healthcare-Associated Infections (HAI) is still a significant cause of mortality and morbidity in this group of patients. This study aimed to evaluate the rates of HAI in patients who were hospitalized in Uludag University Medical Faculty PHO Clinic during the 4-year study period.
**Materials and Methods:** HAI was diagnosed according to the CDC (Center for Disease Control and Prevention) 2008 criteria. We recorded the number of patients admitted, the number of patients with HAI, the total number of HAI episodes, and the length of stay in hospital. We calculated HAI rate and HAI density (per 1000 patient-days).
**Results:** During the four years, 3069 hospitalizations were recorded in 607 PHO patients (5.05 admissions per patient). 38.6% of the patients were female, and 61.4% male. The mean age was 100.8 ± 63.6 months. The mean duration of hospitalization was 14 ± 17.16 days. A total of 232 HAI episodes were recorded in 141 hospitalizations. HAI rate was 7.5%, and HAI density was 5.36/1000 patient-days.
**Conclusion:** The HAI rates in our PHO unit were comparable to those of developed countries and lower than those of developing countries and prior results from our country.

## Öz

**Giriş:** Pediatrik Hematoloji-Onkoloji (PHO) hastalarının tedavileri konusunda gelişmeler ile hastaların sağkalım süreleri her geçen gün uzamaktadır. Ancak Sağlık Bakımı İlişkili Enfeksiyonlar (SBİE) halen bu hasta grubunda önemli

bir mortalite ve morbidite nedenidir. Bu çalışmanın amacı, 4 yıllık çalışma döneminde Uludağ Üniversitesi Tıp Fakültesi PHO Kliniğine yatırılan hastalarda SBİE oranlarını değerlendirmektir.
**Gereç ve Yöntem:** SBİE tanıları Hastalık Kontrol ve Önleme Merkezi (CDC) 2008 kriterlerine göre konuldu. Kabul edilen hasta sayısı, SBİE olan hasta sayısı, toplam SBİE atağı sayısı, hastanede kalış süreleri kaydedildi. SBİE hızı ve SBİE dansitesi (1000 hasta günü) hesaplandı.
**Bulgular:** Dört yıl boyunca, 607 PHO hastasında toplam 3069 hastane yatışı kaydedildi (hasta başına 5,05 başvuru). Hastaların %38,6'sı kadın, %61.4'ü erkekti. Ortalama yaş 100,8 ± 63.6 aydı. Ortalama hastanede kalış süresi 14 ± 17.16 gündü. Toplam 141 yatışta 232 SBİE atağı kaydedildi. SBİE hızı %7,5 ve SBİE dansitesi 5,36/1000 hasta günü olarak bulundu.
**Sonuç:** Merkezimizdeki PHO kliniğinde SBİE oranları gelişmiş ülkelerdeki değerlerle kıyaslanabilir düzeyde bulunurken, gelişmekte olan ülkelere ve ülkemizden yayınlanan önceki sonuçlara göre daha düşüktü.

## Introduction

Hospital infections, healthcare-associated infection (HAI), or nosocomial infections are usually used synonymously in the literature to describe local and/or systemic disease caused by pathogenic microorganisms or toxins originating from the hospital environment in a patient without active infection on admission or plausible incubation of infection. Surveillance of HAI is defined as the continuous, systematic collection and analysis of infection-related data needed for the evaluation, planning, implementation, and interpretation of healthcare facilities (1). In Turkey, the Ministry of Health issued an official regulation called "Infection Control Regulation for Inpatient Treatment Institutions" in 2005. As per these regulations, establishing an infection control committee is mandatory to prevent HAI development in all inpatient healthcare facilities in Turkey (2).

Pediatric cancer patients are an important risk group for life-threatening HAI; therefore, children admitted to Pediatric Hematology–Oncology (PHO) units, especially those with leukemia, have a high risk of serious and opportunistic infections and bacteremia due to severe and prolonged neutropenia, injured physical defense barriers and changes in the microbiota. Between 1996–2001, a study including 20 PHO units in eight European countries (8 pediatric units) reported HAI rates of 5.2–13.3% (3). Data from different countries show HAI rates ranging from 3.7–31% in PHO units and HAI densities are reported to vary between 4.8–28 per 1000 patient-days (4-10). In Turkey, there are only a few studies exploring HAI frequencies among PHO patients, and data show HAI rates of 12.8% (9) and HAI density of 13.6–15.6 / 1000 patient-days (11,12).

Although PHO patients are at high risk of HAI, there are only a few articles on this subject. In this study, we aimed to evaluate the HAI rates retrospectively for four years in the PHO unit of our department.

## Materials and Methods

Our study was performed at the PHO unit of Bursa Uludağ University Faculty of Medicine. The PHO department provides health care for patients with pediatric cancer, unexplained anemia, bleeding disorders, and thrombophilia. Patients older than 18 years of age with congenital diseases that may have required PHO unit care before adulthood were also included in the study; thus, some patients included in the study were older than 18 years of age. Ethics committee approval was received before beginning the study from the Ethics Committee of Bursa Uludağ University Faculty of Medicine (Application date: 05.10.2013, approval number: 2013-18/14). HAI data were collected from medical records of patients admitted to the PHO unit from January 1, 2010, to December 31, 2013. Patients' demographic, laboratory, clinical, and radiological data were obtained from the hospital information system. In addition, all pediatric infectious disease consultations were reviewed and recorded. Patients with and without HAI were compared based on these characteristics.

In all patients, HAI diagnoses were based on the 2008 criteria of the Centers for Disease Control and Prevention (CDC) (13). Surveillance data for each year (2010, 2011, 2012, and 2013) were collected based on Ministry of Health guidelines published in 2010 (14). We recorded the following variables for each year: number of patients hospitalized in the PHO unit, total number of hospitalizations, number of patients with HAI, and total number of HAI events in these patients. We calculated the number of HAI attacks per HAI-developed patient. HAI rate was calculated based on

the following formula: (number of HAIs / number of admissions) × 100. HAI density was calculated using the formula: (number of HAIs / total patient-days) × 1000.

*Statistical Analysis*

The SPSS software version 22.0 computer program was used for all statistical analyses. Quantitative variables were described with mean ± standard deviation (SD) and median (minimum–maximum) values; categorical data were described with frequency and percentage. Comparisons between patients with and without HAI were performed with the Mann-Whitney U test in quantitative variables and Pearson Chi-squared tests in categorical variables. The threshold for statistical significance was accepted as $p < 0.05$.

## Results

During the 4-year study period, a total of 3069 hospitalizations in 607 patients were recorded in the PHO unit (5.05 hospitalization events per patient). Overall, 38.6% (1184/3069) of the hospitalization episodes involved females and 61.4% (1885/3069) involved males. Mean age was 100.8 ± 63.6 months, while the median value was 84 (15–267) months. Mean and median length of hospital stay were 14.12 ± 17.36 days and 7 (1–158), respectively. Infection at admission was present in 34.9% of the hospitalization events (1070/3069).

During the 4-year study period, 123 of the 607 patients (20.3%) experienced at least one episode of HAI. The number of total HAI episodes was 232 (1.89 episodes per patient). HAI rate was 7.55% (232/3069), and HAI density was 5.36 per 1000 patient days. Overall and annual HAI data are shown in Table 1.

Of note, HAI diagnosis was made in 6.7% of the patients found to have an infection at admission and 3.5% of patients without infection at admission ($p = 0.032$). In HAI episodes, the mean length of stay at the hospital before diagnosis was 28.27 ± 16.86 days with a median of 23 (2–158) days.

Mean age in patients with HAI was 8.92 ± 5.53 years, while it was 8.34 ± 5.31 years in patients without HAI ($p = 0.142$). The average length of hospital stay in patients with HAI was significantly longer than of patients without HAI (48.30 ± 9.18 days versus 12.46 ± 14.70 days, respectively) ($p < 0.001$).

## Discussion

Surveillance of HAIs is crucial to decrease financial burden, morbidity and mortality in patients and results can be valuable to assess the quality of care provided by healthcare facilities, particularly in patients admitted to PHO units. Infection Control Committees conduct HAI surveillance in order to decrease HAI rates, determine infection types and risk factors, and take measures to prevent HAI development (15). Despite the presence of extensive studies exploring HAIs in an overall manner (16) and the fact that pediatric hospitals have been reported to have a disproportionate frequency of HAI (17,18), data about this topic are limited worldwide, particularly in patients admitted to PHO units (3-12). The present study revealed 232 HAI episodes in the 3069 hospitalizations of 607 patients. HAI rate was 7.55%, and HAI density was 5.36/1000 patient-days.

A multicenter prospective surveillance study including PHO units from 7 university hospitals in Switzerland and Germany, conducted from 2001 to 2005, reported 263 HAI episodes in 181 pediatric oncology patients, and HAI density was found to be 4.8/1000 patient-days (8). Another prospective active surveillance study from Spain identified an HAI rate of 13.3% and an HAI density of 17.7/1000 patient-days due to 135 hospitalizations in 51 PHO patients –of which there were 18 HAI episodes in 12 patients (7). In a 5-year study from Mexico, which included 9420 patients, 479 HAI episodes were seen in 409 patients, and annual HAI rates were found to range from 3.7% to 5.5%, while density ranged from 5.75 to 6 per 1000 patient days (6). These results are primarily similar to our findings. However, in a study conducted in the PHO unit of Casablanca University, Morocco, during an 8-month prospective study in 2011, HAI density was found to be 28/1000 patient-days (4), indicating a significantly higher value compared to our study and the majority of literature concerning this topic. The authors also found that the mean length of stay was significantly longer in patients with HAI compared to those without (16.5 days vs. 5 days), similar to our findings (4). Another active surveillance study of 138 PHO patients in a university hospital in India identified 14 HAI episodes developing in 13 patients. HAI rate was 9.4%, and HAI density was 11/1000 patient days. Additionally, the average length of stay in patients with HAI was 13.8 ± 6.8 days, significantly

**Table 1. Summary of HAI-related data and rates during the four-year study period**

| | Total | 2010 | 2011 | 2012 | 2013 |
|---|---|---|---|---|---|
| **Hospitalizations per patient** (Hospitalizations/patient count) | 5.05 (3069/607) | 6.55 (629/96) | 5.29 (800/151) | 5.85 (826/141) | 3.71 (814/219) |
| **HAI frequency** (Patients with HAI/patient count) | 20.3% (123/607) | 57.3% (55/96) | 13.2% (20/151) | 16.3% (23/141) | 11.4% (25/219) |
| **HAI episodes per patient** (HAI episodes/patients with HAI) | 1.89 (232/123) | 1.78 (98/55) | 1.4 (28/20) | 2.43 (56/23) | 2.00 (50/25) |
| **Length of stay in patients with HAI** (Days, mean ± SD) | 48.30±9.18 | 46.28±1.33 | 44.73±2.22 | 54.41±0.84 | 48.33±0.84 |
| **HAI rate** (HAI episodes / hospitalizations) | 7.55% (232/3069) | 15.58% (98/629) | 3.5% (28/800) | 6.77% (56/826) | 6.14% (50/814) |
| **HAI density / 1000 patient-days** (HAI episodes / patient-days) | 5.36 (232/43320) | 10.14 (98/9656) | 2.64 (28/10570) | 4.65 (56/12039) | 4.52 (50/11055) |

HAI: Healthcare-associated infections, SD: Standard deviation

longer compared to those without HAI (7.5 ± 4.5 days) (5). Finally, a retrospective study conducted in Iran identified an HAI frequency of 31% (n = 62) among 200 patients admitted to the PHO ward (10).

Taking into account the results of prior studies, it appears that HAI rates range between 3.7% to 31%, while HAI densities range between 4.8 to 28 per 1000 patient-days worldwide (3-10). There are only a few studies that have reported HAI surveillance data in Turkey. In a study conducted in 2007, researchers assessed 342 hospitalizations, and a total of 68 HAI episodes were reported in 44 patients; HAI rate was 19.8% (68/342), and HAI density was 15.6/1000 patient-days (11). A second study evaluating 158 PHO patients during a 6-month period identified 43 cases of HAI in 25 patients. HAI rate was 24.4% (calculated according to study data), and HAI density was 13.6/1000 patient-days (12). Both studies from Turkey were found to have demonstrated higher HAI rates and densities compared to our results of 7.55% and 5.36/1000 patient days, respectively. In other pediatric studies including patients from different wards, HAI densities were generally between 3.3 to 7.0/patient-days (apart from intensive care units with values reaching 28.2/patient-days) in studies conducted in Brazil, Iran, South Africa, Turkey (19-22), indicating expectedly lower HAI prevalence in other pediatric clinics compared to PHO units.

In comparison to studies from developed countries, like Germany and Switzerland (HAI density 4.8/1000 patient-days), the HAI density at our clinic was higher (8), except for Spanish data from 2001 (HAI density 17.7/1000 patient days) (7). Our HAI density was relatively lower compared to other developing countries like Morocco (HAI density 28/1000 patient days), India (HAI density 11/1000 patient days), and Iran (HAI rate 31%) (4,5,10). Our results were comparable with the extensive study conducted in Mexico (HAI density 5.75–6/1000 patient days) (6). These differences may be explained by differences between countries and hospitals in terms of healthcare access, preventive measures and other patient- and healthcare-related factors. However, interestingly, our results were also lower when compared with other Turkish studies (HAI rates of 19.8% and 24.4%, and HAI densities of 15.6 and 13.6 per 1000 patient days) (11, 12). Table 2 summarizes previous studies and our results.

Evaluation of annual data showed that the highest HAI frequency, HAI rate and HAI density values were observed in 2010. Although HAI frequency demonstrated a decreasing trend from 2010 to 2013, other characteristics remained largely stable. Hospitalizations per patient and length of hospital stay in those diagnosed with HAI remained consistent throughout the 4-year study period.

The study from Mexico which provided annual data showed HAI frequencies of 4.1%, 5.5%, 3.4%, 3.7%, 5.1% and 4.7% from 2004 to 2009. HAI densities were reported for only 2008 and 2009, which were 5.8 and 5.5 per 1000 patient days, respectively (6). When compared with the annual data of the study from Mexico, the consistency of results appears to be similar to our findings. However, we reported

**Table 2. HAI rates and densities in the literature**

| Location | Period | Age (year) | Number of Patients or hospitalizations | Patients with HAI | HAI episode count | HAI rate (%) | HAI density (/1000 patient-days) | Ref. |
|---|---|---|---|---|---|---|---|---|
| Germany-Switzerland (prospective) | 2001-2005 | 0-23 | 411 | 181 | 263 | - | 4.8 | 8 |
| Spain (prospective) | 2001 | 0-18 | 135[1] | 12 | 18 | 13,3 | 17.7 | 7 |
| Mexico (prospective) | 2004-2009 | - | 9420 | 409 | 479 | 3.7-5.5 | 5.75-6 | 6 |
| Morocco[2] (prospective) | 2011 | 0-14 | | | | - | 28 | 4 |
| Northern India (prospective) | 2007-2008 | 0-18 | 138 | 13 | 14 | 9,4[3] | 11 | 5 |
| Turkey (prospective) | 2007 | 0-18 | 342 | 44 | 68 | 19.8 | 15.6 | 11 |
| Turkey (prospective) | 2010 | 0-18 | 176 | 25 | 43 | 24.4[4] | 13.62 | 12 |
| Turkey (retrospective) | 2010-2013 | 0-23 | 3069 | 141 | 232 | 7.55 | 5.36 | Our study |

[1]: 135 hospitalizations of overall 51 patients occurred.
[2]: The number of patients is unknown due to a lack of data via the article abstract.
[3]: The HAI rate possibly should be 10.1% (14/138) according to the given data.
[4]: Not mentioned in the article (however, according to the given data in the article, calculated by us)
HAI: Healthcare-associated infections

considerably higher values in 2010 compared to our results in the following years and also compared to the annual data from Mexico (6). The lower HAI frequencies and densities after 2010 may be explained by the establishment and greater recognition of the HAI committee, increased adherence to HAI surveillance, better understanding of the needs of PHO patients, and possibly advances in patient care. Although in the studies from Spain, Morocco, İndia, and İran pediatric hematology oncology patients, HAIs were analyzed, without mentioning the etiologic diagnosis, similar to our study (4,5,7,10). Germany-Switzerland and Mexico studies were conducted only with pediatric cancer patients, and our HAI densities were found to be similar to those of these studies (6,8).

In a random-allocation study from the United States, which explored the changes in all HAI events during a 4-year period on a national scale, it was found that there was a relative decline in the number of HAIs from 2011 to 2015 (4.0% to 3.2% overall, and 10% to 8.5% in patients meeting HAI assessment criteria) (23). Even though this study included adults and collected data from all medical disciplines, an interesting finding was that the decline in HAI was attributed mainly to the decreased frequency of catheter-related urinary infections and surgical-site infections (23).

The primary limitation of our study is its retrospective nature, which may have caused minor bias due to variations in diagnosis, assessment, management and documentation. It is also likely that patients diagnosed with HAI or infection at admission received closer monitoring, leading to ascertainment bias. However, the relatively long duration (4 years), high patient and hospitalization numbers, and extended length of stay data are valuable properties of our study.

The other limitation of our study is that the data we present in our study are from our centers alone. The current changes in the field necessitate further multi-center research. This will highlight the need for future studies to validate and expand upon the findings presented in our study.

In conclusion, since HAI could cause severe consequences in immunocompromised patients like those admitted to PHO units. During the 4-year study period, the HAI rate was found to be 7.55%, and the HAI density was 5.36/1000 patient days. Comparisons with prior studies have shown that HAI frequencies may be associated with resource availability, and HAI rate

and density values were lower in our center compared to less-developed countries and previous studies from our country. In addition, studies reporting annual data seem to show consistent values, suggesting the need for new methods that can reduce HAI frequency via surveillance measures.

*Ethics*

*Ethics Committee Approval:* The study was initiated after obtaining approval from the Bursa Uludağ University Ethics Committee (Application date: 05.10.2013, approval number: 2013-18/14).

*Conflict of Interest:* No conflict of interest was declared by the authors.

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