

Epidemiology and Risk Factors of Hospital-Acquired Pneumonia in Tertiary Pediatric Hospital, Tbilisi, Georgia

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Abstract

Introduction: Hospital-acquired pneumonia (HAP) is one of the most common complications among hospitalized children. This study aimed to determine the epidemiology and risk factors of HAP in the tertiary pediatric hospital in Tbilisi, Georgia.

Methods: The study included pediatric patients admitted to the Iashvili Central Children's Hospital from March 2023 to January 2024. The following data were recorded: age, sex, hospital ward, and risk factors, including comorbid disease, Hb<10 g/dL, pH<7.35, invasive techniques, surgery, hospital admission in the previous month, and interval from admission to presentation of HAP.

Results: The study was performed on 36 patients with a median age of 36 months. Most of the patients (58%) were males. The most common causes of the admission were upper respiratory tract infection (9 patients, 25%), fever (7 patients, 19%), and bronchitis (5 patients, 14%). Seventeen patients (47%) had histories of hospitalizations within the last 30 days. Most cases (20 out of 36) were late-onset HAP. The median time of HAP onset was 8 days. The median length of the hospital stay was 17 days. Twenty-two out of 36 patients experienced a prolonged length of hospital stay of more than ten days. Most of the patients (24 patients, 67%) had comorbidities. The most frequent comorbidities were developmental delay (6 patients) and epilepsy (5 patients). Logistic regression showed a significant relationship between HAP and the presence of comorbidities, prior hospitalization, prolonged hospitalization and anemia.

Conclusion: Early identification of risk factors may be useful in identifying patients at high risk of HAP development.

Keywords: Nosocomial Infections; Hospital-Acquired Pneumonia; Epidemiology; Risk Factors; Georgia

Abbreviations

HAI: Healthcare-Associated Infections; WHO: World Health Organization; HAP: Hospital-Acquired Pneumonia; NP: Nosocomial Pneumonia; VAP: Ventilator-Associated Pneumonia; NV-HAP: Non-Ventilator HAP; LOS: Length of Stay; PICU: Pediatric Intensive Care

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Unit; ICCH: Iashvili Central Children Hospital; ATS: American Thoracic Society; API: Analytical Profile Index; CI: Confidence Interval; IQR: Interquartile Range

Introduction

Nosocomial infections, also referred to as healthcare-associated infections (HAI), are one of the most common complications among hospitalized children. According to the World Health Organization (WHO), seven of 100 hospitalized patients in high-income countries, or 15 patients in middle to low-income countries, acquire an HAI during their hospital stay [1]. Hospital-acquired pneumonia (HAP), or nosocomial pneumonia (NP), is a lower respiratory infection that was not incubated at the time of hospital admission and presents clinically two or more days after hospitalization. Ventilator-associated pneumonia (VAP) is defined as pneumonia that presents more than 48 hours after endotracheal intubation [2].

HAP includes two subgroups: non-ventilator HAP (NV-HAP) and ventilator-associated pneumonia (VAP). Both NV-HAP and VAP are associated with substantial clinical and economic burdens, including prolonged hospital length of stay (LOS), higher overall healthcare costs, and increased morbidity and mortality [3,4].

Many studies have identified HAP in pediatric intensive care unit (PICU) as a relatively frequent problem. However, only some studies have reported the epidemiology and risk factors for HAP outside the PICU [5-7].

Currently, there is no national surveillance system for HAI in Georgia. Effective national programs are needed to control hospital-acquired infections, but setting effective programs without information about the prevalence and epidemiology of HAI is impossible. Limited studies about HAIs in Georgia have been conducted, all of them in adult patients [8,9].

Purpose of the Study

The purpose of this study was to determine the epidemiology and risk factors of nosocomial pneumonia in the tertiary pediatric hospital in Tbilisi, Georgia.

Methods

Study setting

The Iashvili Central Children Hospital (ICCH), where the data for the study was collected, is the only pediatric multi-profile referral center (level 3) in Georgia, consisting of 240 beds and ~8,500 patients from 0 to 18 years of admission annually. This is the largest pediatric hospital in Georgia. Currently, the ICCH provides 56 different services, and 10 of them are possible just in this hospital. Among the unique units is the Department of Respiratory Medicine, which provides medical care for all patients with acute or chronic respiratory disorders.

This hospital's PICU setting consists of 16 beds. The PICU accepts severe patients from all the regions of Georgia, as well as patients from other departments of the ICCH, such as the department of respiratory medicine, abdominal medicine, nephrology, surgery, trauma, oncology, hematology, and neuroscience, it also provides post-op care for pediatric surgical patients except cardio surgery. Two pediatric critical care specialists (anesthesiologist-reanimatologist according to the Georgian standards) and one junior doctor provide diagnostic and treatment to patients admitted in the PICU setting.

The study obtained ethical approval from the ethical committee of the Tbilisi State Medical University.

Study sample and methodology

The prospective cross-sectional study included pediatric patients admitted to the ICCH from March 2023 to January 2024.

HAP was defined as the presence of a new infiltrate on a chest radiograph after 48 hours of hospital admission or within ten days after previous discharge, along with at least 2 of the following criteria: fever (temperature $>38.0^{\circ}\text{C}$), tachypnea, dyspnea, cough, abnormal respiratory auscultation, leukocytes $> 15,000/\text{mL}$ or leukopenia $< 3,000/\text{mL}$ and CRP $> 50 \text{ mg/dL}$.

Length of hospital stay (LOS) was the duration of hospitalization from time to admission until hospital discharge or death, and the cutoff for prolonged hospital stay was > 25 days.

The following data were recorded for all patients on clinical chart review: age, sex, hospital ward, and risk factors, including comorbid disease, Hb $<10 \text{ g/dL}$, pH <7.35 , previous antibiotic therapy, invasive techniques (tracheotomy, nasogastric tube), surgery, hospital admission in the previous month, and interval from admission to presentation of pneumonia. The primary clinical information was also collected.

The onset of HAP was classified according to American Thoracic Society (ATS) guidelines: early-onset if the signs and symptoms appear within five days of admission, and late-onset if it appears after five days of admission or more [10].

Clinical samples were examined for bacterial pathogens using modern methods of bacteriological diagnostics, namely sample cultivation, identification of bacterial agents, and biochemical characterization using the analytical profile index (API) system. Also, the biochemical activity of additional samples was determined by the Poenix50 automated system.

To establish the etiological structure of HAP, the following bacteria were determined: *Pseudomonas aeruginosa*, *Acinetobacter Baumannii*, *Enterobacteriaceae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Methicillin-resistant Staphylococcus aureus*, *Haemophilus influenzae*, *Stenotrophomonas maltophilia*.

Statistical analysis

Data were analyzed in R studio for Windows, version 2023.03.1 Build 446 [11]. Using different statistical tests, we assessed various variables as potential risk factors for hospital-acquired pneumonia. We had data of 36 children with hospital-acquired pneumonia and 17 patients as a control group. A probability of less than 0.05 at a 95% confidence interval (CI) was considered statistically significant.

Differences in proportions were compared using the chi-square test as appropriate. Logistic regression was used as a proper and commonly used test for assessing the association between a binary response variable (such as hospital-associated pneumonia) and one or more explanatory variables. It is particularly well-suited for this scenario because it allows you to model the probability of the binary outcome as a function of the explanatory variables.

Variables significantly associated with HAP were put into the multivariate logistic regression model, where HAP was the dependent (response) variable and factors significantly associated with HAP were independent (explanatory) variables.

Results

The study was performed on 36 patients during 11 months in the ICCH in Tbilisi, Georgia. Among them, 24 patients developed HAP in the Department of respiratory medicine, 8 in the PICU, 2 in the Department of nephrology, and 2 in the Department of abdominal medicine.

Patients were divided into age groups according to the National Institute of Child Health and Human Development [12]: infant (1-12 months), toddler (13-24 months), childhood (25-132 months), and adolescence (133-204 months).

The median age was 36 months [Interquartile Range (IQR): 2 - 168]. Most of the patients (58%) were males.

The most common causes of the initial admission were upper respiratory tract infection (9 patients, 25%), fever (7 patients, 19%), and bronchitis (5 patients, 14%).

Seventeen patients (47%) had histories of hospitalizations within the last 30 days. Most cases were late-onset HAP: 20 out of 36 patients had the signs and symptoms of pneumonia after five days of admission. The median time of HAP onset was eight days (IQR: 3 - 25).

The median length of the hospital stay was 17 days (IQR: 6 - 25). Twenty-two out of 36 patients experienced prolonged LOS of more than 10 days.

Most of the patients (24 patients, 67%) had comorbidities, and some had more than one comorbid condition. The most frequent comorbidities were developmental delay (6 patients) and epilepsy (5 patients) (Table 1).

Age groups	N (%)
Infant (1-12 months) (n [%])	11 (30%)
Toddler (13-24 months) (n [%])	6 (17%)
Childhood (25-132 months) (n [%])	17 (47%)
Adolescence (133-204 months) (n [%])	2 (6%)
Sex	
Male (n [%])	21 (58%)
Female (n [%])	15 (42%)
Cause of admission (n [%])	
Upper respiratory tract infection, unspecified (ICD-10: J06.)	9 (25%)
Fever, unspecified (ICD-10: R50.9)	7 (19%)
Bronchitis, unspecified (ICD-10: J20.9)	5 (14%)
Surgery	3 (8%)
Bronchiolitis unspecified (ICD10: J21.9)	2 (5%)
Unspecified Kidney failure (ICD10: N19)	2 (5%)
Nausea and Vomiting (ICD10: R11.2)	2 (5%)
Bacterial infection, unspecified (ICD10 A49.9)	1 (3%)
Anemia Unspecified (ICD10: D64.9)	1 (3%)
Viral infection, unspecified (ICD10: B34.9)	1 (3%)
Burn of unspecified degree of multiple sites (ICD10: T25)	1 (3%)
Viral intestinal infection, unspecified (ICD10: A08.4)	1 (3%)
Acute pericarditis, unspecified (ICD10: I30.9)	1 (3%)
LOS	

Up to ten days	14 (39%)
More than ten days	22 (61%)
Underlying disease	
Developmental Delay	6
Epilepsy	5
Down syndrome	4
Cerebral palsy	4
Blood disease	4
Congenital heart disease	3
Renal disease	3
Gastrointestinal disease	1
None	12

Table 1: Characteristics of the study population.

Bacterial pathogens were isolated just in 7 patients and due to small number the results were not analyzed. But it should be noted that, majority of them were MDR pathogens, for example *Escherichia coli* was resistant against ampicillin, ceftriaxone, cefuroxime, ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole; *Serratia marcescens* - against amoxicillin-clavulanic acid, ampicillin, ceftriaxone, cefuroxime, colistin, ertapenem, meropenem, tigecycline.

The following risk factors were assessed: age, sex, comorbid conditions, LOS, prolonged hospitalization of more than ten days, histories of hospitalizations within the last 30 days, pH<7.35, Hb<10.

Our analysis examined the association between prior hospitalization within one month before admission to the clinic and the likelihood of hospital-associated pneumonia. While the logistic regression model suggested a positive relationship between prior hospitalization and the risk of hospital-associated pneumonia, the results did not reach statistical significance (p value = 0.994). However, chi-squared test showed opposite, there appears to be a statistically significant relationship (X-squared = 11.785, DF = 1, p-value=0.000597) between hospitalization and the likelihood of developing hospital-associated pneumonia. These different results could be caused because of unbalanced data and further analysis with bigger sample and more balanced dataset is recommended to find more reliable results.

Based on the logistic regression analysis, there is no statistically significant association between sex and the likelihood of hospital-associated pneumonia (p value = 0.973). The chi-squared test showed the same results (X-squared = 1.4986e-31, DF = 1, p-value = 1).

Logistic regression showed a significant relationship between HAP and presence of comorbidities (p value = 0.00891). Individuals with comorbidities have a higher likelihood of hospital-associated pneumonia compared to those without comorbidities. The chi-squared statistic (X-squared = 5.998, DF = 1, p-value = 0.01432) also suggests that there is a significant association between comorbidity and the likelihood of developing hospital-associated pneumonia.

Positive statistically significant association (p value = 0.00415) was also detected between HAP and prolonged hospitalization (> 10 days). This finding suggests that prolonged hospitalization may be a risk factor for developing pneumonia during the hospitalization period. This finding aligns with the results obtained from chi-squared test revealed a statistically significant association between the length of hospital stay and the occurrence of hospital pneumonia (X-squared = 11.013, DF = 1, p-value = 0.0009047).

The results of logistic regression suggest that there’s no significant association between pneumonia and pH level, as evidenced by the non-significant coefficient for pH (p value = 0.993). This implies that changes in pH level do not substantially impact the odds of pneumonia occurrence.

The logistic regression examined pneumonia occurrence in relation to age. The results show age is not significantly associated with pneumonia (p value = 0.204). However, the intercept is significant (p value < 0.001), indicating pneumonia odds are significant when age is zero. Overall, age alone may not be strongly considered as a risk factor for pneumonia occurrence.

The association between nasogastric feeding and hospital acquired pneumonia was explored by logistic regression. The results showed that patients who received nasogastric feeding tended to have a slightly higher chance of developing pneumonia compared to those who did not, although this difference was not strong enough to be considered statistically significant at the typical level, we use for deciding if results are real (p-value = 0.0523). However, it’s important to note that there is still a possibility of a relationship, and more research with larger groups of patients is needed to confirm if this association is real.

We also explored the relationship between hemoglobin level and the likelihood of hospital-associated pneumonia. The results reveal a statistically significant association (p value = 0.01509) between Hb<10 and the probability of pneumonia diagnosis. This finding indicates that lower hemoglobin levels may be a risk factor for the development of pneumonia during hospitalization.

In table 2 the results of individual logistic regression analyses for each predicting risk factor are shown to determine their association with hospital-acquired pneumonia.

Characteristics	OR	95%CI	p-Value
Prior hospitalization within one month before admission	0.998	-135.95-NA	0.994
Sex	0.98	-1.22-1.15	0.973
Age	0.998	-0.005-0.001	0.204
pH <7.35	1.01	-1.55-1.56	0.993
Hb <10 g/dL	0.59	-0.98 - -0.14	0.01509
Comorbidities	5.75	0.5-3.17	0.00891
Prolonged hospitalization	22.4	1.36-6.06	0.00415
Nasogastric feeding	1.45	0.005-0.734	0.0523

Table 2: The results of individual logistic regression analyses for each predicting factor.

OR: Odds Ratio, CI: Confidence Interval.

Discussion

Both developed and developing countries are faced with the burden of healthcare-associated infections. Prevention is the key measure to reduce the morbidity and mortality of HAIs. Accurate data on HAP and VAP rates are essential for evaluating current infection prevention activities and planning further interventions in hospitals and at the national level. Although there are quite a few data from epidemiological studies about these infections in pediatric hospitals, a few papers come from resource-limited countries such as Georgia. This is the first report on HAP epidemiology and risk factors in the pediatric hospital in Georgia.

In our study, the average length of stay in the pediatric wards was 17 days, more than 10 days for most patients (22 patients, 61%). Our findings showed a high rate of length of stay in hospital wards outside of PICU. A similar prolonged rate of hospital stay was shown in

the study from Brazil (14.1 days) [13], Iran (14 days) [14] and Lithuania (11.7 days) [15]. In a study conducted in Saudi Arabia, the mean length of stay was lower - 7.43 days [16]. Similar duration was shown in a study performed in Ethiopia - 6 days (IQR: 3 - 9 days) [17]. The prolonged length of stay in our study might be associated with patients with complex chronic conditions and longer hospital stay, as it was shown by Edwards, *et al.* [18].

In our study, a positive statistically significant association (p value = 0.00438) was detected between HAP and prolonged hospitalization (> 10 days). Prolonged hospitalization was found to be a major risk factor in studies conducted in South Africa [19], Ethiopia [20], Bangladesh [5], Iran [14], Lithuania [15], and Brazil [21]. Despite this positive relation, it is not clear that decreasing the length of hospital stay may reduce the development of HAP.

In our study, 17 patients (47%) had histories of hospitalizations within the last 30 days. This ratio is as high as it was in the papers from South Africa (68%) [22] and 42% [6], but higher than data from Ethiopia (12%) [17]. The chi-squared test showed a statistically significant relationship ($X^2 = 11.785$, $DF = 1$, p -value = 0.000597) between prior hospitalization and the likelihood of developing hospital-associated pneumonia. A few studies show a similar association [7,23]. Not many authors consider recent hospitalization as a risk factor for the development of HAP, but a high rate of patients with histories of hospitalizations indicated that it might be one of the essential factors for HAP occurrence.

The present study also demonstrated that the occurrence of HAIs was higher among male participants than women. Twenty-one (58%) of the study participants were male, with an overall male-to-female ratio of 1.4:1. This result was also supported by many studies [15,17,21,22,24]. At the same time, studies conducted in Iran and Bangladesh showed the prevalence of NI in females [25,26].

The mean time of diagnosis of HAP was eight days. A study from Ethiopia showed a similar period: 7.2 days [17]. A study from Indonesia indicated a longer period: 15.5 days [27]. Guidelines from the American Thoracic Society and Infectious Diseases Society of America stated that early-onset HAP had a better prognosis because patients with early-onset HAP have a lower rate of multi-drug-resistant causative pathogens than patients with late-onset HAP [10].

According to our findings, underlying diseases are statistically significant predictors of HAP risk. Comorbid illnesses increase patients' susceptibility and predispose them to infections. Although underlying comorbidities are not modifiable risk factors, they are useful in identifying patients at high risk of HAP. Similar results were indicated in studies from Ethiopia [17], Brazil [21], South Africa [22], and Saudi Arabia [28].

Age under 6 months was suggested as a significant risk factor for HAI in a study performed in Vietnam [29], HAP was found mostly in children under 5 years in a study from Indonesia [27] and Ethiopia [20]. In the same time, similar to our findings, no association between patients age and risk of HAP development was determined in studies from Iran [25], southeast Ethiopia [17] South Africa [22] and Kenya [30].

Our results reveal a statistically significant association (p value= 0.01509) between $Hb < 10$ and the probability of HAP diagnosis. This finding indicates that lower hemoglobin levels may be a risk factor for the development of pneumonia during hospitalization. In general, anemia is common in hospitalized patients and is associated with hypoxia, which predisposes to nosocomial infections. The similar results were shown in other studies as well [7,31].

Limitation of the Study

Our study has some limitations. First, we had a relatively small sample size, thus reducing the statistical power and the ability to study subsets. Second, we did not perform any viral isolation, which could have been common causes of HAP in our study population. Third, we

focused on a small number of risk factors for HAP and some important variables were not included. Fourth, we were not able to identify the most common bacterial pathogens, hence the etiology of HAP in pediatric patients was not established. Besides these limitations, our study is the first study done in pediatric hospital on the epidemiology and risk factors for HAP in Georgia, which may further help to strategize the infection prevention plans and could be used for treatment strategies for children with HAP.

Conclusion

HAP is a common and preventable complications that lead to significant morbidity, mortality, and healthcare costs. Hospitalized children are a particularly vulnerable population that should be prioritized for HAI prevention national programs. Our study revealed that the hospital stays for more than ten days, comorbid conditions, prior hospitalization within one month before admission to the clinic, and anemia were significantly associated with HAI. Further studies are needed to implement and evaluate adequate infection prevention plans.

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