Incidence and risk factors for hospital-acquired infection among paediatric patients in a teaching hospital: a prospective study in southeast Ethiopia

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ABSTRACT

Objectives In order to maximise the prevention of hospital-acquired infections (HAIs) and antimicrobial resistance, data on the incidence of HAIs are crucial. In Ethiopia, data about the occurrence of HAIs among hospitalised paediatric patients are lacking. We aim to determine the incidence and risk factors of HAIs among paediatric patients in Ethiopia.

Setting A teaching hospital in southeast Ethiopia.

Participants 448 hospitalised paediatric patients admitted between 1 November 2018 and 30 June 2019.

Primary and secondary outcome measures Incidence and risk factors of hospital-acquired infections.

Results A total of 448 paediatric patients were followed for 3227 patient days. The median age of the patients was 8 months (IQR: 2–26 months). The incidence rate of HAIs was 17.7 per 1000 paediatric days of follow-up; while the overall cumulative incidence was 12.7% (95% CI 9.8% to 15.8%) over 8 months. Children who stayed greater than 6 days in the hospital (median day) (adjusted risk ratio (RR): 2.58, 95% CI 1.52 to 4.38), and children with underlying disease conditions of severe acute malnutrition (adjusted RR: 2.63, 95% CI 1.61 to 4.97) had higher risks of developing HAIs.

Conclusions The overall cumulative incidence of HAIs was about 13 per 100 admitted children. Length of stay in the hospital and underlying conditions of severe acute malnutrition were found to be important factors associated with increased risk of HAIs.

INTRODUCTION

There is a ‘perfect storm’ on hospital-acquired infections (HAIs) among hospitalised patients at any point in time throughout the globe. HAI is defined as an infection occurring in a patient during the process of care in a hospital or other healthcare facilities that is not manifested or incubating at the time of admission.1 Currently, it is a growing public health problem which concerns both the medical and the general community, and a rising issue for patient safety and quality of care in every level.2–8 A study by Sheng et al9 reported that 80% of hospitalised patient deaths were linked to nosocomial infection. Available evidences also showed that financial burden, increased resistance of microorganisms to antimicrobials, prolonged hospital stay and sometimes deaths, are caused by HAIs.10–12

Worldwide, it is estimated that hundreds of millions of patients every year in both developed and developing countries are affected by HAIs.7 In some Australian public hospitals, HAIs affect one in every 74 hospitalisations.13 In Europe, the total annual number of patients with HAIs in 2011–2012 was estimated around 3.2 million. The prevalence of patients with at least one HAI in acute care hospitals was 6.0% (country range 2.3%–10.8%).14 Moreover, throughout Europe, HAIs accounted for 16 million additional days, with total costs estimated at approximately €7 billion.14–16 In the USA, approximately 2 million patients developed HAIs, and nearly a hundred thousand of these patients were estimated to die annually. This
ranked HAIs as the fifth leading cause of death in acute care hospitals, and the risk of acquiring infection is 2–20 times higher in some developing countries.17 18

In some developing countries, the magnitude of HAIs remains underestimated and uncertain.12 There is little information available on the epidemiology of HAIs in African countries.19 20 Although data are sparse, evidence suggested that HAIs are considerably adding to the available high burden of infections in some sub-Saharan African countries.21 A systematic review by Nejad et al22 reported that hospital-wide HAI prevalence in Africa varied between 2.5% and 14.8%. This review has shown that published studies were only conducted in 10 African countries—emphasized there were paucities of information available among the epidemiology of HAIs in many African countries. In addition to this, a recent review by Irek et al indicated that there was a scarcity of studies on HAIs in Africa—of the 35 eligible articles retrieved, more than half (n=21, 60%) were from East Africa only.20 In addition, most of the HAIs literature only focused on adults, and the data on HAIs among the paediatric population in sub-Saharan Africa were hardly available.12 23 24 For example, a systematic review conducted by the WHO in the year 2010 identified no reports on paediatric nosocomial bacteraemia in some African countries between 1995 and 2008.15

In Ethiopia, little is known about the incidence and prevalence of HAIs in the neonatal and paediatric populations. Moreover, previously conducted studies focused only on adults, and many of these were limited to surgical site infections.25–28 With an estimated prevalence of 10.9%–24 66.5%,27 The overall cumulative incidence was 35.8 per 100 patients.26 Furthermore, urinary tract and bloodstream infections were found to be the most common forms of HAIs in Ethiopia.29–33 Surgery after admission,23 26 underlying medical conditions,23 25 patients with catheters,23 25–26 infection on mechanical ventilators,26 immunodeficient patients,23 25 26 patients’ age,23 25 26 hospital types,32 the types of ward and prolonged hospitalizations33 were found to be important factors associated with increased risks of HAIs in Ethiopia.

Up to date, there are no surveillance programmes at the regional or national levels which targeted HAIs in Ethiopia. The available evidence on HAIs in the country was originated from primary studies. Moreover, to the best of our knowledge, there is not a single published report on the incidence and risk factors of HAIs among paediatric patients in Ethiopia. In order to maximize the prevention of HAIs and antimicrobial resistance in Ethiopia, epidemiological data on the incidence of HAIs are crucial because without a valid and precise assessment of HAIs, the problem remains unnoticed. Therefore, this study was designed to determine the incidence and risk factors of HAIs among paediatric patients in Goba Referral Hospital, southeast Ethiopia. The current study will help policymakers to improve their decision-making and inputs for healthcare professionals, for the improvement of patient care.

METHODS

Study design and setting

A hospital-based prospective follow-up study was conducted from 1 November 2018 to 30 June 2019, at Madda Walabu University Goba Referral Hospital, southeast Ethiopia. Goba Referral Hospital is the only referral and teaching hospital in the Bale zone, serving over 1 787 575 million people. Goba Referral Hospital is located 445 km far from the capital city of Ethiopia. According to the 2018 annual report of Goba Referral Hospital, the average outpatient flow is over 9 661, and the annual admission is over 7 886 patients, of which 1335 were admitted in the paediatric ward and neonatal intensive care unit (NICU). The hospital has a total of 127 inpatient beds—of which 30 and 15 are in the paediatric ward and NICU, respectively.

Study population and eligibility criteria

All patients (age less than 18 years) admitted to the paediatric ward and NICU were enrolled, and those who at least stayed for 48 hours, were eligible for the study. Enrolled patients who showed signs of infections and/or symptoms of infection within the first 48 hours were excluded from the study.

Data collection procedures

First, consent was sought from each of the child’s parent/guardian before commencing any study procedures. On admission, all children were evaluated clinically to exclude community-acquired infections by a paediatrician. Afterwards, sociodemographic and clinical data were collected through a structured questionnaire using individual patient chart investigation approach, accordingly, a detailed clinical history of patients were taken and recorded. Patients with no new signs or symptoms of infection after the first 48 hours from admission were included and followed prospectively for the development of HAIs during their stay in the hospital. Data were collected from enrolled patients on a daily basis: children were followed by a paediatrician daily, charts were reviewed, and discussions with nurses and physician caring for the patients were held. HAIs were confirmed by senior paediatrician specialists working in the respective NICU and paediatric ward (figure 1).

Data were collected by trained physicians and one paediatrician. The Centers for Disease Control and Prevention (CDC)/National Health Care Safety Network surveillance definition for HAIs was used.34 In this study, the usage of any antimicrobials and information on the use of different medical devices at the time of hospital admission and before the diagnosis of HAIs were recorded, respectively (see online supplemental file 1).

Data quality control

The data collection tool was adapted from different related pieces of literature based on the available evidences of HAIs.1 23 26 32 To ensure the quality of data, the data collection tool was pretested before the data collection.
collection period. The training was given for data collectors on the study procedures, and with practical exercise sessions. Data collection was closely supervised by a principal investigator, and the collected data were checked for completeness, accuracy and consistency. In order to minimise the potential effects of confounder variables, multivariable logistic regression model was used, and analyses were adjusted to known confounder, such as age. In addition, the researchers try to reduce selection bias by including all admitted patients in our follow-ups. Moreover, to reduce the effect of observer bias, the data collectors have no preconceived expectations of what they should find in an examination.

**Operational definition**

HAI—a localised or systemic condition that results from an adverse reaction in the presence of an infectious agent or its toxin, and occurring 48 hours or longer after hospital admission, which was not incubating at the time of admission.14 19 23 26 32 34

Severe anaemia—haemoglobin <50 g/L (for patients older than 28 days) or haemoglobin <90 g/L (for neonates).

Late-onset neonatal sepsis—infection occurring after birth, but excluding infections known to have been transmitted across the placenta.

**Study variables**

The outcome variable of the study was the occurrence of HAI. The presence of HAI was confirmed when the patients met the criteria for signs and symptoms determined by the CDC,34 where the independent variables included: sociodemographic characteristics (age of the child, sex, place of residence and previous hospitalisation), and clinical and other related variables (duration of hospitalisation, insertion of a urinary catheter, presence of peripheral intravenous catheter, received antimicrobial, American Society of Anesthesiology classification, intubation, surgery after admission, underline disease refers to severe acute malnutrition (SAM) presented at the time of admission, mechanical ventilator and HIV status).

**Data processing and analysis**

Data were entered into Epi-data V.3.1 and exported to Stata V.14 statistical software for further analysis. Descriptive
were men with an overall male-to-female ratio of 1.24:1. Moreover, 390 (71.2%) of the study participants were from rural areas. The median hospital stay of the patients was 6 days (IQR: 3–9 days), and among them, 24 (5.4%) died. The overall incidence density rate of the admitted paediatric mortality was 7.44 per 1000 paediatric days of follow-ups (table 1).

Clinical characteristics of patients
In this study, 46 (10.3%) of the participants had histories of hospitalisations within the last 30 days. Fifty-four (12.1%) of the children were diagnosed with SAM at the time of their admission. Severe anaemia was reported among 41 (9.2%) respondents. Overall, 171 (38.2%) patients received antimicrobials at the time of the study (table 1).

Incidence and type of HAI
During the study period, 448 paediatric patients were followed for a total of 3227 patient days. A total of 57 patients experienced HAIIs, and none of the study participants were identified with more than one episode of HAIIs. The mean time of diagnosis of HAIIs in Goba Referral Hospital is 7.20 (95% CI 6.72 to 7.66) patient days. The overall incidence rate of HAIIs was 17.7 per 1000 paediatric days of follow-ups, while the cumulative incidence was 12.7% (95% CI 9.8% to 15.8%) over 8 months. The mean length of stay for the infected paediatric patients was 11.5 days (95% CI 9.5 to 13.4), while it was lower for the remaining patients, at 6.5 days.

Table 2 illustrates the proportion of HAIIs among the paediatric patients in Goba Referral Hospital. Hospital-acquired pneumonia (HAP) was the most common type of HAI which was observed among the paediatric patients with a proportion of 56.1% (95% CI 43.9% to 68.4%), followed by late-onset neonatal sepsis 10.5% (95% CI 5.5% to 19.3%), and the least HAIIs observed were early onset of neonatal sepsis and surgical site infections, with an overall proportion of 1.8% each. In this study, the stratification of the types of HAIIs by ward of admission revealed significant variability (p value=0.007) (figure 3).

Risk factors of HAIIs
Table 3 showed the risk factors of HAIIs among the paediatric patients in Goba Referral Hospital. Bivariate analysis of RR has indicated that hospital duration (>6 days), patients who received antimicrobial medications, presence of drainage tubes and children diagnosed with SAM were predisposed to HAIIs.

In the adjusted model, the risk of HAIIs was 2.58 times more likely to be higher among children who stayed longer than or equal to 6 days (median day) than those who stayed less (ARR: 2.58, 95% CI 1.72 to 4.38). Patients with SAM conditions had 2.83 times higher risks of developing HAIIs compared with its counterparts (ARR: 2.83, 95% CI 1.61 to 4.97). Sociodemographic and some
In this study, we estimated the attributable risk, which estimates the excess risk of disease in those exposed compared with those non-exposed. The excess occurrence of HAIs among children with underlying SAM diseases attributable to their SAM condition is 13 per 100 (table 4).

**DISCUSSION**

HAIs are current global challenges that increase morbidities, mortality and massive economic cost. Yet, there remain limited data on the occurrences of HAIs in hospitalised paediatric patients in sub-Saharan Africa, including Ethiopia. This study was designed to determine the incidence and risk factors of HAIs among paediatric patients in a teaching hospital, southeast Ethiopia. The overall incidence rate of HAIs was 17.7 per 1000 paediatric days of follow-up while the cumulative incidence was 12.7% (95% CI 9.8% to 15.8%) over 8 months. Children who stayed longer than the median day (6 days) in the hospital, and children with underlying disease conditions (SAM), had higher risks of developing HAIs.

In this study, the overall incidence rate of HAIs was 17.7 per 1000 paediatric days of follow-ups. This finding is lower than a related prospective study by Ali et al from southwest Ethiopia, which reported an incidence of HAIs of 28.15 per 1000 patient days. The difference might be associated with the nature of this study which involved only paediatric patients including those in intensive care; whereas, the study by Ali et al included adult study participants. Also, variations in some studies could be attributed to differences in geographical locations and the study settings (as in the case of Ali et al where the study they included a specialised hospital). A previous before-and-after study conducted in a teaching hospital in Indonesia

| Variables | Category | n (%) |
|-----------|----------|-------|
| Patient age, median (IQR): 8 months (2–26 months) | | |
| Sex | Male | 248 (55.4) |
| | Female | 200 (44.6) |
| Ward | Neonatal intensive care unit | 201 (44.9) |
| | Paediatrics | 247 (55.1) |
| Resident | Urban | 129 (28.8) |
| | Rural | 319 (71.2) |
| Previous hospitalisation* | Yes | 46 (10.3) |
| | No | 402 (89.7) |
| Mechanical ventilation | Yes | 76 (17.0) |
| | No | 372 (83.0) |
| Presence of peripheral intravenous catheter† | Yes | 430 (96.0) |
| | No | 18 (4.0) |
| Presence of urinary catheters | Yes | 9 (2.0) |
| | No | 439 (98.0) |
| Drainage tube inserted** | Yes | 53 (11.8) |
| | No | 395 (88.2) |
| Underlying severe acute malnutrition (SAM) diseases‡ | Yes | 54 (12.1) |
| | No | 394 (87.9) |
| Surgery after admission | Yes | 47 (10.5) |
| | No | 401 (89.5) |
| Patient received antimicrobials§ | Yes | 171 (38.2) |
| | No | 221 (49.3) |
| | Unknown | 56 (12.5) |
| Severe anaemia | Yes | 41 (9.2) |
| | No | 375 (83.7) |
| | Unknown | 32 (7.1) |
| Hospital duration (median day) | ≤6 | 237 (52.9) |
| | >6 | 211 (47.1) |
| HIV status | Positive | 2 (0.4) |
| | Negative | 393 (87.7) |
| | Not tested | 53 (11.8) |
| American Society of Anesthesiology classification | Normally health patient | 72 (16.1) |
| | Patient with mild systemic diseases | 235 (52.5) |
| | Severe systemic disease that is not incapacitating | 100 (22.3) |
| | Incapacitating systemic disease that is a constant threat to life | 36 (8.0) |
| | Unknown | 5 (1.1) |
involved children whom were admitted to the paediatric intensive care unit (ICU) and paediatric ward, reported the incidence density rate of HAI 29.1 per 1000 patient days, which is similar to our findings.36 One of our findings has also revealed that the overall cumulative incidence of HAIs was 12.7%; this is comparable to those reported from a study in the USA (11.9%)37 which was conducted in the paediatric ICU, and in Poland (13.5%).38 Also, the present 12.7% of HAIs noted in our study population fell in the ranges of 9.8%–15.8%, and is reported elsewhere,14 40 41 and the WHO pooled estimated for low-income countries 10.1%.18 Conversely, similar studies from Turkey reported a much higher prevalence of HAIs among children ranging between 22.2% and 68.4%,42 43 and in a multicentre prospective study from Europe reported 18.5%.44 The high burden of HAP among hospitalised paediatric patients has important implications in terms of length of hospital stay, healthcare cost and mortality. The overall mortality attributed to HAP has been as high as 30%–50%.57 In this study, ventilator-associated pneumonia (VAP) developed in 9.21% (7/76) of children undergoing mechanical ventilation. Our estimate is in line with studies conducted on children reporting VAP, which occurred in 3%–10% of ventilated paediatric ICU patients.36 58–60

The most common type of HAI observed in this study was HAP, which contributed to a proportion of 56.1% of the total HAIs. It may not be a surprise to see such a high proportion of HAI in the NICU and paediatric ward since most of the patients admitted in intensive care are incapacitated and critical. Moreover, compared with adults, infants and neonates are immunologically immature, and in many cases, vulnerable.49 50 The finding was similar to the study done in Tikur Anbessa Hospital, Ethiopia.33 It is also true for other settings—in Iran 43.7%,51 India 50%,52 Vietnam 41.9%,53 Morocco 34.5%,54 Saudi Arabia 46.7%,55 China 52.2%56 and in a European multicentre prospective study 53%.44 The high burden of HAP among hospitalised paediatric patients has important implications in terms of length of hospital stay, healthcare cost and mortality. The overall mortality attributed to HAP has been as high as 30%–50%.57 In this study, ventilator-associated pneumonia (VAP) developed in 9.21% (7/76) of children who underwent mechanical ventilation. Our estimate is in line with studies conducted on children reporting VAP, which occurred in 3%–10% of ventilated paediatric ICU patients.36 58–60

In this study, the risk of developing HAIs was three times higher among children who stayed longer than or equal to the median 6 days than their counterparts. Despite this positive association, this is not a proof that decreasing the length of stay neither increasing admission days increases/decreases the occurrence of HAIs. Possible revered causation may be one of the mechanisms why this prolonged length of stay is associated with HAIs. Moreover, there is evidence that HAIs cause a prolonged length of stay.61–65 In our findings, the presence of underlying diseases, such as SAM, was recognised as the main risk factor for HAIs. This was consistent with the finding from another study in Ethiopia,24 that underlying illnesses increased the susceptibility of patients and predisposed them to infections secondary to the reduction of the patient’s immune response that exacerbated the illnesses through which in many cases, had significant factors that contributed more to the acquisition of HAIs in neonates and paediatric patients.41 66–67

**Table 2** Proportion of hospital-acquired infections among paediatric patients in Goba Referral Hospital, Ethiopia (n=57)

| Hospital-acquired infections | Number | Proportion | 95% CI |
|-----------------------------|--------|------------|--------|
| Pneumonia/lower respiratory tract infections* | 32 | 56.1 | 43.9 to 68.4 |
| Late-onset neonatal sepsis | 6 | 10.5 | 3.5 to 19.3 |
| Intravenous line site infections | 5 | 8.8 | 1.8 to 15.8 |
| Urinary tract infections | 4 | 7.0 | 1.8 to 14.0 |
| Systemic infections | 4 | 7.0 | 1.8 to 14.0 |
| Skin/soft tissue infections | 2 | 3.5 | 0.0 to 8.8 |
| Measles | 2 | 3.5 | 0.0 to 8.8 |
| Early-onset neonatal sepsis | 1 | 1.8 | 0.0 to 5.3 |
| Surgical site infections | 1 | 1.8 | 0.0 to 7.0 |

*including ventilator-associated pneumonia (VAP) (n=7) and VAP developed in 9.21% (7/76) of children undergoing mechanical ventilation.
Limitations of the study
Several limitations on this prospective study needed to be considered. First, we did not assess the healthcare workers’ infection prevention practices that would have been associated with the prevalence of HAIs. Second, the researchers did not examine the number of HAIs after the patients were discharged. Third, despite that we followed the patients until their discharge, the full burden of HAI could not be captured in this specific study, and is limited to in-hospital assessment only, leaving outpatients whom may have potentially developed HAIs after discharge. Fourth, we focused on a small number of risk factors for HAIs and some important variables were not included. Fifth, the used analysis does not take any time-varying risk into account. Sixth, since there was limited information on the patients’ medical record folders, more social determinant variables were not collected. In addition, this study is not free from the effects of information bias as we do not use ‘blinding’. Another limitation of the study is that we could not adjust the results for the effect of social determinant variables on HAIs because the information on these social determinant variables was not collected in our study. Finally, laboratory cultures to isolate organisms as a guide were not used, in addition to the clinical criteria, to confirm the results of HAIs because of financial constraints, laboratory facilities and expertise. Given the lack of microbiology data, endogenous infections may be misclassified as HAIs. Since the study was conducted in a teaching referral hospital, the generalisation of the study findings was limited to these facilities.

CONCLUSIONS
The present study revealed that the cumulative incidence of HAIs was 13 per 100 admitted children, and the overall incidence rate of HAIs was 17.75 per 1000 paediatric days. Length of stay in the hospital and patients with SAM conditions were associated with increased risk of HAIs.

Table 3  Bivariate association of factors for the occurrence of hospital-acquired infections (HAIs) among paediatric patients in Goba Referral Hospital, southeast Ethiopia 2019 (n=448)

| Variables                        | Category         | Presence of HAIs | Crude RR       |
|---------------------------------|------------------|------------------|----------------|
|                                 |                  | Yes (57)         | No (391)       |
| Sex                             | Male             | 30               | 218            | 0.88 (0.55–1.45) |
|                                 | Female           | 27               | 173            | 1               |
| Age (months)                    | 1–12             | 33               | 252            | 0.78 (0.48–1.28) |
|                                 | >12              | 24               | 139            | 1               |
| Residence                       | Urban            | 12               | 117            | 0.65 (0.36–1.20) |
|                                 | Rural            | 45               | 274            | 1               |
| Hospital duration (median day)  | ≤6               | 17               | 220            | 1               |
|                                 | >6               | 40               | 171            | 2.64 (1.54–4.51)*|
| Admission unit                  | NICU             | 27               | 174            | 1.10 (0.68–1.79) |
|                                 | Paediatrics      | 30               | 217            | 1               |
| Patient received antimicrobials | Yes              | 17               | 154            | 1               |
|                                 | No               | 27               | 194            | 1.22 (0.69–2.17) |
|                                 | Unknown          | 13               | 43             | 2.33 (1.21–4.50)*|
| Previous hospitalisation        | Yes              | 7                | 39             | 1.22 (0.58–2.53) |
|                                 | No               | 50               | 352            | 1               |
| Mechanical ventilation          | Yes              | 12               | 64             | 1.30 (0.68–2.71) |
|                                 | No               | 45               | 327            | 1               |
| Presence of urinary catheters   | Yes              | 2                | 7              | 1.77 (0.50–6.17) |
|                                 | No               | 55               | 384            | 1               |
| Drainage tube inserted          | Yes              | 14               | 39             | 2.42 (1.42–4.12)*|
|                                 | No               | 43               | 352            | 1               |
| Severe acute malnutrition       | Yes              | 13               | 41             | 2.15 (1.24–3.73)*|
|                                 | No               | 44               | 350            | 1               |
| Surgery after admission         | Yes              | 4                | 43             | 0.64 (0.24–1.69) |
|                                 | No               | 53               | 348            | 1               |

*P value is <0.05 (crude).
NICU, neonatal intensive care unit; RR, risk ratio.
Further studies are strongly recommended to identify other important factors including isolating of bacterial, fungal and viral agents responsible for HAIs in the region.

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**Table 4 Multivariable logistic regression analysis on factors associated with hospital-acquired infections (HAIs) among patients in Goba Referral Hospital, southeast Ethiopia 2019 (n=448)†‡**

| Variables                      | Category | Patient with HAIs (n=57) | Adjusted RR     | Attributable risk§ |
|-------------------------------|----------|-------------------------|-----------------|-------------------|
| Hospital duration             | ≤6       | 17                      | 1               |                   |
|                               | >6       | 40                      | 2.58 (1.52–4.38)† | 0.12              |
| Patient received antimicrobials| Yes      | 17                      | 1               |                   |
|                               | No       | 27                      | 1.25 (0.71–2.19) |                   |
|                               | Unknown  | 13                      | 1.93 (0.84–4.42) |                   |
| Drainage tube inserted        | Yes      | 14                      | 1               |                   |
|                               | No       | 43                      | 1.77 (0.88–3.54) |                   |
|                               | Unknown  | 13                      | 1               |                   |
| Severe acute malnutrition     | Yes      | 13                      | 2.83 (1.61–4.97)† | 0.13              |
|                               | No       | 44                      |                   |                   |

†Hosmer-Lemeshow test (p=0.166).  
‡Adjusted for age, sex, admission unit, mechanical ventilation and presence of a urinary catheter.  
§Attributable risk is the difference between the risk HAIs in the exposed group and the unexposed group.  
RR, risk ratio.
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