# Incidence and risk factors of health-care-associated infection in the neonatal intensive care unit of Assiut University Children's Hospital

Gehad S. EL_Deen Mahmoud Mohammed, Asmaa H. Shoriet, Safwat M. Abdel-Aziz

Department of Pediatrics, Faculty of Medicine, Assiut University, Assiut, Egypt

Correspondence to Gehad S. EL- Deen Mahmoud, Master Degree (MD), Department of Pediatric, Faculty of Medicine, Assiut University, Assiut, Egypt.
Tel.: 01097602024;
e-mail: gahadsalah2020@gmail.com

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**Introduction**
One of the most common causes of mortality and morbidity in neonates, particularly in developing countries is hospital-acquired infections. Healthcare-associated infections (HCAI) are common in pediatric wards and are also one of the major causes of death in neonatal intensive care units (NICUs). Risk factors involved in nosocomial infection (NI) including gestational age, birth weight, severity of illness, and its related length of hospital stay and devices used are assessed.

**Objective**
The objective of study was to detect the incidence, anatomical sites, causative organisms, and risk factors related to HCAI in NICU in Assiut University Children Hospital.

**Materials and methods**
A cross-sectional (observational descriptive) study was done in the NICU of the Assiut University Children Hospital, during a period of 12 months (from February 2018 to February 2019). A total of 150 noninfected neonates at admission were included, where blood, pus, cerebrospinal fluid, and urine specimen were collected and processed.

**Results**
Out of 150 neonates, 107 (71.3%) developed NI. Most of the infections were caused by *Staphylococcus aureus* (22.7%) and *Klebsiella* spp. (16.0%). Bloodstream infection was the main site for NI in neonates (68.3%), followed by respiratory infection (20.8%). The reported risk factors for NI were low birth weight and prematurity. The outcome of HCAIs was death in 52% of neonates.

**Conclusion**
HCAIs was reported to have high incidence rate in neonates admitted in the NICU, especially in premature and low birth weight neonates. Early detection of NI and related risk factors remain the way to manage this problem.

**Keywords:**
health-care-associated infections, nosocomial infection, neonatal intensive care unit

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## Introduction

Health-care-associated infection (HCAI) is an infection acquired during hospitalization that was not incubated at the time of admission [1]. One of the most common causes of mortality and morbidity in neonates, particularly in developing countries is hospital-acquired infections (HAIs) [2]. The rate of infection has been reported to increase with decreasing gestational age and birth weight [3]. HCAI was found to be related not only to the patient's primary disease process, but also related to actions of health-care workers. The use of central venous catheters was the most common intervention associated with infection in NICU [4].

Diagnosis of infection, especially in preterm neonates, is difficult because symptoms of infection are nonspecific and vague. Moreover, the diagnostic procedures are different in the NICU [5].

The major problem in NICUs that are associated with prolonged morbidity, high mortality, and significant hospital costs remains nosocomial infection (NI) [6]. So, the aim of an infection surveillance program must be to reduce the incidence of HCAI and the associated costs.

Neonates in NICU are exposed to various procedures that provide a way of entry for microorganisms that cause these neonates more liable to HCAI including intubation and ventilation, central venous catheters, peripheral venous lines, total parenteral nutrition (TPN), and urinary catheters [7]. Neonate represents one of the most vulnerable populations

among the pediatric group, especially neonates hospitalized in a NICU [8].

## Materials and methods

### Study design and setting

This cross-sectional (observational descriptive) study was conducted in the NICU of the Assiut University Children Hospital, during a period of 12 months (from February 2018 to February 2019).

### Study cases

All newborns admitted to the NICU during the study period and showing the inclusion criteria were included in this study.

### Patient inclusion criteria

(1) Age of cases that included in the study: neonates (0–28 days after birth).
(2) Duration of admission: neonates who were admitted for more than 48 h in hospital**.**
(3) Cases without any sign of infection at admission**.**

### Patient exclusion criteria

(1) Age: more than 28 days.
(2) Neonates who were admitted for less than 48 h or died before 48 h of admission.
(3) Neonates who were admitted for infection reasons (such as pneumonia, MAS, AGE, and skin infections).
(4) Neonates with potential infection (premature rupture of membranes, chorioamnionitis, TOF).
(5) Neonates with congenital infections.

### Data collection

All cases included in the research was subjected to the following:

(1) Meticulous history taking including name, age, sex, birth weight, perinatal history (ask about length of pregnancy) 'full-term or pre-term,' ask about risk factors such as complete obstetric history to detect the risk factors of sepsis such as maternal fever greater than 38°C, maternal urinary tract infections (UTIs), premature rupture of membranes (>18 h), chorioamnionitis, meconium-stained amniotic fluid, ask about the mode and site of delivery, type of feeding: 'breastfeeding or formula-feeding,' ask about the cause of NICU admission (any disease in neonates that affect the general condition will predispose to infection). Ask about symptoms of sepsis such as lethargy and poor feeding and also about antibiotics and procedures used (central venous catheter, endotracheal tube/mechanical ventilation, peripheral intravenous lines, nasogastric tube, and urinary catheter).
(2) Full clinical examination:
    (a) General examination: including vital sign.
    (b) Systemic examination: chest, cardiac, abdominal, and neurological examination.
    (c) Daily examination with recording progress notes for every day.
(3) Investigations:
    (a) Complete blood picture: to detect bloodstream infection and bacteremia. Leukocytosis (white blood cells >11 × $10^9$//l) or leucopenia (white blood cells <4 × $10^9$//l) also help in the evaluation of the infection in an NICU patient; also anemia (red blood cells < 4 × $10^{12}$ and hemoglobin <10 g/dl in newborn) and thrombocytopenia (platelet <150 × $10^9$/l) may present in cases of infection.
    (b) C-reactive protein: normal value (0–5 mg/dl), raised in cases of infection.
    (c) Urine analysis: help in the diagnosis of UTI.
    (d) Chest radiograph: to detect nosocomial pneumonia.
    (e) Capillary blood gases.
    (f) Cultures: blood, cerebrospinal fluid, endotracheal aspirate (BAL), urine and surgical site. Cultures are the last and the more accurate step in the diagnosis of infection and its site in the body.

### Ethical considerations

(1) The study was approved and monitored by the Medical Ethics Committee, Assiut Faculty of Medicine.
(2) The investigators explained the steps and value of the research to all eligible participants. Those who agreed to be included in the study signed a fully informed consent.
(3) Risk–benefit assessment. no risks
    As the study is observational, there are no additional risks to the patients other than the recognized risks of their standard care.
(4) Confidentiality (dealing with data and data dissemination should be confidential).
(5) Statement describing the research procedure to be given to the participants.

## Results

The majority of studied neonates were males (55.3%), female (44.7); of them 63.3% were delivered by cesarean section and 36.7% by NVD. Gestational age

for the studied neonates was preterm (58.7%) and full term (41.3%); 32.7% had birth weight less than 1500 g was, 38.7% had a birth weight of 1500–2500 g, and 28.7% had a birth weight of more than 2500 g. Regarding length of stay in the NICU 3.3% of neonates stayed less than 7 days); 2.7%) had stayed for 7–15 days; and 94% stayed greater than 15 days. Also, it represents that among the infected neonates 48% recovered and 52% died, as shown in Table 1.

As regard procedures that was used for the cases included in this study were Umbilical catheter inserted in 84.7%, endotracheal tube used in 80% of studied cases. The majority of studied cases was on TPN (93.3%), peripheral IV cannula inserted in 15.3% of studied cases, 6.7% only was on nasogastric tube and enteral feeding, as shown in Table 2.

As regards the microbial profile and the distribution of isolated microorganisms from positive blood cultures, the most common pathogens were *Staphylococcus aureus* (22.7%), *Escherichia coli* (12.7%), *Klebsiella* spp. (11.3%), *Pseudomonas aeruginosa* (5.3%), *Citrobacter diversus* (5.3%), *Proteus* (2.0%), and group B *Streptococcus* spp. (1.3%), as shown in Fig. 1.

The most common isolated microorganisms from positive endotracheal aspirate cultures were *Klebsiella spp.* (16%), *S. aureus* (6.7%), *E. coli* (2%), group B *Streptococcus* spp. (1.3%), and *Citrobacter diversus* (0.7%), as shown in Fig. 2.

Bloodstream infection was the common site of NI (68.3%), followed by respiratory tract infection (20.8%), surgical site infection (7.7%), and UTI (3.3%) as shown in Table 3.

Table 4 shows the incidence rate of NI in relation to gestational age and birth weight. There was a statistically significant difference between the occurrence of infection among the studied newborns and their gestational age and birth weight. A significant association between the occurrence of NI and younger gestational age of less than 37 weeks [$P$ = 0.008, odds ratio (OR)=0.321, confidence interval (CI) = 0.144–0.715] and low birth weight (LBW) ($P$ = 0.004) was found. Also, we found no statistically significant difference between the occurrence of NI and gender ($P$ = 0.127, OR = 1.765, CI = 0.848–3.673), and mode of delivery ($P$ = 0.644,

**Table 1 Demographic features of studied neonates (*n*=150)**

| Characteristics | Categories | *n* (%) (*n*=150) |
|---|---|---|
| Sex | Male | 83 (55.3) |
| | Female | 67 (44.7) |
| Gestational age | PT (<37 weeks) | 88 (58.7) |
| | FT (≥37 weeks) | 62 (41.3) |
| Birth weight (g) | BW (<1500) | 49 (32.7) |
| | BW (1500-2500) | 58 (38.7) |
| | BW(>2500) | 43 (28.7) |
| Mode of delivery | NVD | 55 (36.7) |
| | CS | 95 (63.3) |
| Length of hospital stay | <7 days | 5 (3.3) |
| | 7-15 days | 4 (2.7) |
| | >15 days | 141 (94) |
| Outcome | Death | 78 (52.0) |
| | Recovery | 72 (48.0) |

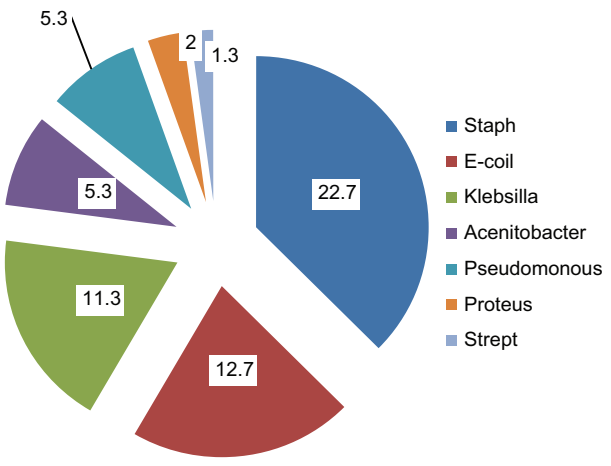
BW, birth weight; CS, cesarean section; NVD, natural vaginal delivery, PT, preterm; FT, fullterm; NGT, nasogastric tube.

**Table 2 Therapeutic interventions**

| Characteristics | Categories | *n* (%) |
|---|---|---|
| Umbilical catheter | No | 23 (15.3) |
| | Yes | 127 (84.7) |
| Mechanical ventilation via endotracheal tube | No | 30 (20.0) |
| | Yes | 120 (80.0) |
| TPN | No | 10 (6.7) |
| | Yes | 140 (93.3) |
| Peripheral IV line | No | 127 (84.7) |
| | Yes | 23 (15.3) |
| NGT and enteral feeding | No | 140 (93.3) |
| | Yes | 10 (6.7) |

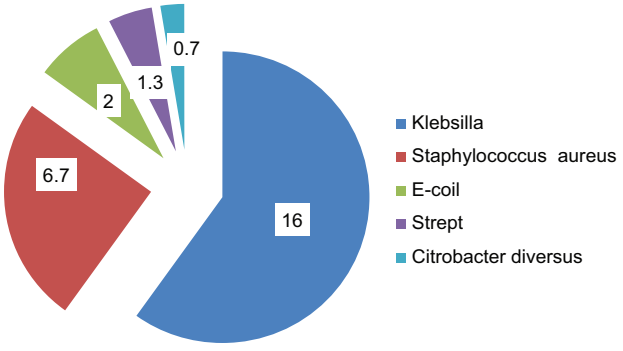
TPN, total parenteral nutrition.

**Figure 1**




Microorganisms isolated from blood culture.

**Figure 2**




Microorganisms isolated from endotracheal aspirate culture.

OR = 1.187, CI = 0.573–2.460) among the studied newborns.

Table 5 shows the distribution of infection according to the procedures used in studied cases. Most of the procedures done for neonates were significantly associated with NIs. The most common procedures associated with NI were umbilical catheter ($P = 0.011$), mechanical ventilation ($P = 0.027$), and peripheral IV line ($P = 0.045$).

As regards the outcome of the infected newborns by NI in the NICU, 48% recovered and 52% died, as shown in Fig. 3.

## Discussion

In our study, the incidence of HAI was 71%. The incidence of HAI in previous studies was found to be between 6.2 and 50.7%. Wide difference in rates of HAI was documented in previous studies in Egypt [9,10]. Abdel-Wahab *et al.* [7] found an incidence rate of 21.4%.

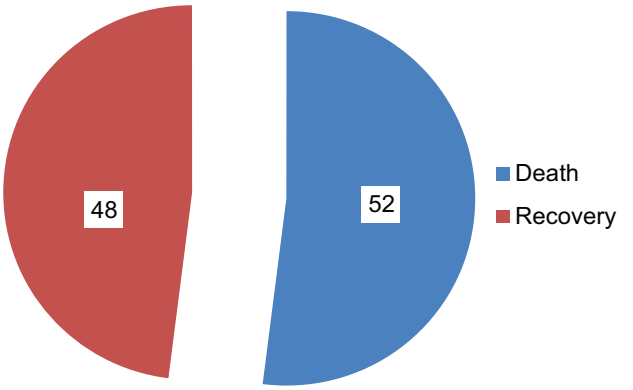
In our study, we found that the most important neonatal risk factors for HAI were LBW of less than 1.5 kg and prematurity. This observation is also found in several previous studies which indicate that the risk of NI increases with a decrease in gestational age and birth weight [11–13]. These neonates are exposed to various procedures such as the use of invasive devices

**Table 3 Type of infection**

| Categories | *n* (%) |
|---|---|
| Bloodstream infection | 125 (68.3) |
| Ventilator-associated pneumonia | 38 (20.8) |
| Surgical site infection | 14 (7.7) |
| UTI | 6 (3.3) |

UTI, urinary tract infection.

**Figure 3**




Outcomes.

**Table 4 Distribution of infection according to the demographic features of studied cases**

| Variables | Category | Infected cases (*n*=107) [*n* (%)] | Noninfected cases (*n*=43) [*n* (%)] | *P* | OR (95% CI) |
|---|---|---|---|---|---|
| Sex | Male (*n*=83) | 55 (51.4) | 28 (65.12) | 0.127 | 1.765 (0.848-3.673) |
| | Female (*n*=67) | 52 (48.6) | 15 (34.88) | | |
| Gestational age | PT (<37 week) (*n*=88) | 55 (51.4) | 33 (76.74) | **0.008**** | 0.321 (0.144-0.715) |
| | FT (≥37 week) (*n*=62) | 52 (48.6) | 10 (23.26) | **0.007**** | |
| | *P* | 0.785 | **<0.001**** | | |
| Mode of delivery | NVD (*n*=55) | 38 (35.51) | 17 (39.53) | 0.644 | 1.187 (0.573-2.460) |
| | CS (*n*=95) | 69 (64.49) | 26 (60.47) | | |
| Weight (g) | BW (<1500) (*n*=49) | 43 (40.19) | 6 (13.95) | **0.004**** | 0.241 (0.094-0.621) |
| | BW (1500-2500) (*n*=58) | 34 (31.78) | 24 (55.81) | | |
| | BW (>2500) (*n*=43) | 30 (28.04) | 13 (30.23) | | |

BW, birth weight; CI, confidence interval; CS, cesarean section; NVD, natural vaginal delivery; OR, odds ratio, **Detect high incidence of infection in neonates associated with gestational age as high in preterm neonates (0.008) and birth weight as high in low birth weight (0.004).

**Table 5 Distribution of infection according to procedures used in studied cases**

| Variables | Category | Infected cases (*n*=107) [*n* (%)] | Noninfected cases (*n*=43) [*n* (%)] | *P* |
|---|---|---|---|---|
| Umbilical catheter | No (*n*=23) | 22 (20.56) | 1 (2.33) | 0.011* |
| | Yes (*n*=127) | 85 (79.44) | 42 (97.67) | |
| Mechanical ventilation (endotracheal tube) | No (*n*=30) | 16 (14.95) | 14 (32.56) | 0.027* |
| | Yes (*n*=120) | 91 (85.05) | 29 (67.44) | |
| TPN | No (*n*=10) | 7 (6.54) | 3 (6.98) | 0.923 |
| | Yes (*n*=140) | 100 (93.46) | 40 (93.02) | |
| Peripheral IV line | No (*n*=127) | 18 (16.82) | 5 (11.63) | 0.045* |
| | Yes (*n*=23) | 89 (83.18) | 38 (88.37) | |
| NGT and enteral feeding | No (*n*=140) | 101 (94.39) | 39 (90.7) | 0.647 |
| | Yes (*n*=10) | 6 (5.61) | 4 (9.3) | |

TPN, total parenteral nutrition, *Detect increase incidence of infection in neonates asscciated with increase use of umbilical catheter (0.01), mechanical ventilation (0.07), intravenous line (0.045).

and broad-spectrum antibiotics during their NICU stay that cause them liable to infection [14].

Sex and mode of delivery were not significantly predisposed to NI in our study. Inversely, some studies have reported that gender and mode of delivery were significant risk factors [15].

In this study, other risk factors such as umbilical catheterization, endotracheal intubation, IV cannula, nasogastric tube, TPN, and duration of hospital stay greater than 15 days have been reported to be associated with an increased risk of HAI. Previous studies have reported similar results [16,17].

In our study, the most common pathogens isolated in neonatal HAI were *S. aureus* (22.7%), *E. coli* (12.7%), *Klebsiella* spp. (11.3%), *P. aeruginosa* (5.3%), *Acinetobacter* spp. (5.3), *Proteus* spp. (2.0%), and group B *Streptococcus* spp. (1.3%). The results of the blood cultures were consistent with previous studies [13,18]. But, other studies have found that Gram-positive organisms are the most microorganisms isolated in neonatal HAI, especially in developed countries [19]. This can be explained by the fact that microorganisms differ with the geography [20].

In the present study, the most common infection in the majority of cases was bloodstream infection (68.3%), followed by nosocomial pneumonia (20.8%). Several studies have reported the same result [10,11], but different from other studies, which described respiratory tract infection as the most prevalent NI [12].

Our results have detected that infected newborns may have a high death rate than neonates without HAI, whereas death rate in our study was 52% compared with the death rate of another study which was 13%, specifically in those with bloodstream infections [21].

## Conclusion

Our study detect a high incidence of HAI within the NICU. LBW and prematurity are associated with increased risk of HAI. This increase in the risk of HAI is associated with increased mortality rate among neonates in NICU. As most of the risk factors for HAI are modifiable and can be changed, this enables the developing countries to follow measures to decrease HAI and its associated complications. It is the way to minimize the occurrence of HAI.

So, we suggest that the infection control measures such as compliance of hand hygiene, limitation of excessive use of umbilical catheter, mechanical ventilation, central venous line, and prevention of improper use of antibiotics will contribute to decrease the incidence of HCAI.

### Recommendations

(1) Having an ongoing HAI surveillance program to detect the incidence of HAI, causative organisms, related risk factors, and death rates
(2) Ongoing surveillance of microorganisms should be followed in all NICUs and also receive regular reports of antibiotic susceptibility from their bacteriological laboratories.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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