Device-associated nosocomial infection in children

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ABSTRACT
Device-associated nosocomial infection is a significant part of nosocomial infection and can cause the majority of its mortality, morbidity, extra lengths of hospital stay and cost.

In a 13-year review, the online database was searched for full articles to find research on epidemiology of device-associated nosocomial infection in pediatric and neonatal wards.

Twenty two papers were included; five articles report data both in pediatric and neonatal intensive care units. The maximum reported value per 1000 device day was in pediatric intensive care unit (36.5). The largest count of involved patients was 391527 in a Chinese trial and 4 were done multinational. Most papers were accomplished in the developing countries and showed that the rates of device-associated nosocomial infection was decreased in before/after study by applying hygienic or educational interventions on safer care.

Device-associated nosocomial infections frequently occur in pediatric and neonatal intensive care units. This condition is preventable by the use of proper hygienic education and we need more attention on the prevention and diagnosis to reduce the rate of its complication, mortality and economic impact.

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Introduction
Nosocomial Infection (NI) is a serious concern of healthcare providers and patients for its high mortality, extra cost and prolonged hospital stay. Multiple factors effect on incidence of NI such as: hand hygiene, clean and safe use of medical devices, local and global infection prevention strategies, nurse-patient ratio, socioeconomic status, antimicrobial drug resistant, antimicrobial prophylaxis, underlying diseases, immunodeficiency, age, weight of neonate, type and quality of instruments, use of H2 blockers or corticosteroids, adequate and
Device associated nosocomial infection in children

qualified medical laboratory services, duration of devices, organizational and institutional characteristics of hospital wards.\(^4\)\(^-\)\(^1\)\(^1\)

Device-associated healthcare associated infections (DA-HAI) are significant part of NI that cause the majority of its mortality, extra length of stay (ELOS) and therefore extra cost of hospitalization.\(^1\)\(^2\)\(^-\)\(^1\)\(^1\)

The burden of NI in some developed countries reports regularly, they use the standard national or local surveillance systems, but it is closet or underestimated or unknown in a lot of the developing countries because of the complexity of NI diagnosis and economic limitation.\(^1\)\(^3\)

In the developed countries, NI affects as many as 50% of patients in intensive care units (ICU) and approximately 5% -15% of hospitalized patients.\(^1\)\(^4\)

Device-associated nosocomial infections (DAI) is a prominent part of NI and the ICU is the most common ward for developing NI.\(^1\)\(^5\)

Concern about healthcare associated infections (HAI) in children and neonates is serious. Although some studies report a lower rate of HAI mortality in this group than the adult patients \(^1\)\(^6\)\(^-\)\(^1\)\(^8\), but the life-long complications and vulnerability of the children especially low birth weight neonates to infections and injuries and difficulties in some diagnostic procedures \(^1\)\(^9\)\(^-\)\(^2\)\(^1\) were warned about this group.

Less effective skin barrier, immature immune system especially in preterm infants, abnormal bacterial defences and migration of granulocyte, drop of maternal IgG in the first few months of life and lower activity of mucous membrane are some of the causes of more worries of children and neonate HAI.\(^2\)\(^2\)\(^-\)\(^2\)\(^4\)

The use of prevention protocols and hygiene education could significantly reduce the rate of NI.\(^2\)\(^5\)\(^-\)\(^2\)\(^7\)

The World Health Organization (WHO) distributes programs such as “guidelines on hand hygiene in healthcare”\(^1\)\(^2\) to limit the rate of healthcare derived infections for both the patients and healthcare givers. In addition, international or local programs and guidelines on hand hygiene, antibiotic administration, clean procedure achievement, wound care, safe use of medical devices, cares on emergency room, proper applying of disinfectants and sterilization\(^2\)\(^8\) protocols on definition of NI, suitable report systems for NI, appropriate patients isolation, the improvement of laboratory settings, ameliorate the surgical procedures and strategies on injection and transfusion\(^2\)\(^9\) safe medical waste management was recommended by the scientific institutions, ministries of health and international health-oriented committees\(^8\)\(^,\)\(^3\)\(^0\) to achieve the accurate incidence of NI, prevent and reduce its medical, social and economic complications.

**Definition**

After 2002, the centers for Disease Control and Prevention of the United States (U.S) combined 3 national health care surveillance systems into a single Internet based system, the National Healthcare Safety Network (NHSN).\(^3\)\(^1\)

Many researchers use the definition criteria based on NHSN case definitions.\(^3\)\(^2\)

The surveillance systems such as CDC-NHSN (formerly the National Nosocomial Infection Surveillance system [NNIS]), German Hospital Infection Surveillance System and Korean Nosocomial Infections Surveillance System (KONIS) distributed in some developed countries, but this is not the case in the developing countries.\(^3\)\(^3\)

The International Nosocomial Infection Control Consortium (INICC) is a project that focuses on determining the incidence of NI and tries to reduce its mortality, extra length of hospital stay (ELOS) and anti-microbial resistance that is based on NNIS methodology and definitions.\(^3\)\(^4\)

Volunteer hospitals can use the INICC to achieve the cost-effective suggestions for reducing the NI complications and rates.
And moreover, CDC-NHSN provides forms and instructions for definition and evaluation of DAI.  

**Healthcare Associated Infection (HAI)**

The HAI defined by the CDC-NHSN as localized or systemic infections resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s) that become apparent in healthcare units or after discharge that they are not complications or extensions of infections already present on admission, unless a change in pathogen was found. HAI may be caused by infectious agents from endogenous or exogenous sources.

Ventilator-associated pneumonia (VAP), central line associated bloodstream infection (CLABSI) and catheter-associated urinary tract infection (CAUTI) is commonly considered as usual DAI. The surgical site infection (SSI) is one of the most common HAI and cause of mortality in the U.S.

**Ventilator Associated Pneumonia (VAP)**

As many authors reported, the VAP is the most common ICU-acquired infection. (Table 1) By the CDC-NHSN definition of pneumonia (PNEU) was divided to:

1. Clinically Defined Pneumonia (PNU1)
2. Pneumonia with Common Bacterial or Filamentous Fungal Pathogens and Specific Laboratory Findings (PNU2)
3. Viral, Legionella, and other Bacterial Pneumonias with Definitive Laboratory Findings (PNU2)
4. Pneumonia in Immunocompromised Patients (PNU3)

PNEUs spotted as ventilator-associated when patient was intubated and ventilated at the time of, or within 48 hours before the onset of the event.

In some study risk factors for VAP in children and adult were genetic syndrome, reintubation, gastric aspiration, mechanical ventilation for >3 days, chronic obstructive pulmonary disease, positive end-expiratory pressure, transport out of PICU, primary BSI, prior antibiotic use, continuous enteral feeding guidelines, bronchoscopy, immunodeficiency, immunosuppressant drug, neuromuscular blockade.

For the prevention of VAP, the elevation of the head of the bed to 45° to prevent aspiration, rigorous hand washing, focused educational programs, ventilator circuit maintenance, continuous aspiration of subglottic secretions, judicious and appropriate antimicrobial use, reducing the duration of intubation, protocolized weaning and the daily interruption of sedation are recommended.

**Central Line Associated Bloodstream Infection (CLABSI)**

As the CDC-NHSN was defined, the primary bloodstream infections (BSI) was a laboratory confirmed bloodstream infection (LCBI) when it is not secondary to a community-acquired infection or not matched with another criterion of HIA in other body sites. When a BSI-LCBI associated with central vascular catheter (CVC) or umbilical catheter use at the time of, or within 48 hours before the onset of the BSI, it is called Central line-associated BSI (CLABSI).

BSI is reported as the most frequent HAI of pediatric intensive care in some researches. It was estimated that as many as 65% to 70% of CLABSI may be preventable with the implementation of evidence-based or non-technologic strategies. The risk factors that were associated with BSI: congenital heart disease, developmental delay, failure to thrive, and genetic syndrome, receipt of transfusion, transport out of the PICU, the use of a central line, the use of multiple CVCs, the use of an arterial catheter, the receipt of steroid therapy, and the receipt of total parenteral nutrition, mechanical ventilation, dialysis, longer duration...
of CVC use, the increase count of CVCs use and the use of extracorporeal membrane oxygenation. 35, 59-61

**Catheter Associated Urinary Tract Infection (CAUTI)**

Urinary tract infections (UTI) were divided by the CDC-NHSN in two groups on defined criterion: Symptomatic (SUTI) and asymptomatic bacteriuria UTI (ABUTI). When the UTI is associated with an indwelling urinary catheter at the time of or within 48 hours before the onset of the symptom or diagnosis of UTI, named Catheter-associated UTI (CAUTI). The risk factors for bacteriuria in urinary catheterized patients are age >65, duration of catheter placement >14 days, contamination of collection bag, periurethral contamination with pathogenic microorganisms, contamination of collection bag, periurethral contamination with pathogenic microorganisms, No systemic antibiotics, female gender, diabetes mellitus, severe fatal underlying disorder, lack of aseptic techniques during catheter placement. 62-64

**Epidemiology**

The overall statistics on HAI shows that: in the developed countries 5% to 15% of hospitalized patients affected by HAI and it founded as many as 50% in ICU. 6, 14 The rate of HAI was higher in the developing countries 65 but as mentioned above, the true incidence of HAI is ambiguous in these regions. 13

**Mortality**

The HAI upraises both hospital and ICU mortality. 49 Januel et al. 66 found 14.6% mortality for ICU-acquired HAI which was 6.1%, 3.2%, 1.7%, and 0.0% for specific site infection: pulmonary infection, central venous catheter infection, bloodstream infection and urinary tract infection, respectively. Reunes et al. 67 suggest bedridden and increasing age as independent risk factors for death in elderly ICU acquired BSI. In a trial for evaluation, the mortality of HAI according to Foglia et al. report that crude mortality rates in patients infected with antibiotic-resistant organisms were greater than those infected with antibiotic-susceptible organisms. 68

Lopes et al. found in their trial that the predictive factors for mortality related to NI in pediatric was undergoing invasive procedures and the use of two or more antibiotics. 69 As Vincent et al. reported the “factors independently heighten the risk of hospital death were comorbid cancer, heart failure, immunosuppression, or cirrhosis; infection with Pseudomonas, Enterococcus, or Acinetobacter species; older age; greater disease severity; and treatment with mechanical ventilation or renal replacement therapy on the day of the study”. 14

Data on crude mortality and extra mortality of DAI is mentioned in table 1.

**Microbiology**

Microorganisms related to the DAI was somehow different from the source of infection, type of devices used, age of patients and predisposing factors. 62, 64, 70

The data for 2003 from the Center for Disease Control and Prevention’s National Nosocomial Infection Surveillance summary demonstrate that, in the US intensive care units (ICUs), 28.5% of enterococcal infections were resistant to vancomycin, 59.5% of Staphylococcus aureus infections were resistant to methicillin, 20.6% of Klebsiella pneumoniae infections were resistant to third-generation cephalosporins, and 29.5% of Pseudomonas aeruginosa infections were resistant to quinolones. 71

The patients with a history of transplantation or underlying lung disease were more commonly infected with antibiotic-resistant organisms. Additionally, patients infected with antibiotic-resistant organisms were more commonly infected with antibiotic-resistant organisms.
resistant organisms more frequently had a history of transfer from outside hospitals or genetic syndromes.\textsuperscript{68}

The risk factors for colonization with antibiotic-resistant, gram-negative organisms on admission to the PICU include previous PICU admissions, intravenous antibiotic use in the past 12 months, and exposure to long-term care facilities.\textsuperscript{72}

**Costs**
The HAI imposes significant economic consequences on both national and international healthcare systems.\textsuperscript{73} In the USA, the direct medical cost of preventable HAI was comparable to the costs of diabetes mellitus and it’s complications ($4.5 billion), stroke ($6.7 billion) and chronic obstructive lung disease ($4.2 billion).\textsuperscript{74} In Germany, Frank et al. reported that approximately 2.4 billion euro are spent annually in 1998-1999 only for the treatment of HAI.\textsuperscript{52} Rosenthal et al. found that nosocomial pneumonia approximately duplicates the cost of treatments in Argentina.\textsuperscript{75} Chen et al. report that nosocomial infection increase the total cost by 3306 dollars per patient.\textsuperscript{76} Chen et al. in another study report that HAI imposes 3.52 times the mean cost for patients without HAI.\textsuperscript{77}

**Extra length of stay**
The length of hospital stay was significantly increased by HAI; Chen et al.\textsuperscript{76} found 18.2 extra days of hospitalization per each case due to HAI in China. Rosenthal et al. reported 8.95 days extra LOS caused by nosocomial pneumonia per patient. The data on ELOS in DAI is collected in table 1.

**Efforts for prevention Protocols and Guidelines on DAI**
DAI is a major part of HAI and largely preventable if prevention protocols are widely utilized.\textsuperscript{6, 7, 78} In the U.S, four research areas perform significant research on HAI prevention: Agency for Healthcare Research and Quality (AHRQ), the Center for Disease Control and Prevention (CDC), the Center for Medicare & Medicaid Services (CMS), and the National Institute of Health (NIH). The National Action Plan to Prevent Healthcare-Associated Infections is a roadmap to eliminate HAI in the U.S shown to reduce HAI significantly. This roadmap is supported by the Department of Health & Human Services (HHS). Many national and international scientific complexes focused on patient safety, healthcare quality and HIA prevention, some of these collaborative efforts are listed below:

- WHO hand hygiene: Clean Care is Safer Care.\textsuperscript{6}
- African Partnerships for Patient Safety (WHO).\textsuperscript{8}
- The evolving threat of antimicrobial resistance - Options for action.\textsuperscript{79}
- Guidelines for the Prevention of HAI (CDC).\textsuperscript{7}
- Guideline for hand hygiene in health-care settings (CDC).\textsuperscript{80}
- Guidelines for Preventing Hospital-acquired Infections.\textsuperscript{81}
- American Society for Parenteral and Enteral Nutrition (ASPEN).\textsuperscript{82}
- Australasian Society for Parenteral and Enteral Nutrition (AuSPEN).\textsuperscript{83}
- Center for Healthcare Related Infection Surveillance and Prevention (CHRISP)(I-Care Program. Australia).\textsuperscript{84}
- International Federation of Infection Control (IFIC).\textsuperscript{85}
- Canadian Nosocomial Infection Surveillance Program (CNISP).\textsuperscript{86}
- European Society for Clinical Nutrition and Metabolism (ESPEN).\textsuperscript{87}
- Infectious Diseases Society of America (IDSA).\textsuperscript{88}
- Association for Professionals in Infection Control and Epidemiology (APIC).\textsuperscript{89}
- Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA).
- British Committee for Standards in Hematology (BCSH).
- A Strategy for the Control of Antimicrobial Resistance in Ireland (S A R I).

**Methods**

The online database was searched for full articles published from March 2000 to April 2013 with English language restriction to retrieve articles on epidemiology of Device Associated Nosocomial Infection (DAI): catheter associated Urinary tract infection (CAUTI), ventilator associated pneumonia (VAP) and central line associated bloodstream infection (CLABSI) in children and neonates. PubMed, Google Scholar, Scopus and Cochrane were searched using the following terms: "nosocomial infection”, “hospital acquired”, “device associated”, “rate”, “pediatric”, "neonate”. The Cochrane Library was searched, and hand search was done for the retrieved references.

To confirm the quality of the studies, only the studies that use standardized definitions like as NNIS were included. The studies that were reports costs, mortality, morbidity, hospital stay, localization, type of intensive care unit (ICU) and epidemiology of DAI were included in our review. The included studies were classified in three groups: CUT, VAP and BSI. Researches that did not report the rate of DAI per 1000 device days or those that evaluated DAI in immunodeficient patients were excluded. NI from other sources of device like cardiac ventricular device was spared.

**Results**

From the 23 valuable articles included (table.1), 4 and 3 of these researches report mortality and length of hospital stay respectively. Nine papers focused on only one of three suspected DAI groups. Articles that report data for pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU) was 16 and 13, respectively. 10, 13, 9 of included articles in PICU and 11, 12, 2 of included articles in NICU reported data for VAP, CLBSI and CAUTI, respectively.(Figure 1)

Two articles were retrospective and 3 were scheduled in two phases, before and after educational or other interventions in the same center(s).

The four articles from Rosenthal et al. were performed in more than one country; the largest count of included population was 391527 in a Chinese research. In the six papers that were written in neonates’ field, the information was reported in the specified weight ranges.

**Discussion**

The fact that a large number of retrieved articles was done in the developing countries tell us the efforts in identifying DAI burden and reducing HAI in such countries. Although it will take years, these explanatory data can help the control of HAI especially in low income regions.

In recent years, the INICC volunteer centers have tried to conduct useful and valuable research in the developing countries that can lead to revision in local health policies.

Our review showed great variability in the reported values of DAI. Although most researchers use one of the standard critera, different definition criteria for the diagnosis of DAI explain some of variability of the reported data.
Table 1. Studies included in review (continued…)

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<th>Location</th>
<th>Cases</th>
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<th>VAP Per 1000Dd</th>
<th>CAUTI Per 1000Dd</th>
<th>CLABSI Per 1000Dd</th>
<th>Extra Mortality % (Crude Mortality %)</th>
<th>ELOS (LOS)</th>
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Table 1. Studies included in review (continued…)

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Dd: Days, ELOS: Extra length of Stay, PICU: Pediatric Intensive Care Unit, NICU: Neonatal Intensive Care Unit, Hs1: Academic and Public Hospital, Hs2: Private Hospital.
Figure 1. Included articles characteristics

Most studies were performed in the definition criteria of CDC-NHSN and some are based on local diagnostic methods. Another point that should be noted is that the results of the studies of the non-teaching hospitals have been different from teaching wards. All of the large, well-designed and multi-center studies show the higher prevalence of DAI in the developing countries rather than the developed countries but some of the papers reported lower prevalence paradoxically. Fortunately, like the studies compare HAI rate in teaching and non-teaching hospitals most studies that designed as before-after hygiene or educational interventions shows DAI rate reduction in educated centers. That could be a start for future endeavor for prevention of DAI.

In this review, we excluded many articles that do not match with our criteria but the information about the DAI in countries where have not found such studies, that provided enough or reliable data, is limited and they will probably have a higher incidence of infections in these countries as well as these areas have potential poorer scientific, economic or local infection control program status.

A considerable number of studies have focused on the incidence of infection in pediatrics and neonatal intensive care units which it is a sign of a special attention to this age group due to high sensitivity and susceptibility to these infections and its mortality and complications in low age patients.

Reporting systems in some developed countries provide a thorough annual report on nosocomial infections, but in other countries because of the lack of such a system, the information is often not available or the reports are limited by independent international specialists or institutes.

Although some of these studies included a small number of cases, but most of these studies were based on large number of cases and/or performed multi central.

It seems that in countries where the laws are adequate to detect and defend nosocomial infections in addition to many scientific studies done in HAI, the results of these studies show a greater reduction in infections over the year. As previously mentioned, many factors have an impact on the incidence of nosocomial infections, such as: sufficient staff, state health laws, hygiene in medical procedures, control measures, strict hospital policy on diagnosis and treatment of HAI, continuing education,

Table 2. Minimum and maximum of DAI in wards by type of DAI

<table>
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<tr>
<th>Ward</th>
<th>DAI</th>
<th>Min</th>
<th>Max</th>
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<td>VAP</td>
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<td>CLBSI</td>
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<td>VAP</td>
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<td>CLBSI</td>
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DAI: Device-Associated Nosocomial Infection
Min: Minimum reported value per 1000 Device day
Max: Maximum reported value per 1000 Device day
PICU: Pediatric Intensive Care Unit
NICU: Neonatal Intensive Care Unit
VAP: Ventilator-Associated pneumonia
CAUTI: Catheter-Associated Urinary Tract Infection
CLBSI: Central Line-Associated Bloodstream Infection

99, 103, 106, 116, 110
restriction of medical procedure and minimize device use, appropriate application of disinfectants and antibiotic and many more.

Conclusion
The DAI as the major part of HAI frequently occurs in pediatric and neonatal intensive care units, especially in the developing countries. The fact that DAI is preventable by using proper hygiene training tell us the need for more attention on the prevention and diagnosis to reduce the rate of complication, mortality and economic impact.

Momentous Abbreviations
NI: Nosocomial Infection
DA-HAI: Device associated healthcare associated infections
DAI: Device-Associated Nosocomial Infection
PICU: Pediatric Intensive Care Unit
NICU: Neonatal Intensive Care Unit
VAP: Ventilator-Associated pneumonia
CAUTI: Catheter-Associated Urinary Tract Infection
CLBSI: Central Line-Associated Bloodstream Infection
CVC: Central Vascular Catheter
Dd: Device-days
ELOS: Extra length of Stay-Day
WHO: World Health Organization
NHSN: National Healthcare Safety Network
CDC: Centres for Disease Control and Prevention of United Stat
INICC: International Nosocomial Infection Control Consortium

Conflict of Interest
None declared.

Funding/Support
None declared.

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Device associated nosocomial infection in children

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Device associated nosocomial infection in children


