INTRODUCTION

Nosocomial or hospital-acquired infection has been defined as an infection acquired by patients while they are in hospital or by members of hospital staff. Hospital acquired infections could be described as an untoward effect of hospitalization to which both patients and health care workers are at risks ***(Ricks and Dethia, 2007).***

Risk factors include the patient's underlying illness, selected medications, and the type of health care facility. In a study seven risk factors were determined for ICU-acquired infection: increased length of stay (more than 48 hours), mechanical ventilation, diagnosis of trauma, central venous catheterization, pulmonary artery catheterization, urinary catheterization, and stress ulcer prophylaxis ***(Irwin and Rippe. 2008).***

The relative prevalences of the 4 most common nosocomial infections in intensive care units (ICUs) in the United States -- pneumonia, bloodstream infections, urinary tract infections (UTIs), and surgical site infections changed between 1975 and 2003. Pneumonia and bloodstream infections increased in prevalence by approximately 5%, while UTIs and skin and soft tissue infections (SSTIs) decreased by approximately 40% and 15%, respectively. The prevalences of pneumonia and bloodstream infection and skin and soft tissue infections(SSTIs) are similar in both medical ICU and surgical ICU patients (≤3% difference), although UTIs are notably more common in the medical (30%) than the surgical ICU (18%) ***(Laura et al., 2008).***

Infection control guidelines concern three main approaches, which can be schematized as follows. First, methods and techniques are needed to prevent cross-contamination and to control the potential sources of pathogens that could be transmitted from patient to patient or from Health Care Worker (HCW) to patient. These methods and techniques include appropriate protocols for cleansing, disinfecting, and caring for various pieces of equipment and devices. Second, guidelines are needed for the appropriate use of surgical antibiotic prophylaxis or empirical therapy among selected groups of patients. Third, strategies to limit the emergence of resistant microorganisms need to be developed. In addition, specifically targeted measures against various types of Nis(nosocomial infections)also have been proposed ***(Saint and Matthay, 1998).***

Preventing nosocomial infections is important to reduce the use of antibiotics Many hospitals have reduced the number of nosocomial infections through infection control programmes and novel interventionsBy optimizing the use of antibiotics within intensive care units, patient outcomes are improved, better initial antibiotic administration is provided, and the chances of further antibiotic resistance are minimized In addition to the strategies described in this review. Clinicians must insure that antibiotic administration satisfies minimal requirements, such as proper dosing, drug interval administration, monitoring drug levels, and avoiding harmful drug interactions. Not satisfying these minimal requirements will lead to patients receiving suboptimal antibiotic concentrations, which increases the likelihood of treatment failures, antibiotic resistance, and patient toxicity ***(Boyce et al., 1997).***

EPIDEMIOLOGY OF NOSOCOMIAL INFECTION IN ICU

1- Definitions

Infection

Infection is a microbiologically proven clinical diagnosis of inflammation, local and/or generalized. This includes not only clinical signs, but also the presence of at least a moderate(2+) number of leukocytes and micro-organisms of more than or equal to 10colony-forming units/ml(10 cfu/ml) in diagnostic samples obtained from an internal organ, or the isolation of a micro-organism from blood, cerebro-spinal flid, or pleural fluid ***(Silveteri et al., 2005).***

Nosocomial Infection

Nosocomial or hospital-acquired infection has been defined as an infection acquired by patients while they are in hospital or by members of hospital staff. Hospital acquired infections could be described as an untoward effect of hospitalization to which both patients and health care workers are at risks ***(Ricks and Dethia, 2007).***

Colonization

Colonization is defined as the presence of a micro-organism in an internal organ that is normally sterile (e.g, lower airways,

bladder), without an inflammatory response of the host ***(Silveteri et al., 2005).***

Sepsis

Is defined as clinical signs of generalized inflammation caused by micro-organisms and/or their products ***(Silveteri et al., 2005).***

Septicemia

Is sepsis combined with a positive blood culture ***(Silveteri et al., 2005).***

Decontamination

Decontamination is a process which removes or destroys micro-organisms to render an object safe for use. It includes cleaning, disinfection and sterilization ***(Garner, 2006).***

Disinfection

Disinfection is aprocess that reduces the number of pathogenic micro-organisms, but not necessarily bacterial spores, from inanimate objects or skin, to a level which is not harmful to health **(Garner, 2006)**

Asepsis

Is the prevention of contact with micro-organisms ***(Garner, 2006).***

Lower respiratory tract infection:

1- Pneumonia:

New or increased production of purulent sputum and/or fever 38°c with clinical signs(ie, rales, dullness to percussion) and/or chest radiograph showing new or progressive infiltrate, consolidation, cavitations, or pleural effusion not attributable to another disease ***(Eggimann and Petit, 2001).***

2-Ventilator-associated Pneumonia:

New radiographic infiltrate for at least 48h from the last chest radiograph and at least two of the Following: 1-fever 38.5°C or 35°C,2- leukocytes 10, 000/L or 3- 500/L, Purulent sputum, or 4- isolation of pathogenic bacteria from lower Respiratory tract ***(Eggimann and Petit, 2001).***

Blood stream infection:

Primary blood stream infection refers to a bacteremia for which there was no documented distal source and includes those infections resulting from an Iv line or arterial line infection. ***(Eggimann and Petit, 2001).***

2- Epidemiology of Nosocomial Infections (NIs)

Epidemiologic data collected from surveillance activities are used to determine NI rates and may be used to monitor their evolution and to detect any unusual variation that may be

Potentially suspect of outbreaks or high endemic rates of NI. Importantly, NI rates vary widely according to the type of ICU and

the population served. They may also vary with the type of surveillance) ***(Raymond and Aujard, 2000).***

A prevalence of 20.6% was reported in the European Prevalence of Infection in Intensive Care study, which included 10, 038 patients from 1, 417 European ICUs in 1995. Pneumonia was the most common NI (46.9%), followed by lower respiratory tract infection other than pneumonia (17.8%), urinary tract infection (UTI) (17.6%), and laboratory-confirmed bloodstream infection (12%) ***(Vincent et al., 2012).***

Importantly, NIs are easier to compare if they are presented as incidence densities related to device use (*eg*, endotracheal tube, central venous catheter [CVC], or urinary catheter) ***(Eggimann et al., 2000).***

An incidence of 9.2%, corresponding to an incidence density of 23.7 episodes per 1, 000 patient-days, was reported for the 164, 034 patients in 119 ICUs surveyed from 1986 through1990 in the National Nosocomial Infection Surveillance (NNIS) system ***(Jarvis et al., 2011).***

Data collected from 112 European medical ICUs between 1992 and 1997 indicated that NIs developed in 7.8% of hospitalized patients (14, 177 of 181, 993 patients), corresponding to an incidence density of 19.8 episodes per 1, 000 patient-days. UTIs (31%) were the most common, with 95% occurring in catheterized patients. Pneumonia, which was ventilator-associated in 86% of cases,

represented 27% of all NIs, and bloodstream infections represented 19% (laboratory-confirmed, 18.2%, and clinical sepsis, 0.8%), of which 87% were found to be catheter-related ***(Richards et al., 1999b).***

NI device-related rates (*ie*, catheter-related UTI, central venous catheter-related bloodstream infections, and ventilator-associated pneumonia) were 5.5, 4.0, and 7.1, respectively, episodes per 1, 000 device-days for European coronary ICUs, 6.4, 5.3, and 6.8, respectively, for medical ICUs, 4.8, 6.9, and 4.0, respectively, for pediatric ICUs, and 4.6, 5.1, and 12.5, respectively, for surgical ICUs ***(Richards et al., 1998).***

Comparable incidences of NIs have been reported in ICUs from other developed countries ***(Pittet et al., 1999a).***

Moreover, preliminary data from the National Nosocomial Infection Surveillance (NNIS) system suggested that risk-adjusted NI rates decreased over time for these three infections that are continuously monitored in ICUs ***(Richards et al., 1998).***

3- Risk Factors of NIs

The length of ICU stay is the predominant risk factor for nosocomial infection followed by the use of medical devices ***(Osmons et al., 2003).***

In the NNIS surveillance study, nosocomial infection rates for nosocomial pneumonia, bloodstream infections, and urinary tract

infections have correlated strongly with device use ***(Richards et al., 2000)***

Other risk factors include the patient's underlying illness, selected medications, and the type of health care facility. In a study seven risk factors were determined for ICU-acquired infection: increased length of stay (more than 48 hours), mechanical ventilation, diagnosis of trauma, central venous catheterization, pulmonary artery catheterization, urinary catheterization, and stress ulcer prophylaxis ***(Irwin and Rippe. 2008).***

Although therapeutic agents are superior to no prophylaxis in preventing stress ulcer bleeding, there is a growing concern about potential complications of prophylaxis, particularly nosocomial pneumonia. The incidence of nosocomial pneumonia is approximately 20-fold higher in mechanically ventilated patients, in whom the mortality rate from the pneumonia can be as high as 60% ***(Tryba and Cook, 2011).***

Gastric alkalinization and colonization with gram-negative bacilli is thought to play a causal role, rendering pH-altering drugs potentially disadvantageous. Although a persistently alkaline gastric environment increases the likelihood of bacterial colonization, it is unclear if this is influenced by the pharmacologic agent used for stress ulcer prophylaxis, as several meta-analyses have provided conflicting results ***(Ortiz et al., 2010).***

Studies show a higher incidence of nosocomial pneumonia in patients treated with antacids when compared with sucralfate, a drug that does not alter the gastric pH and appears to have bactericidal properties ***(Tryba, 2007).***

Other studies and one meta-analysis have shown no statistically significant difference in the rate of pneumonia in sucralfate and H2RA(H2 receptor antagonist) treated mechanically ventilated patients ***(Pickworth et al., 2009).***

Teaching hospitals with higher rates of device utilization have had higher device-associated infection rates ***(Richards et al., 2000).***

As in adult ICUs the most important risk factors for nosocomial infection in Pediatric ICUs appears to be the length of ICU and rate of device utilization ***(Richards et al., 1999a).***

A potential risk factor is hyperglycemia; Hyperglycemia is common in the ICU setting due to underlying disease, physiologic stress, and parenteral nutritional support. In vitro investigations suggest that hyperglycemia can impair polymorphonuclear leukocyte and monocyte phagocytic and bactericidal activities ***(Van den Berghe, 2004).***

A large randomized trial performed in a single surgical ICU found that tight control of blood glucose during the ICU stay (maintaining blood glucose 80 to 110 mg per dL) reduced overall mortality, the incidence of bacteremias, and the number of patients who required more than 10 days of antibiotic therapy ***(Van den Berghe et al., 2001).***

However, a subsequent study of the impact of tight glycemic control on outcomes in a medical ICU did not find the same benefit, and further investigation of both the risk of infection with hyperglycemia as well as optimal treatment is needed ***(Van den Berghe et al., 2006).***

4- Pathophysiology of NIs

The colonization of the host by potentially pathogenic microorganisms is a prerequisite for the further development of most NIs and may occur from exogenous or endogenous sources. As a consequence of the severity of the underlying diseases with possibly impaired host defenses, and in the presence of risk factors, critically ill patients are particularly susceptible to a rapid colonization by endemic pathogens of the hospital flora. The endemic transmission of exogenous staphylococci and other potential pathogens by the hands of health-care workers (HCWs) is well-documented **(Vicca.1999).**

Many NIs are believed to arise from the endogenous flora of the skin, oropharyngeal, or Gastro-intestinal (GI) tracts due to treatments such as chemotherapy, corticosteroid therapy, or antibiotic therapy, and also by the use of invasive devices such as intravascular or urinary catheters and nasogastric or endotracheal tubes. This flora also is responsible for the majority of surgical wound infections ***(Rangel et al., 1999).***

Pathogens responsible for nosocomial infections.

The most common pathogens responsible for ICU infections in North American medical centers are Staphylococcus aureus(S aureus) (24.1%), Pseudomonas aeruginosa (P. aeruginosa) (12.2%) and Escherichia coli (E. coli) (10.1%). More than half of all S aureus and P aeruginosa isolates are collected from respiratory samples, while the most common source for E coli isolates are urine samples (32.1%) ***(Streit et al., 2004).***

In one report, gram-positive organisms were responsible for most of the nosocomial ICU infections documented in the National Nosocomial Infections Surveillance (NNIS) System**.** In this data set, coagulase-negative staphylococci (CoNS) were responsible for 42.9% of bloodstream infections, whereas S aureus was implicated in 27.8% of pneumonia cases. The most prevalent gram-negative pathogen was P aeruginosa, which was associated with 18.1% of pneumonia cases ***(Gaynes et al., 2005).***

- **Changes in pathogen prevalence over time.**

According to United State NNIS data, little change has occurred in the prevalences of most gram-negative pathogens (including Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterobacter spp) associated with occurrence of pneumonia in the ICU between 1986 and 2003**.** One exception is Acinetobacter baumannii, which increased significantly during this interval. Gram-positive pathogens, which have shown substantial increases in prevalence in both ICU and non-ICU

hospital settings, include methicillin-resistant S. aureus (MRSA) and vancomycin-resistant enterococci (VRE) ***(Gaynes et al., 2005).***

- **Resistance**

Several factors encourage the development and spread of resistance among pathogens in the ICU which include:

- Previous exposure to antibiotics.
- Inappropriate use of antibiotics, particularly broad-spectrum agents.
- Length of hospital stay.
- Insufficient nursing/support staff.
- Poorly enforced infection control practices.

(Rao, 2009).

Drug use and duration of therapy

Antibiotics are highly prescribed among hospitalized patients. In a study of 9471 patients, showed that 25.1% and 33.9% of patients in medical and surgical clinics respectively were prescribed one or more antibiotics. However, the corresponding rates in medical and surgical ICUs were much higher, 52.5% and 81.1%, respectively ***(Usluer et al., 2005).***

Mortality rates are higher among patients treated with antibiotics for extended periods. The number of antibiotics used during treatment and the duration of ICU hospitalization were significantly correlated with higher rates of mortality ***(Hartmann et al., 2004).***

Emergence of multidrug resistant bacteria

Longer periods of drug use have also been associated with the development of multidrug resistance (resistance to 3 or more antimicrobial classes)**.**A study in 239 ICU patients in which longer periods of antibiotic use and the use of fluoroquinolones were independently associated with increased risk of emergence of multidrug-resistant MRSA(methicillin resistant staphylococcus aureus) and ESBL(extended spectrum B-lactamase) producing gram-negative pathogens ***(Nseir et al., 2005).***

The prevalence of multidrug-resistant pathogens isolated from patients at hospital admission has increased in recent years**.** A study in a tertiary care hospital in Boston between 1998 and 2003 examined changes in the prevalence of multidrug-resistant gram-negative bacilli isolated from patients within 24 hours of admission and the results showed that the prevalence of multidrug-resistant E coli, Klebsiella spp, and Enterobacter cloacae at admission were significantly higher at the end of the study period; of the 4 pathogens monitored, only P aeruginosa did not show a significant increase in prevalence ***(Pop-Vicas and D'Agata, 2005).***

Inappropriate antimicrobial therapy

The rising prevalence of nosocomial infections caused by multidrug-resistant pathogens greatly increases the chances of patients receiving inappropriate antibiotic therapy, defined as a lack

of effective treatment at the time of identification, the use of an antibiotic that does not have demonstrated efficacy against a specific pathogen, and/or the use of an antibiotic to which an infecting pathogen is resistant ***(Kollef et al., 1999).***

Inappropriate empiric antibiotic therapy was a significant risk factor among ICU patients undergoing percutaneous tracheostomy who developed nosocomial pneumonia as a postoperative complication ***(Jacobs et al., 2003).***

Cost of resistant infection

The acquisition of any nosocomial infection increases treatment costs, particularly colonization with resistant pathogens. Costs are incurred for the following care:

- General hospital costs (e.g., cost of bed per day).
- Isolation of infectious patients who then require separate supplies, housekeeping, waste disposal, and staffing.
- Acquisition and/or administration of antimicrobial agents.
- Requirements for specialized staff (e.g., nurses, physicians, infection control staff).
- Unforeseen complications.
- Additional procedures.

(Howard et al., 2001)

Length of stay/mortality

Prolonged ICU stays are associated with an increased risk of infection with resistant pathogens. In a study in ICU patients with

primary bloodstream infections, showed that treatment in an ICU for more than 7 days doubled a patient's chance of infection with resistant pathogens including MRSA, ceftazidime-resistant Enterobacter spp, VRE. or ciprofloxacin or imipenem-resistant P aeruginosa. Moreover, late-onset infections were 2 to 3 times more likely to be caused by resistant pathogens than early-onset infections ***(Fridkin, 2011).***

Infection in the ICU is also associated with increased patient mortality. In a survey of 893 ICU patients hospitalized for longer than 48 hours**,** reported a significant correlation between nonsurvivorship and acquisition of microbiologically confirmed infections, as well as the development of severe sepsis ***(Osmon et al., 2003).***

On 193 hospitalized patients infected with either E coli or K pneumoniae, mortality rates were 13.0% among 123 patients infected with fluoroquinolone-resistant pathogens, but only 5.7% among 70 patients infected with fluoroquinolone-susceptible pathogens ***(Lautenbach et al., 2005).***

Important resistant pathogens:

- **Methicillin-Resistant Staph Aureus (MRSA).**

Compared with MSSA (methicillin sensetive staphylococcus aureus), MRSA is associated with increased morbidity and mortality, prolonged length of hospitalization, and higher treatment costs. The most widely prescribed treatment for MRSA is vancomycin; however, linezolid or quinupristin-dalfopristin are used in cases of serious infection, and fluoroquinolones plus rifampin or trimethoprim-sulfamethoxazole can be used in cases of less serious infection ***(Kopp et al., 2004).***