

# Evaluation of Infection and Antimicrobial Selection Patterns in Ain Shams University Neonatal Intensive Care Unit

Thesis

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Presented by

Ayah Mohammed Zaki Shabana

(M.B.B.CH.)
Faculty of Medicine – Ain Shams University

Supervised by

#### Prof. Dr. Safaa Shafik Imam

Professor of Pediatrics
Faculty of Medicine – Ain Shams University

#### Prof. Dr. Ghada Abdel Wahed Ismail

Professor of Clinical Pathology Faculty of Medicine – Ain Shams University

#### Dr. Ola Galal Badr El-Deen

Assistant Professor of Pediatrics Faculty of Medicine – Ain Shams University

> Faculty of Medicine Ain Shams University 2013

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# List of Abbreviations

BSI	Blood Stream Infection
BW	Body Weight
CBC	Complete Blood Count
CDC	Centers for Disease Control
CHG	Chlorhexidine Gluconate
CLABSI	Central Line Associated Blood Stream Infection
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CNS	Central Nervous System
CONS	Coagulase-Negative Staphylococcus
CRP	C-Reactive Protein
CS	Cesarean section
CSF	Cerebrospinal Fluid
CVC	Central Venous Catheter
CVC/UC	Central Venous Catheter/Umblical Catheter
DAI	Device Associated Infection
E coli	Escherichia coli
ELBW	Extremely Low Birth Weight
EOS	Early-Onset Sepsis
ESBL	Extended spectrum beta lactamase
GA	Gestational Age
GBS	Group B Streptococcus
GIT	<b>Gastrointestinal Tract</b>
H.influenza	Haemophilus influenza
HAI	Hospital acquired infection
I:T ratio	Immature to Total White Blood Cells Ratio
ΙΕΝ γ	Interferon $\gamma$
IL6	Interleukin 6
IL8	Interleukin 8
IM	Intramuscular
INICC	<b>International Nosocomial Infection Control Consortium</b>
IV	Intravenous
K.pneumonia	Klebsiella pneumonia
LBW	Low Birth Weight

LOS	Late-Onset Sepsis
MDGs	Millennium Development Goals
MRSA	Methicillin-Resistant Staphylococcus aureus
MV	Mechanical ventilation
NCPAP	Nasal Continuous Positive Pressure Ventilation
NDM	New Delhimetallo-betalactamase
NGT	Nasogastric tube
NICHD	The National Institute of Child Health and Human
	Development
NICU	Neonatal Intensive Care Unit
P.aeruginosa	Pseudomonas aeruginosa
PCR	Polymerase Chain Reaction
PCT	Procalcitonin
PIA	Polysaccharide Intercellular Adhesion
PROM	Premature Ruptue Of Membrane
ROM	Rupture Of Membranes
S. aureus	Staphylococcus aureus
S.agalactiae	Streptococcus agalactiae
SIRS	Systemic Inflammatory Response Syndrome
TNF-α	Tumor Necrosis Factor-α
TPN	Total Parentral Nutrition
UTI	Urinary Tract Infection
VAP	Ventilator Associated Pneumonia
VLBW	Very Low Birth Weight
VRE	Vancomycin-Resistant Enterococci
WBC	White Blood Cells
WHO	World Health Organization
Wk	Week
Spp.	Species

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# Introduction

In September 2000, world leaders made a commitment to build a more equitable, prosperous and safer world by 2015 and launched the Millennium Development Goals (MDGs). Millennium Development Goal 4 is to reduce the number of child deaths by two thirds of the 1990 level to 31 per 1,000 live births by 2015 (*Lawn et al.*,2006).

However, neonatal mortality has fallen at a slower rate than early child mortality. Consequently, about half of all childhood deaths in developing countries occur in the neonatal period. Global neonatal mortality is estimated at 30 per 1,000 live births (*Bryce et al.*,2005).

Bacterial infections are thought to be the second most important cause worldwide accounting for 26% of the deaths, but in countries with the highest neonatal mortality rates, infection may account for a greater proportion (*Talbert et al.*,2010).

Improvement in outcome and successful treatment depends on early initiation of appropriate antibiotic therapy. The pattern of causative organisms has been constantly changing and the frequent emergence of resistant bacteria compounds the problem further. This highlights the need for surveillance of sepsis for optimum therapy. Knowledge of likely causative organisms and their antimicrobial sensitivity pattern could aid in choosing prompt and appropriate therapy (*Bhat et al.*,2011).

Infection with antimicrobial resistant organism results in delay in starting effective antibiotic therapy, fewer possible treatment options and increased morbidity and mortality, with prolonged hospital stay and greater costs of hospitalization (*Patel and Saiman*, 2010).

Antibiotic stewardship, including appropriate choice and administration of antibiotics, de-escalation of therapy, and a multidisciplinary team approach to managing neonatal sepsis, is recommended to limit inappropriate antibiotic use and prevent the development of antimicrobial resistant organism (*Ballot at al.*,2012).

# Aim of the study

#### The aims of this study are:

- 1) To document the incidence of neonatal sepsis either earlyonset, late-onset or nosocomial.
- 2) To detect the most common isolates in the neonatal intensive care unit.
- 3) To evaluate the antimicrobial selection and prescription practices; in relation to antimicrobial susceptibility and resistance patterns of these isolates.
- 4) To tailor antibiotic policy based on local resistance pattern as a step for application of antimicrobial stewardship.

# Review of Literature

## **NEONATAL SEPSIS**

#### **Definition:**

Neonatal sepsis is defined as a clinical syndrome of bacteremia with systemic signs and symptoms of infection in the first 4 weeks of life. When pathogenic bacteria gain access into the bloodstream, they may cause overwhelming infection without much localization (septicemia), or may be predominantly localized to the lung (pneumonia) or the meninges (meningitis) (*Paolucci et al.,2012*).

## **Etiology:**

Infectious agents can be transmitted to a neonate in many ways. Trans-placental transmission is well documented for congenital viral infections, but not for perinatal bacterial infections, with the exceptions of infections caused by Treponema pallidum and Listeria monocytogenes. Ascending intra-amniotic infection followed by aspiration of infected amniotic fluid can result in systemic neonatal infection.

Approximately 1% to 4% of neonates born to mothers with intra-amniotic infection develop systemic infection. Neonatal infection can also be acquired during vaginal delivery from bacteria colonizing the mother's lower genital tract.

Inadequate hand washing by the nursery staff can promote the spread of microorganisms from an infected to an uninfected infant or from the hands of colonized caregivers to the newborn.

The use of instrumentation, including endotracheal tubes, nasogastric feeding tubes, umbilical catheters, central venous catheters and urinary catheters, also increases the risk of neonatal infection (*Edwards*, 2011).

### **Incidence of Neonatal Sepsis:**

- The exact incidence of serious sepsis in the newborn is uncertain and underreporting is common (*McIntosh*, 2002).
- The incidence of primary sepsis is 1-5 per 1000 live births. The incidence is much higher for very low birth weight infants (BW <1500g) with early onset of sepsis (EOS) of 15-19 per 1000 and late onset nosocomial sepsis at 21%. The mortality rate is high (13-25%); higher rates are seen in premature infants and those with early fulminant disease (*Gomella et al.*,2009).
- The incidence of sepsis is expected to increase at a rate of 1.5% per year (*Aneja and Fink*,2007). Although mortality from severe sepsis has decreased modestly over the past three decades, its incidence is increasing dramatically (*Warner and Moldawer*,2008).

## **Neonatal Sepsis and Mortality**

Every year an estimated 4 million babies die in the first 4 weeks of life (the neonatal period). A similar number are stillborn and 0.5 million mothers die from pregnancy-related causes. Three-quarters of neonatal deaths happen in the first week, the highest risk of death is on the first day of life (*Lawn et al.*, 2005).

Almost all (99%) neonatal deaths arise in low-income and middle-income countries, yet most epidemiological and other research focuses on the 1% of deaths in rich countries. Globally, the main direct causes of neonatal death are estimated to be preterm birth (28%), severe infections (26%) and asphyxia (23%). Neonatal tetanus accounts for a smaller proportion of deaths (7%), but is easily preventable (*Stoll*,2005). Low birth weight is an important indirect cause of death. Maternal complications in labor carry a high risk of neonatal death, and poverty is strongly associated with an increased risk. Preventing deaths in newborn babies has not been a focus of child survival or safe motherhood programs (*Lawn et al.*,2005).

Appropriately targeted research is required to guide investment in effective interventions, especially in low resource settings. Setting global priorities for research to address neonatal infections is essential and urgent (*Bahl et al.*,2009). While we neglect these challenges, 450 newborn children die every hour, mainly from preventable causes, which is unconscionable in the 21<sup>st</sup> century (*Lawn et al.*,2005).

Newborn infections claim an estimated 1.4 million lives each year and remain responsible for approximately one-third of the world's 4.0 million neonatal deaths(*Lawn et al.*,2006).

Although effective and simple interventions for prevention and treatment of newborn infections exist, they do not reach the majority of neonates in developing countries (*Darmstadt et al.*,2005).

This gap between knowledge and practice is due in large part to poor coverage with health services, shortage of health care providers and issues related to access to referral services. The result is that a large proportion of neonatal infection deaths occur in community settings, frequently at home (*Bahl et al.*,2009).