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

Thesis

Submitted for partial fulfillment of Master Degree

In *Pediatrics*

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

Acknowledgement

First and for most, thanks to God who have lightened my path to become a humble student of a noble profession and granted me the ability to accomplish this work.

I would like to express my sincere feelings of appreciation and admiration to ***Prof. Safaa Shafik Imam*** *;Professor of Pediatrics, Faculty of Medicine, Ain-Shams University for her tremendous support that helped me through this work. I am deeply grateful for her more than words can ever express.*

Also I would like to thank and express my appreciation to ***Prof. Ghada Abdel Wahed Ismail*** *Professor of Clinical Pathology, Faculty of Medicine, Ain-Shams University, for her kind help and valuable guidance*

I would like also to express my deep feelings of gratitude to ***Dr. Ola Galal Badr El-Deen;*** *Assisstant professor of Pediatrics, Faculty of Medicine-Ain Shams University for her indescribable support and meticulous revision of this work.*

Finally yet importantly, I would like to express my gratitude to my parents for their love and support and for everyone who participated in some way to let this work come to such final picture, I owe my thanks and gratitude.

Contents

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 Staphylococc*us**
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	**Gastrointestinal Tract**
H.influenza	***Haemophilus influenza***
HAI	**Hospital acquired infection**
I:T ratio	**Immature to Total White Blood Cells Ratio**
IFN γ	**Interferon γ**
IL6	**Interleukin 6**
IL8	**Interleukin 8**
IM	**Intramuscular**
INICC	**International Nosocomial Infection Control Consortium**
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***

List of Tables

List of Figures

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 early-onset, 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 ***(Mclntosh,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 21st 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).***