Neonatal Sepsis; Bacterial Profile, Serological Markers, and Risk Factors in Major Hospitals in Sana'a (EMRO-TDR Unit Reference RPPH 18-8)

Yemen

SECTION A. GENERAL INFORMATION

- **PI name: Adeeb Salah**

- **Reporting Period:** First report; May to June 2019

- **Objectives of the study:**

  - **General:** this study aims to

1. Determine the common bacterial species associated with neonatal sepsis, their antibiotic susceptibility pattern and the possible associated risk factors
2. Investigate associated acute phase reactive proteins/cells of neonatal sepsis

  - **Specific:** this study aims to

1. Isolate and identify bacterial agents responsible for neonatal sepsis in major hospitals in Sana'a city, Yemen.
2. Determine the susceptibility pattern of bacterial isolates to commonly used antibiotics.
3. Evaluate the risk factors associated with neonatal sepsis.
4. Investigate the utility of some biomarkers (e.g. complement reactive proteins, pro-calcitonin) and inflammatory cells in detecting neonatal sepsis.

SECTION B. TECHNICAL REPORT:

INTRODUCTION:

Sepsis is a state of severe inflammatory response due to production of enormous quantities of several pro-inflammatory cytokines; especially TNF and IL-1. The diagnosis of neonatal sepsis is still controversial. This is due to lack of accurate diagnostic and prognostic testing. Blood culture is the gold standard diagnostic test; however, it can be negative even in severe cases. Complete blood count with some serological markers such as C-reactive protein (CRP), Amyloid A and pro-calcitonin are being used to support the diagnosis. Though the utility of these markers is still under investigation (1, 2).

Most cases of early-onset sepsis, within the first 7 days of life, are acquired at or shortly before birth. Early onset sepsis suggests transplacental or ascending infections from the maternal genital tract, whereas late onset sepsis, within 7 to 28 days of life, is associated with the postnatal nosocomial or community environment (3,4) Despite antibiotic therapy, neonatal sepsis remains frequent and devastating condition and a major cause of mortality among preterm neonates in developing countries. It is responsible for 30% to 50% of annual neonatal deaths. According to World Health Organization estimate, there are about 5 million neonatal deaths each year, 98% occurring in developing countries 30% to 50% due to neonatal sepsis. Lack of appropriate hygiene during labor and delivery and postnatal care have been suggested as major contributors to infectious morbidity in newborns in developing countries (5).

Bacterial pathogens causing neonatal sepsis and their antibiotic susceptibility pattern may change over time and differ between countries. Group B Streptococcus (GBS) and E. coli are recognized as the dominant early onset sepsis pathogens and coagulase negative staphylococci (CONS) as the dominant late onset sepsis pathogen followed by GBS and Staph aureus, in developed countries. Conversely, gram-negative organisms are more common and are mainly represented by Klebsiellae, E. coli and Pseudomonas followed by gram-positive organisms (Staphylococcus aureus, CONS, Streptococcus pneumoniae, and Streptococcus pyogenes) in developing countries (2,4). This diversity may be due to the changing pattern of antibiotics use and changes in pathogen lifestyle.

Due to current situation in Yemen, local conflict and displacement, 10% of women and children are malnourished and more than 50% of Yemeni people have no access to health services (WHO report). Moreover, risen costs of health services and inappropriate use of antibiotics severely affect health of mothers and neonates. These factors may provoke change in causative agents together with their change in antibiotics susceptibility patterns. Thus, necessitating for more data based on evidence of neonatal sepsis. Therefore, this study aims to assess the causative bacterial species, their antimicrobial susceptibility pattern and possible associated risk factors of neonatal sepsis. In addition, it will investigate associated reactive proteins (CRP, Pro-calcitonin) and cellular response during neonatal sepsis in major NICUs in Sana'a. Outcomes will ease the diagnosis and therapeutic intervention, and it will provide a basis for further studies in infectious diseases both locally and globally.

METHODOLOGY:

Study design: An observational, prospective, cross-sectional study that will analyze data related to neonates who have clinical signs and symptoms and confirmed laboratory tests of sepsis.

Study population: study will include all neonates with neonatal sepsis, during the first three months of study period.

Sample size: All neonates with suspected neonatal sepsis hospitalized in three consecutive months (Frist 3 months of the study). Around 200 neonates will be included.

Sampling method: All hospitalized neonates with suspected neonatal sepsis

Data collection:

1. All data will be collected and recorded on standardized protocols.
2. Questionnaire will be used by NICU's doctor to collect socio-demographic data and associated risk factors of mothers and neonates.
3. Blood samples will be collected by well-trained nurse.
4. Specimens will be analyzed for diagnostic and research purposes.

Ethical considerations:

This study is approved by the ethical committee of the faculty of medicine.

Consent form will be taken from patients' family.

Filled forms and data will be stored in password-protected files and will be destroyed at the end of the study.

Activity implementation:

Time period	Activities
May-June 2019	During this period, we performed many activities to facilitate the processes including; 1. We finalized the criteria of the questioner. 2. We collected team members from NICUs in Sana'a (Al-Thawra hospital, C-plus hospital, Alsabben). 3. We trained members on taking informed consent, using questioner and on collecting and handling specimens. 4. We ensured that material and methods will be according to standard protocols. 5. We purchased available required materials. 6. We printed questioners, informed consent and other data collection forms. 7. We prepared material (Blood culture bottles, C.B.C materials, antibiogram, CRP solutions, ..) for purchase upon receiving fund.

Preliminary Results:

There is no accurate data about neonatal sepsis in Yemen. Bacteriological profile still unclear as well as risk factors. We noticed that NICU doctors don't perform blood culture for suspected neonatal sepsis cases due to 1. absence of incubators 2. rarity of positive cases 3. and high cost of the procedure.

References:

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2. Dong Y, Speer C P. Late-onset neonatal sepsis: recent developments. Arch Dis Child Fetal Neonatal. 2014;0:F1–F7.
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4. Simonsen KA, Anderson-Berry AL, Delair SF, H. Dele Daviesa HD. Early-Onset Neonatal Sepsis. Clinical Microbiology Reviews. 2014; 27 (1): 21–47.
5. Ballot D, Nana T, Sriruttan C, Cooper P. Bacterial Bloodstream Infections in Neonates in a Developing Country. ISRN Pediatrics Volume 2012, Article ID 508512, oi:10.5402/2012/508512.