CAUSATIVE ORGANISMS, ANTIBIOTIC SENSITIVITY PATTERNS AND RISK FACTORS ASSOCIATED WITH NEONATAL SEPSIS AT MOI TEACHING AND REFERRAL HOSPITAL, KENYA

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DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER OF MEDICINE CHILD HEALTH AND PEDIATRICS, MOI UNIVERSITY.

DECLARATION

Student's declaration

This thesis is my original work done during the Master of Medicine in Child Health and Pediatrics degree course of Moi University School of Medicine

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Supervisors' declaration

This research thesis has been submitted for examination with our approval as University supervisors.

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ABBREVIATIONS AND ACRONYMS

AOR	Adjusted Odds Ratio
CRP	C - Reactive Protein
GBS	Group B streptococcus
IREC	Institutional Research and Ethics Committee
IQR	Interquartile range
LOS	Late onset neonatal sepsis
MTRH	Moi Teaching and Referral Hospital
NBU	Newborn Unit
NICU	Neonatal Intensive Care Unit
OR	Odds Ratio
SPSS	Statistical Package for Social Sciences
WHO	World Health Organization

OPERATIONAL DEFINITIONS

- **Neonatal sepsis:** A clinical syndrome in an infant 28 days of age or younger, manifesting by systemic signs of infection and/or isolation of a bacterial pathogen from the blood stream.
- **Term infant:** Infant born at a gestational age of 37 or more completed weeks
- **Preterm infants:** Infant born at less than 37 weeks of gestation
- **Causative organisms:** Micro-organisms isolated during the course of an infection
- **Early-onset neonatal sepsis (EOS**): Neonatal sepsis with onset of symptoms at the age of 72 hours or earlier.
- **Late-onset neonatal sepsis (LOS):** Neonatal sepsis with onset of symptoms after the age of 72 hours.
- **Antibiotic sensitivity**: Susceptibility of bacterial (micro)organisms to antimicrobials.
- A**ntibiotic susceptibility testing (AST):** Laboratory testing carried out on cultured bacteria (isolate) to determine the effectiveness of an antimicrobial to check or inhibit bacterial growth.

ABSTRACT

Background: Neonatal sepsis is a clinical syndrome characterized by systemic signs of infection which can be confirmed by blood culture testing. Previous studies have reported high incidences of hospital associated sepsis; antimicrobial resistance coupled with increased mortality especially in the developing economies. There are limited local studies regarding antibiotic sensitivity patterns and its associated risk factors of neonatal sepsis. This limits empirical antibiotic therapy and local infection control strategies.

Objectives: To determine the causative organisms, antibiotic sensitivity patterns and risk factors associated with neonatal sepsis at Moi Teaching and Referral Hospital (MTRH) newborn unit.

Methodology: A cross-sectional study among 141 neonates with confirmed sepsis receiving care at MTRH new-born unit between September 2017 and July 2018. The participants were sampled consecutively until the desired sample size was achieved. Neonatal clinical characteristics were obtained from the participants' medical records while blood culture samples were collected for antimicrobial susceptibility testing. Data on maternal characteristics were obtained using an interviewer administered questionnaire. Descriptive statistics, Pearson chi-square test of association and odds ratios were conducted using statistical package for social sciences (SPSS) version 24.

Results: Females accounted for 57.4% of the 141 neonates enrolled. The median gestational age and birth weight were 37 (IQR: 22-45) weeks and 2400g (IQR: 800 - 4700) respectively; 78% (n=110) of the neonates were born via spontaneous vertex delivery. A total of 151 bacterial isolates were identified, majority (46.4%; n=70) being *Klebsiella pneumoniae.* followed by *Coagulate negative staphylococcus aureus* (CoNS) 27.8% (n=42). *Klebsiella pneumoniae* was sensitive to meropenem (OR=3.298; 95% CI: 2.219-4.902; p<0.001) and amikacin (OR=1.116; 95% CI: 0.920, 1.354; p=0.270). but resistant to vancomycin (OR=2.455; 95% CI:1.888-3.192; p<0.001), CoNS was sensitive to vancomycin (OR=5.710; 3.478-9.374; p<0.001) but resistant to the rest. Both the neonatal (mode delivery, place of birth, prematurity and 5-minute APGAR score) and maternal (parity, intrapartum pyrexia, age, level of education and urinary tract infection during pregnancy) risk factors showed no significant associations with the occurrence of neonatal sepsis.

Conclusion: The main bacterial causes of neonatal sepsis were *Klebsiella pneumoniae* and CoNS. Both the gram positive and gram-negative bacteria had good sensitivity to meropenem and amikacin. The risk factors evaluated were not associated with the occurrence of neonatal sepsis.

Recommendations: *Klebsiella pneumoniae* being one of the known nosocomial infections, improvement in infection control in the unit is recommended. There is need for evidence-based review of empirical antibiotic therapy regimen containing penicillin, gentamicin, and ceftriaxone due to the prevailing high resistance levels. Future larger studies designed to identify other risk factors for neonatal sepsis should be conducted.

CHAPTER ONE

1.0 INTRODUCTION

1.1 Background information

Neonatal sepsis is a clinical syndrome in an infant aged 28 days or less that manifests by systemic signs and symptoms of infection. It is a major cause of neonatal morbidity and mortality worldwide especially in the developing countries (Shane and Stoll 2014) . Previous epidemiological studies have reported infections as the leading cause of neonatal morbidity and mortality globally (Kang et al. 2011). Neonatal mortality rate in the developed economies is estimated at 0.69 deaths per 1000 live births which is lower than that of developing nations at 0.76 deaths per 1000 live births (Irshad and Hayat 2019). In a systematic review conducted on neonatal sepsis globally, it was reported that approximately 22 neonates per 1000 live births develop sepsis of which 11%-19% of them succumb to the disease (Fleischmann-Struzek et al. 2018). In Europe, a hospital incidence rate of 50 cases per 1000 neonatal unit admissions was reported in Greece (Gkentzi et al. 2019), while in the United Kingdom 49 per 1000 neonatal unit admissions was seen (Cailes et al. 2018). The mortality rate due to neonatal sepsis was estimated at 12% in Nigeria (Shobowale et al. 2017) and 28% in Kenya (Muthwii et al. 2019). Of the 30 million neonates who contract infections annually around the globe, approximately 2 million succumb to neonatal sepsis (Irshad and Hayat 2019).

Neonatal sepsis is caused by bacteria that is classified as either gram-positive or gram-negative based on their gram staining patterns. It can be confirmed by isolating the causative pathogen(s) from the bloodstream of the affected individual (Shane, Sánchez, and Stoll 2017). In the developing countries, gram-positive organisms (*Coagulase negative staphylococcus*-CoNS, *Enterococcus faecalis*, methicillin-

resistant and methicillin-susceptible *Staphylococcus aureus*- MRSA/MSSA and *Streptococcus pneumoniae*) are the predominant causative organisms (Shrestha et al. 2018). Gram-negative bacteria *(Klebsiella pneumoniae, Serratia marcescens, Acinetobacter baumannii and Escherichia coli*) have been associated with neonatal sepsis in developed countries (Sivanandan, Soraisham, and Swarnam 2011). In the developing countries, *Klebsiella* is the main causative organism of most neonatal sepsis while CoNS has been associated with sepsis in developed countries (Muller-Pebody et al. 2011).

In the Gulf states region of Kuwait, Saudi Arabia and United Arab Emirates, *Klebsiella spp*. and *Enterobacter spp.* were found to be sensitive to third generation cephalosporins such as cefotaxime and ceftriaxone (Hammoud et al. 2017). In the United Kingdom, early onset neonatal sepsis associated with gram negative bacteria has been reported to be susceptible to a combination of penicillin and gentamicin (94%), amoxicillin and cefotaxime (100%), amoxicillin and other penicillin (98%) and cefotaxime monotherapy at 96% (Muller-Pebody et al. 2011). However, a majority of the gram-positive bacteria resisted these treatment combinations. Cefotaxime was demonstrated not to be effective against *Enterococci spp, Acinetobacter spp* and *Listeria monocytogenes* while these late onset sepsis causing organisms are susceptible to gentamicin (Muller-Pebody et al. 2011). Frequent use of third generation cephalosporins drive the development of resistant bacterial pathogens in neonatal intensive care units with emergence of extended spectrum beta lactamase producing strains.

A combination of neonatal, maternal and environment risk factors predispose neonates to sepsis. Neonatal sepsis is classified, according to the time of onset of

symptoms, as either early onset where symptoms manifest earlier than 72 hours of life or late onset which manifests after 72 hours of life (Shane and Stoll 2014; Chacko and Sohi, n.d.; Y. Dong and Speer 2015; Y. Dong, Glaser, and Speer 2019). Early onset neonatal sepsis (EONS) is associated with causative factors (Abdellatif et al. 2019) of maternal origin and is often transmitted during antenatal period or labour (vertical transmission). Late onset neonatal sepsis (LONS) causative organisms are either community acquired or nosocomial among hospitalized neonates (Greenberg et al. 2017; Y. Dong, Glaser, and Speer 2019; H. Dong, Cao, and Zheng 2017). Most early onset neonatal sepsis is associated with both maternal and neonatal factors (Ramasethu and Kawakita 2017). Maternal factors include age of the mother, level of education, intrapartum pyrexia, parity, antenatal clinic attendance and presence of urinary tract infection during pregnancy (Shane and Stoll 2014; Gebremedhin, Berhe, and Gebrekirstos 2016). Neonatal risk factors include APGAR (appearance, pulse, grimace, activity and respiration) score, mode of delivery and maturity levels (Seale et al. 2014; Greenberg et al. 2017). Gram-positive organisms have been reported as the main causative organism for late onset neonatal sepsis (Hammoud et al. 2017). These gram-positive microbes could be from either exogenous or endogenous environmental factors (Legeay et al. 2015; Stockmann et al. 2014; Y. Dong, Speer, and Glaser 2018). The exogenous factors include the physical environment of birth and care which encompasses hygiene, medical equipment, procedures and traffic while endogenous factors include the flora of the patient (Stockmann et al. 2014).

1.2 Problem Statement

Neonatal sepsis is one of the leading causes of morbidity and mortality among newborns globally (Kang et al. 2011; Obiero et al. 2015). Most of the neonates presenting with sepsis are likely to succumb to the disease if it is not promptly addressed. Its case mortality rate is higher in developing countries compared to the developed ones with an estimated prevalence of 12% and 28% in Nigeria (Shobowale et al. 2017) and Kenya (Muthwii et al. 2019) respectively. At a tertiary teaching hospital in Kenya, the rate of neonatal mortality attributed to sepsis was quite high among those born with a low birthweight (Njuguna, Kiptoon, and Nyandiko 2014). Although studies on neonatal sepsis have been conducted around the African continent, the major causative organisms of neonatal sepsis in Western Kenya as well as their antibiotic sensitivity patterns is not adequately documented. This is despite the fact that empirical data suggesting that a combination of neonatal, maternal and environment risk factors could predispose neonates to sepsis (Shane and Stoll 2014). This study therefore aimed at determining the causative organisms, antibiotic sensitivity patterns and risk factors associated with neonatal sepsis.

1.3 Justification

There has been increasing reports of global antimicrobial resistance necessitating the institution of antibiotic stewardship (Shane and Stoll 2014; Shane, Sánchez, and Stoll 2017). In Kenya, neonates with multidrug resistant *K. pneumoniae* were reported not to respond to commonly used antibiotics such as third generation cephalosporins and gentamicin (Apondi et al. 2016). Identification of the causative organisms and their sensitivity patterns to commonly used antibiotics in the local setting will inform local infection control strategies. This is because there are limited local studies on antibiotic sensitivity patterns thus the need for profiling them to guide empirical therapy choice.

The risk factors for neonatal sepsis vary between geographic regions and demographic settings, thus necessitating more local studies. The findings from this study will inform policy makers on better treatment protocols for neonatal sepsis.

1.4 Research Question

What are the causative organisms, the antibiotic sensitivity patterns and risk factors of bacterial causes of neonatal sepsis at Moi Teaching and Referral Hospital?

1.5 Objective

1.5.1 Broad Objective

To determine the causative organisms, the antibiotic sensitivity patterns and risk factors associated with bacterial causes of neonatal sepsis at Moi Teaching and Referral Hospital newborn unit.

1.5.2 Specific Objectives

1. To determine the causative organisms of bacterial neonatal sepsis at Moi Teaching and Referral Hospital newborn unit.
2. To determine the antibiotic sensitivity of organisms causing neonatal sepsis at Moi Teaching and Referral Hospital newborn unit.
3. To determine risk factors associated with bacterial causes of neonatal sepsis at Moi Teaching and referral Hospital Newborn unit.

CHAPTER TWO

2.0 LITERATURE REVIEW

Neonatal sepsis is a major cause of neonatal morbidity and mortality globally, with the greatest burden reported in the developing countries (Shane and Stoll 2014) . Approximately 6.7% of the neonates from around the world who contract sepsis annually succumb to the disease (Irshad and Hayat 2019).

2.1 Causative Organisms of Neonatal Sepsis

Neonatal sepsis is caused by bacteria that is either gram-positive or gram-negative based on the gram staining patterns. In the developing countries, gram-positive organisms such as *Coagulase negative staphylococcus*-CoNS, methicillin-resistant and methicillin-susceptible *Staphylococcus aureus*- MRSA/MSSA and *Streptococcus pneumoniae*) are the predominant causes (Shrestha et al. 2018). Gram-negative bacteria such as *Klebsiella pneumoniae, Acinetobacter baumannii and Escherichia coli* have been associated with neonatal sepsis in developed countries (Sivanandan, Soraisham, and Swarnam 2011).

Neonatal sepsis (Irshad and Hayat 2019) is further classified according to the time of onset of symptoms as either early or late onset neonatal sepsis(Shane and Stoll 2014; Chacko and Sohi, n.d.; Y. Dong and Speer 2015; Y. Dong, Glaser, and Speer 2019). Early onset neonatal sepsis (EONS) is associated with causative factors (Abdellatif et al. 2019) of maternal origin and is often transmitted during labour or antenatally (vertical transmission). The most common bacterial causes of neonatal sepsis include: *Klebsiella spp, Escherichia coli, Staphylococcus aureus* and Group B streptococci (Downie et al. 2013). Late onset neonatal sepsis (LONS) causative organisms are either community acquired or nosocomial among hospitalized neonates (Greenberg et al. 2017; Y. Dong, Glaser, and Speer 2019; H. Dong, Cao, and Zheng 2017). The

causative organisms for LONS include *Streptococcus pneumoniae, Streptococcus pyogenes, Staphylococcus aureus, Group B streptococc*us and *Non-typhoidal salmonella* (Zaidi et al. 2009). In a systematic review on neonatal sepsis comprising of thirty four studies conducted around the globe, 20 studies reported that *Staphylococcus aureus* was the most common causative bacteria, followed by *Klebsiella pneumoniae* and *Escherichia coli* (Huynh et al. 2011). N*on-fermenting* gram-negative bacteria were the most isolated among neonates presenting with sepsis. *Staphylococcus aureus* was the most predominant among neonates with late onset neonatal sepsis (Sundaram, Kumar, and Narang 2009). However, studies in Tanzania (Blomberg et al. 2005; Mhada et al. 2012) found that early onset sepsis was primarily due to, *Staphylococcus aureus* and *Escherichia coli*, while late onset sepsis was due to *Klebsiella spp, Staph. aureus* and *Escherichia coli*. Group B streptococcus was isolated in blood culture tests from 11 studies (Blomberg et al. 2005; Mhada et al. 2012; Kiwanuka et al. 2013; Macharashvili et al. 2009; Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006; Ojukwu et al. 2006; Sigaúque et al. 2009; Talbert et al. 2010; Darmstadt, Batra, and Zaidi 2009; Mir et al. 2011; Gray 2007). Similarly in a retrospective analysis of blood cultures over an 11 year period conducted at the Moi Teaching and Referral Hospital in Kenya, *Klebsiella spp* was the predominant organism of neonatal sepsis at the newborn unit (Apondi et al. 2016).

2.2 Antibiotic Sensitivity Patterns of Organisms Causing Neonatal Sepsis

Neonatal sepsis is caused by either gram-positive or gram-negative organisms. In Tanzania, 68% of *Klebsiella. pneumonia* and *Escherichia coli,* both gram-negative, were resistant to gentamicin and totally resistant (100%) to ampicillin (Mhada et al. 2012). The World Health Organization (WHO) recommended first line treatment for neonatal sepsis include penicillin (or ampicillin) and gentamicin combination. In the

event of staphylococcal infection, ampicillin is replaced by cloxacillin or flucloxacillin. The second line regimen include third generation cephalosporins such as ceftriaxone or cefotaxime. Antimicrobial susceptibility to *Klebsiella spp* to first line antibiotic regimen has been reported to be decreasing (Downie et al. 2013). The duration of antibiotic treatment may be influenced by the clinical status of the neonate, blood culture positivity and the pathogens isolated (Saini et al. 2011). In a systematic review of 12 studies on antibiotic resistance (Huynh et al. 2011), the authors reported resistance of gram-negative bacteria (excluding *Klebsiella spp.*) to penicillin/ ampicillin. *Klebsiella spp.* was reported to be 96% resistant to penicillin/ampicillin in Kenya (Talbert et al. 2010) and 100% resistant in Tanzania (Mhada et al. 2012). *Klebsiella* was further resistant to gentamicin (49% and 77%) and third generation cephalosporins (43% and 18%) in Kenya (Talbert et al. 2010) and Tanzania (Mhada et al. 2012) respectively.

More than half (55%) of *Escherichia coli* isolated in a study in Georgia (Macharashvili et al. 2009) and all (100%) of those isolated in Uganda (Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006) resisted penicillin/ampicillin. In Kenya and Tanzania, *Escherichia coli* was resistant to penicillin in proportions of 78% (Talbert et al. 2010) and 93% (Mhada et al. 2012) respectively. There was no resistance to Gentamicin from gram negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) in Pakistan (Mir et al. 2011). The resistance of *Escherichia coli* to gentamicin was reported in Uganda at 29% (Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006), Kenya at 10% (Talbert et al. 2010) and 43% in Tanzania (Mhada et al. 2012). *Escherichia coli* was not resistant to third generation cephalosporins in a study conducted in Malawi (Gray 2007); However, 6% (Mugalu,

Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006) 17% (Talbert et al. 2010) and 14% (Mhada et al. 2012) resistance were reported in Uganda, Kenya and Tanzania respectively. *Staphylococcus aureus* was reported to be resistant to methicillin (a penicillin) in 67% of all the bacterial isolates in an Ethiopian study. In Kenya, *Acinetobacter baumanii* was resistant to penicillin at 56%, Gentamicin (27%) and third generation cephalosporins at 35% in a study conducted at the Aga Khan Hospital (Talbert et al. 2010). At Moi Teaching and Referral Hospital, the authors (Njuguna, Kiptoon, and Nyandiko 2014) of a study reviewing the causes for neonatal mortality among low-birth weight newborns recommended blood culture testing among neonates with suspected neonatal sepsis to identify the bacterial causes and their antibiotic sensitivities at the facility's newborn unit.

2.3 Risk Factors for Neonatal Sepsis

Neonatal sepsis is associated with a myriad of maternal and neonatal risk factors. In a study conducted in Oman, the maternal risk factors identified were chorioamnionitis, prolonged rapture of membranes, lack of intrapartum steroids use and intrapartum antibiotic use. Only the history of maternal steroid use was associated (p-value = 0.020) with having a gram-negative infection for neonatal sepsis (Abdellatif et al. 2019) . In Uganda, primiparity, intrapartum pyrexia (p=0.06) were not significantly associated with the occurence of neonatal sepsis whereas prolonged rapture of membranes, lack of antenatal clinic attendance (p=0.02) and prolonged duration of labour (Mugalu, Nakakeeto, Kiguli, and Kaddu–Mulindwa 2006) were significantly associated. A seven times likelihood, AOR = 7.43 (95% CI: 2.04 – 27.1) was reported in Ethiopia among mothers with prolonged rapture of membranes and having a new-born with sepsis (Gebremedhin, Berhe, and Gebrekirstos 2016). In Taiwan (Kung et al. 2016), a statistically significant association between maternal steroid use and

neonatal sepsis (p=0.009) was reported. However, there was no statistically significant association between prolonged rapture of membranes (p=0.840) and neonatal sepsis (Kung et al. 2016).

Neonatal risk factors identified from previous studies included: sex, age, birth weight, gestational age, mode of delivery and place of delivery. In Nepal (Yadav et al. 2018), the authors reported that gender was not associated with neonatal sepsis ($p > 0.05$), however, neonates older than three days ($p<0.05$), low birth weight ($p<0.05$) and gestational age of 37 weeks or more ($p<0.05$) were statistically associated with neonatal sepsis. In Uganda (Mugalu, Nakakeeto, Kiguli, and Kaddu–Mulindwa 2006), female neonates (p=0.01) and neonatal age below seven days (p=0.01) were statistically associated with neonatal sepsis. A study conducted in Ethiopia (Gebremedhin, Berhe, and Gebrekirstos 2016) reported than male neonates were 1.5 times (AOR =1.5; 95% CI: 0.6 ,3.60) more likely to contract neonatal sepsis compared to their female counterparts, however, this relationship was not statistically significant. Neonates with a birth weight of at least 2,500 grams were less likely to be diagnosed with neonatal sepsis compared to those with a birthweight below 2,500 grams. Similar findings were also reported among neonates born through caesarean section (Gebremedhin, Berhe, and Gebrekirstos 2016). In Taiwan (Kung et al. 2016), there was no statistically significant association between birth weight (p=0.052), gestational age (p=0.333) and being born outside a hospital (p=0.119) and neonatal sepsis.

Candida spp. has been reported to cause high proportion of bloodstream infections among preterm neonates (Spiliopoulou et al. 2012). They often complicate the clinical course of preterm neonates with underlying disease; with common central nervous

system involvement and neurologic impairment (Legeay et al. 2015). The risk of neonatal candidemia has been reported to be increased by central mechanical ventilation and extended antimicrobial use (Legeay et al. 2015; Kung et al. 2016).

In Europe and North America, Group-B streptococcus (GBS) was the leading cause of neonatal sepsis with an incidence of 0.5 to 3 cases per 1,000 live births (Tsolia et al. 2003). Administration of intrapartum antimicrobial prophylaxis (IPAP) among women colonized with GBS has been reported as an effective measure of reducing early onset neonatal sepsis (EONS) among neonates born from those mothers (Bennett, Raphael Dolin, and Blaser 2019). Previous studies have indicated that GBS is a less common cause of neonatal sepsis in other continents, where gram negative organisms are isolated more frequently. Maternal bacterial colonization rates have been shown to vary in various countries and socioeconomic and ethnic groups in the same country. This could correlate with invasive infectious rates in neonates. In Athens-Greece, maternal colonization rate was higher among middle class pregnant women (Tsolia et al. 2003). The estimated GBS colonization rates in the USA and Canada range between 15-40% and 7-28% in European countries (Polin et al. 2012; Shane and Stoll 2014; Vergnano et al. 2011). Furthermore, studies in Greece reported 29% vertical transmission of GBS in which 22.5% of these mothers did not receive intrapartum antibiotic prophylaxis (Gkentzi et al. 2019). Maternal colonization rates have thus been associated with increased GBS infection rates among newborns (Gkentzi et al. 2019; Tsolia et al. 2003).

CHAPTER THREE

3.0 METHODOLOGY

3.1 Study design

This study adopted a cross sectional study design among to determine the bacterial causes of neonatal sepsis and their antibiotic sensitivity patterns among neonates admitted in a newborn unit of a tertiary teaching hospital.

3.2 Study site

The study was conducted at the newborn unit of Moi Teaching and Referral Hospital (MTRH). The facility is located in the Uasin Gishu County headquaters town of Eldoret, Kenya. It is the second largest national teaching and referral health facility located in the western part of the country. It has a bed-capacity of over 1000 serving the surrounding areas and referrals from far flung areas of the western and central parts of Kenya and neighboring countries. The hospital provides various services ranging from primary to tertiary care. It serves a large population of over 24 million people in the urban and rural populations.

The hospital's newborn unit (NBU) is located at the Riley Mother and Baby Hospital (RMBH) wing which is an extension of the teaching hospital set-up in 2009. It has a bed (crib) capacity of 70 but is often admits up to 185% of its capacity. Because of this congestion, there is increased risk of infection transmission among the newborns. The management protocol for neonatal sepsis in this newborn unit involves diagnosis of the disease using blood culture laboratory assays and this is followed up with pharmacological management. Empirical therapy for the newborns with suspected neonatal sepsis, the first-line regimen involves a combination of penicillin-gentamicin and third generation cephalosporins as second line treatment. Other commonly used antimicrobials include carbapenems, aminoglycosides, macrolides and glycopeptides.

3.3 Target population

All neonates admitted into the newborn unit during the study period

3.4 Study population

This study enrolled neonates admitted to the Newborn Unit of MTRH who had been diagnosed with neonatal sepsis clinically.

3.4.1 Inclusion criteria

i. Neonates with confirmed sepsis through a positive blood culture result.

3.4.2 Exclusion criteria:

Neonates whose parents did not consent to take part in the study.

3.5 Study period

The study was carried out between September 2017 and July 2018.

3.6 Sample Size

The sample size determination was computed by using Fischer's formula for finite populations. According to a study done in Port Harcourt Teaching Hospital in Nigeria, 33.1% of the study participants had neonatal septicemia (West and Tabansi 2014). An average of 20 blood culture tests were being done at MTRH NBU monthly with an isolation rate was about 30 to 40 percent. This could translate to approximately 240 samples within 12 months period. To estimate our sample size, we used the finite population correction formula (Daniel, 1999) as follows:

$$n = \frac{NZ_{\alpha/2}^2 \times p \times (1-p)}{d^2(N-1) + Z_{\alpha/2}^2(p(1-p))}$$

Where:

$n =$ The anticipated sample size with finite population correction

$N =$ The population size

$Z_{\alpha/2} = 1.96$, standard normal variate

$p =$ Estimated prevalence of positive cultures in the population

$d =$ Margin of error at 5%

Calculating sample size yields the following figure.

$$n = \frac{(240 \times 1.96^2) \times (0.331 \times 0.669)}{(0.05^2 \times 239) + (1.96^2 \times 0.331 \times 0.669)}$$

$$n = \frac{204.1632}{1.4482} = 141 \text{ participants.}$$

3.7 Study Procedure and Data Collection Techniques

3.7.1 Sampling Technique

Neonates who were suspected to have sepsis were screened for eligibility and sampled consecutively until the desired sample size was achieved.

3.7.2 Study Procedure

Neonates suspected to have sepsis had blood culture and sensitivity samples collected as part of routine care. The samples were processed as per good clinical laboratory standards of Moi Teaching and Referral Hospital whose microbiology laboratory has been accredited by the Kenya National Accreditation Services (KENAS). Blood cultures were taken after cleansing the skin site with 70% isopropyl alcohol for 30 seconds followed by 1-2% tincture iodine and isopropyl alcohol again. 1 mL blood sample were drawn from a peripheral vein and inoculated into BactT/Alert (Paed Plus) bottle. These were then put into a BACTEC incubator and observed for 5 days before reporting as negative. Identification of bacteria and antibiotic sensitivity testing were done by standard bacterial methods as per the manufacturing guidelines.

Parents of neonates with positive blood culture test results were approached by a trained research assistant or researcher for discussions on the study objective, procedures, risks and benefits. Those who were willing to have their newborns

participate in the study were consented using a written informed consent form. Maternal characteristics (parity, intrapartum pyrexia, urinary tract infections in pregnancy, level of education and age) information were collected using a structured interviewer administered questionnaire. Neonatal characteristics (gender, maturity, mode of delivery, place of delivery, birth weight and APGAR score) and clinical data were obtained from the medical records through chart review by the researcher and the information keyed into a data collection tool. Blood culture and sensitivity results were obtained from the laboratory reports in the participants' in-patient files.

3.8 Data Analysis and Presentation

The bacterial isolates were classified as either gram-positive or gram-negative. The sensitivity of the various antimicrobials was assessed for the various isolates. The results were presented using tables. Data analysis was done using the statistical package for social sciences (SPSS) version 24.

Descriptive statistics were used to summarize the data. The median and the corresponding inter-quartile range were used to summarize continuous variables such as age, weight, APGAR score and time of onset of the symptoms among others. Categorical variables such as the gender, place of birth, mode of delivery and type of isolate were summarized using frequencies and percentages. Inferential statistics techniques using test of association and risk estimates were used to assess the relationships between the dependent and independent variables.

3.9 Ethical considerations

Permission to undertake the study was sought from the Institutional Research and Ethics Committee (IREC) Moi University and the MTRH administration. An informed signed consent was obtained from the mothers of the neonates. There was no coercion or enticement for the parents to have their babies to participate in the study. All participants were accorded standard consideration and treatment as the rest of the neonates.

The mothers were informed of the study objectives, procedures, risks and benefits. Participants' information was processed and stored safely by the principal investigator and confidentiality was ensured. The study findings and recommendations will be shared with appropriate stakeholders through research conferences and scientific publications.

CHAPTER FOUR

RESULTS

4.0 Description of Study Participants

In this study, 141 neonates were enrolled majority 81 (57.4%) of whom were female. The median gestational age was 37 weeks with the youngest being 22 weeks while the oldest neonate was 45 weeks. Spontaneous vaginal delivery (SVD) was the commonest mode of delivery for 110 (78%) of the neonates. The median birth weight was 2400 grams (IQR: 800 - 4700) with 66 (47.5%) having a normal birth weight.

Table 1: Neonatal Characteristics

Neonatal characteristic	**N**	**Frequency (%) / Median (IQR)**
Gender	141	
Male		60 (42.6%)
Female		81 (57.4%)
Gestational Age	125	37 (22 - 45) weeks
Mode of Delivery	141	
Spontaneous vaginal delivery		110 (78%)
Caeserian section		31 (22%)
Birth Weight in grams	139	2400g (800 - 4700)
ELBW (≤999g)		6 (4.3%)
VLBW (1000-1499g)		24 (17.3%)
LBW (1500-2499g)		41 (29.5%)
Normal (2500-3999g)		66 (47.5%)
Macrosomia (≥4000g)		2 (1.4%)
Maturity	141	
Preterm		98 (69.5%)
Term		43 (30.5%)

The median age of the mothers enrolled was 24 (IQR: 15 - 40) years majority (54.1%; n=72) of whom were primiparous. Nearly all (93.1%; n=108) respondents attended antenatal clinic, more than half (56.6%; n=69) were unemployed with the more than one-quarter having attended a tertiary educational institution (Table 2).

Table 2: Characteristics of the participants' mothers

Maternal characteristic	**N**	**Frequency (%) / Median (IQR)**
Age	136	24 (15 - 40) years
Parity	133	
Primiparous		72 (54.1%)
Multiparous		61 (45.9%)
2		29 (21.8%)
3		20 (15%)
4		2 (1.5%)
5		4 (3%)
6		3 (2.3%)
7		3 (2.3%)
ANC Attendance	116	
Yes		108 (93.1%)
No		8 (6.9%)
UTI during pregnancy	130	
Yes		19 (14.6%)
No		111 (85.4%)
Employment Status	122	
Employed		53 (43.4%)
Unemployed		69 (56.6%)
Level of Education	132	
Primary		50 (37.9%)
Secondary		45 (34.1%)
Tertiary		37 (28%)

4.1 Causative organisms of bacterial neonatal sepsis at Moi Teaching and Referral Hospital's newborn unit.

This study enrolled 141 neonates of whom some had multiple isolates reported during blood culture testing. This led to a total of 151 bacterial isolates identified. Majority (46.4%; n=70) of these identified isolates were *Klebsiella spp* followed by *Coagulate negative staphylococcus* (27.8%; n=42). There were low frequencies of *Acinetobacter baumanii* (6.6%; n=10), *Staphylococcus aureus* (4.7%; n=7), *Enterococcus fecalis* (3.3%; n=5) and *Escherichia coli* (2.6%; n=4) reported (Table 3).

Table 3: Frequency of Bacterial Isolates at MTRH newborn Unit

Bacterial isolate	**Frequency**	**Percent (%)**
Acinetobacter spp.	10	6.6
Alcaligenes spp.	1	0.7
Coagulate negative staphylococcus	42	27.8
Enterobactor spp	4	2.6
Enterococcus fecalis	5	3.3
Escherichia coli	4	2.6
Klebsiella spp.	70	46.4
Methicillin resistant staphylococcus aureus	1	0.7
Methicillin susceptible staphylococcus aureus	3	2
Micrococcus spp.	1	0.7
Pseudomonas auroginosa	1	0.7
Pseudomonas spp.	1	0.7
Staphylococcus aureus	7	4.7
Streptococcus virdans	1	0.7
	151	**100**

4.2 Antibiotic sensitivity patterns of organisms causing neonatal sepsis at Moi Teaching and Referral Hospital newborn unit.

The sensitivity testing was done for all the isolates identified. However, since *Klebsiella spp.* (a gram-negative bacteria) and *Coagulase Negative Staphylococcus* (CoNS) were the majority and formed the bulk of the burden of neonatal septicaemia in the newborn unit, this study focuses more on these two isolates. *Klebsiella spp.* was significantly more sensitive to meropenem (OR=3.298; 95% CI: 2.219-4.902). However, its sensitivity to amikacin (OR=1.116; 0.920-1.354) and cefepime (OR=1.157; 0.167-8.002) was not found to be statistically significant. Furthermore, there was a significantly higher likelihood of *Klebsiella spp* being sensitive to Vancomycin (OR=2.455; 1.888-3.192, p<0.001) compared to other commonly used antibiotics as shown in Table 4.

Table 4: *Klebsiella spp* Antibiotic Sensitivity and Resistance Patterns (N=70)

Antibiotic	**Pearson chi-square test**					
		Pattern	Odds Ratio	95% Confidence Interval of the Difference		p-value
	n(%)			Lower	Upper	
Vancomycin	70 (100)	Resistant	2.455	1.888	3.192	<0.001
Meropenem	57 (81.4)	Sensitive	3.298	2.219	4.902	<0.001
Ceftriaxone	66 (94.3)	Resistant	1.076	0.990	1.061	0.161
Amikacin	54 (77.1)	Sensitive	1.116	0.920	1.354	0.270
Cefepime	68 (97.1)	Sensitive	1.157	0.167	8.002	0.882
Gentamycin	66 (94.3)	Resistant	1.076	0.990	1.061	0.161
Cefotaxime	67 (95.7)	Resistant	1.077	0.983	1.180	0.122

Coagulase negative staphylococcus (CoNS) – a gram-positive bacteria - was significantly sensitive to vancomycin (p-value <0.001; OR=5.710; 3.478-9.374). It also had higher odds for being sensitive to amikacin (OR=1.497; 0.884-2.535) however, this relationship was not found to be statistically significant. Furthermore, this study reports that CoNS was resistant to the remaining antibiotics tested, with the resistance statistically significant for meropenem as shown on Table 5.

Table 5: *Coagulase Negative Staphylococcus* (CoNS) antibiotic sensitivity pattern (N=42)

Antibiotic	**Pearson chi-square test**					
	n(%)	Pattern	Odds Ratio	95% Confidence Interval		p-value
				Lower	Upper	
Cefepime	42 (100)	Resistant	1.038	1.001	1.077	0.208
Cefotaxime	41 (97.6)	Resistant	1.086	1.004	1.175	0.116
Vancomycin	33 (78.6)	Sensitive	5.710	3.478	9.374	<0.001
Penicillin	31 (73.8)	Resistant	0.985	0.937	1.036	0.481
Meropenem	38 (90.5)	Resistant	2.739	2.061	3.642	<0.001
Amikacin	27 (64.3)	Sensitive	1.497	0.884	2.535	0.142
Gentamycin	36 (85.7)	Resistant	1.005	0.868	1.162	0.951
Ceftriaxone	40 (95.2)	Resistant	1.070	0.974	1.176	0.238

4.3 Risk factors for neonatal sepsis at Moi Teaching and referral Hospital Newborn unit

Neonatal risk factors such as spontaneous vaginal delivery, hospital delivery, prematurity, low birth weight and 5-minute APGAR score after birth of less than 6 were not found to be associated with the occurrence of neonatal sepsis (Table 6).

Table 6: Neonatal Risk factors associated with Neonatal Sepsis at MTRH newborn unit.

Neonatal Characteristics	***Klebsiella sp.***	**CoNS**
Mode of Delivery (N=141) SVD = 110 (78%) CS = 31 (22%)	p-value = 0.256 RR = 0.868 (0.698 – 1.080)	p-value = 0.557 RR = 1.278 (0.531 – 3.076)
Birthplace (n=134) Hospital = 125 (93.3%) Home = 9 (6.7%)	p-value = 0.144 RR = 1.476 (0.733 – 2.975)	p-value = 0.207 RR = 0.508 (0.194 – 1.332)
Maturity (N=141) Term = 98 (69.5%) Preterm = 43 (30.5%)	p-value = 0.106 RR = 0.826 (0.652 – 1.045)	p-value = 0.792 RR = 1.094 (0.561 – 2.135)
Apgar Score at 5 minutes (N=105) ≤6 = 37 (35.2%) >6 = 68 (64.8%)	p-value = 0.259 RR = 1.532 (0.733 – 3.202)	p-value = 0.352 RR = 0.082 (0.669 – 1.163)

There were no statistically significant relationships demonstrated between maternal factors and occurrence of neonatal sepsis. These factors including primiparity, intrapartum pyrexia, maternal age, level of education, urinary tract infection during pregnancy, prolonged rapture of membranes and mode of delivery with the corresponding p-values and risk ratios are indicated as shown on table 7.

Table 7: Maternal Risk Factors Associated with Neonatal Sepsis

Maternal Characteristics	***Klebsiella sp.***	**CoNS**
Parity (Primi/ Multigravida)	p-value = 0.322 RR – 1.116 (0.895 – 1.391)	p-value = 0.484 RR – 0.787 (0.401 – 1.543)
Intrapartum Pyrexia	p-value = 0.814	p-value = 0.331
Maternal Age	p-value = 0.630	p-value = 0.404
Level of Education	p-value = 0.365	p-value = 0.191
UTI in pregnancy	p-value = 0.304	p-value = 0.164

CHAPTER FIVE

DISCUSSION

5.0 Introduction

This study purposed to determine the causative organisms, antibiotic sensitivity patterns and risk factors associated with neonatal sepsis at the newborn unit of Moi Teaching and Referral Hospital. This section compares the current study's findings with those from other setups to determine reasons for concurrence or contrast.

5.1 Causative organisms of bacterial neonatal sepsis at Moi Teaching and Referral Hospital's newborn unit.

Neonatal sepsis could be caused by various pathogenic bacteria that could be classified as either gram-positive or gram-negative based on their gram staining patterns. In this study, the leading causative organism of neonatal sepsis among all the enrolled children was *Klebsiella spp* (a gram-negative bacteria) accounting for nearly half of all the bacterial isolates. The second most common bacteria isolated among the neonates enrolled in the study was *Coagulase negative Staphylococcus aureus* (CoNS) a gram-positive bacterium that accounted for more than one-quarter of all the bacteria isolated. Although there were other bacteria isolated from the neonates enrolled, their proportions were negligible with *Acinetobacter baumannii* (a gram-negative bacteria) being the third most prevalent bacteria isolated.

These results are consistent with previous studies conducted in Kenya (Talbert et al. 2010) and India (Verma et al. 2015). In the Kenyan study conducted at Kilifi District Hospital, *Klebsiella spp* was the most prevalent of all the bacterial isolates obtained from the enrolled neonates and the leading gram negative bacteria seen (Talbert et al. 2010). This similarity could be attributed to the fact that both studies were conducted in public hospitals in the same country where infection control strategies and study

population are similar. In the Indian study, it was reported that *Klebsiella spp* was the most common (48.1%) bacteria seen at the neonatal intensive care unit (NICU) of S.P. Medical College tertiary hospital in Bikaner – Rajasthan (Verma et al. 2015). This similarity could be attributed to similarity in study settings, in that; both MTRH and S.P. Medical College are tertiary hospitals in developing economies where neonates presenting with infection are often referred to.

However, the results from this study contrasted with those from Kenya (Kohli-Kochhar, Omuse, and Revathi 2011), Bangladesh (Mannan et al. 2018) and Arab States in the Gulf region – Kuwait, Saudi Arabia and the United Arab Emirates - (Hammoud et al. 2017). In the Kenyan ten year (2000 - 2009) retrospective review conducted in Aga Khan university hospital – a private teaching hospital -, CoNS was the most prevalent (27%) of the bacteria isolated from the neonates followed by *Klebsiella spp* (Kohli-Kochhar, Omuse, and Revathi 2011). This difference in study findings could be attributed to the difference in study settings and design. The current study was conducted at a public teaching hospital which receives neonates from all socioeconomic backgrounds while the Aga Khan study was conducted in a private teaching hospital which likely receives children from affluent background. While the current study adopted a cross-sectional descriptive study design, the Aga Khan study was a retrospective and over a long period which is may be fraught with incomplete data. This could explain the inconsistencies in study findings.

In the Bangladesh study conducted at Ad-din Medical College Hospital (AMCH) in Dhaka; it was reported that CoNS (68.4%) was the most prevalent followed by *Acinetobacter baumannii* at 18.4% (Mannan et al. 2018). There was no *Klebsiella spp* reported. This difference could be attributed to differences in study designs as the

Bangladesh study was prospective over a period of nine-months while the current study was cross-sectional. The Bangladesh study further employed other investigatory techniques such as C-Reactive Proteins (CRP), complete blood count (CBC) and blood slide for malarial parasites which were not investigated in the current study.

In the Gulf Region states (Hammoud et al. 2017), it was reported that CoNS was the most prevalent (34.65%) followed by *Klebsiella spp (*22.8%*), E. coli* (4.845) and *Acinetobacter spp* (4.59%). This prospective study conducted in the five NICUs of Kuwait, United Arab Emirates (UAE) and Saudi Arabia was different from the current study due to its study design, target population (late onset sepsis) and sample size (n=780). This could explain the difference in the study findings.

5.2 Antibiotic sensitivity of organisms causing neonatal sepsis at Moi Teaching and Referral Hospital newborn unit

Klebsiella spp. was sensitive to meropenem (OR=3.298; 95% CI: 2.219-4.902, p<0.001) and amikacin (OR=1.116; 0.920-1.354, p=0.270). However, there were significantly higher odds of *klebsiella* resistance to vancomycin (OR=2.455; 1.888-3.192, p<0.001) compared to gentamicin (OR=1.076 0.990-1.061, p=0.161). The sensitivity data in this study were similar to those found in India (Verma et al. 2015) where *Klebsiella* was found to be sensitive to amikacin and resistant to penicillin. Gentamicin sensitivity results are also similar to a study in the Gulf Region States where there was a 7.09 % increased chance of resistance the gram-negative bacteria to gentamicin (Hammoud et al. 2017). The findings of the current study contrast those from another Kenyan study conducted at the Aga Khan University Hospital, which found *Klebsiella* to be 72.4% sensitive to gentamicin and amikacin at 94.1% (Kohli-Kochhar, Omuse, and Revathi 2011).

Coagulase negative Staphylococcus aureus (CoNS) was sensitive to vancomycin (OR=5.710; 3.478-9.374) and amikacin (OR=1.497; 0.884-2.535), but resistant to the rest of the antimicrobials. These findings are similar to an Indian study which found CoNS to be resistant to gentamicin, ceftriaxone and ceftazidime but sensitive to vancomycin. The current study's findings further match those from Bangladesh (Mannan et al. 2018) where CoNS was reported to be sensitive to vancomycin (74%) but resistant to meropenem (22%). In a previous Kenyan study (Kohli-Kochhar, Omuse, and Revathi 2011), it was reported that CoNS was sensitive to gentamicin (83.4%) which contrasts the findings of the current study. This variation could be attributed to indiscriminate use of gentamicin as empirical first-line antimicrobial over the years without laboratory guidance.

5.3 Risk factors for neonatal sepsis at Moi Teaching and referral Hospital Newborn unit

5.3.1 Maternal Risk Factors and Occurrence of Neonatal Sepsis

In this study, there was no statistically significant relationships demonstrated between maternal factors and occurrence of neonatal sepsis. These factors include primiparity, intrapartum pyrexia, maternal age, level of education, urinary tract infection during pregnancy, prolonged rapture of membranes and mode of delivery. These findings are similar to studies conducted in Saudi Arabia (Al-Zahrani et al. 2015), Uganda (Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006) and South Korea (Kung et al. 2016). In a study conducted at King Abdul Aziz Specialist Hospital in Taif, Saudi Arabia (Al-Zahrani et al. 2015), it was reported that there was no statistically significant association between intrapartum pyrexia (p=0.110) or prolonged rapture of membrane (0.210) and the occurrence of neonatal sepsis. Although this study also adopted a cross-sectional study design, Al-Zahrani and colleagues however stratified

their participants into three groups (proven early-onset neonatal sepsis, clinical early-onset neonatal sepsis and negative infectious status) while the current study only had a single group of neonates with sepsis.

In Uganda's Mulago hospital study (Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006) assessing the aetiology and risk factors for neonatal sepsis, it was determined that primiparity (0.23), intrapartum pyrexia (0.060), prolonged rapture of membranes (0.140) and mode of delivery (0.070) was not significantly associated with the occurrence of neonatal sepsis. These findings were also similar to a study in South Korea (Kung et al. 2016) which found no statistically significant association between prolonged rapture of membranes (0.840) and occurrence of neonatal sepsis.

The findings of this study, however, contrast those found in Ethiopia's public hospitals of Mekelle City in Tigray region (Gebremedhin, Berhe, and Gebrekirstos 2016). This study in Ethiopia found that occurrence of neonatal sepsis was more likely in infants of mothers who had had intrapartum pyrexia (AOR = 6.08), urinary tract infection during pregnancy (AOR = 5.23) and prolonged rapture of membranes (AOR = 7.4).

5.3.2 Neonatal Risk Factors and Occurrence of Neonatal Sepsis

Neonatal risk factors such as spontaneous vaginal delivery, hospital delivery, prematurity, low birth weight and 5-minute APGAR score of ≤6 were, in this study, found not to be associated with the presence of neonatal sepsis in the infants studied. These results matched the findings in Saudi Arabia (Al-Zahrani et al. 2015), Uganda (Mugalu, Nakakeeto, Kiguli, and Kaddu -Mulindwa 2006) and South Korea (Kung et al. 2016). Hospital birth was not associated with occurrence of neonatal sepsis in Uganda (p-value = 0.07) and Korea (0.119) (Mugalu, Nakakeeto, Kiguli, and Kaddu -

Mulindwa 2006; Kung et al. 2016). There was no statistically significant association between prematurity and occurrence of neonatal sepsis reported in South Korea (0.333) (Kung et al. 2016), however, a statistically significant relationship was reported in Saudi Arabia (0.007) (Al-Zahrani et al. 2015). Low birthweight was not significantly associated with neonatal sepsis in Saudi Arabia (0.880) (Al-Zahrani et al. 2015) and South Korea (0.052) (Kung et al. 2016). Five-minute APGAR score of ≤6 was not associated with the occurrence of neonatal sepsis in South Korea (0.052), however, high odds were reported in Ethiopia (AOR = 68.9) (Gebremedhin, Berhe, and Gebrekirstos 2016).

CHAPTER SIX

6.0 CONCLUSIONS, RECOMMENDATIONS AND STUDY LIMITATIONS

6.1 Conclusions:

i. The main causative organism of neonatal sepsis was *Klebsiella pneumoniae.*

ii. Both *Klebsiella pneumoniae* and *Coagulate negative staphylococcus aureus* were sensitive to meropenem and amikacin antibiotics.

iii. Neonatal (place of birth, mode of delivery, maturity and 5-min APGAR score) and maternal risk factors (age, parity, intrapartum pyrexia and urinary tract infection during pregnancy) were not seen to be significantly associated with increased likelihood for neonatal sepsis occurrence.

6.2 Study Recommendations:

i. Infection control measures targeting *Klebsiella pneumoniae* and *Coagulate negative staphylococcus aureus* should be instituted to reduce the prevalence of the organism.

ii. Current first line antibiotic regimen of penicillin and gentamycin should be reviewed.

iii. Future larger studies designed to identify other risk factors for neonatal sepsis should be conducted.

6.3 Study Limitations

The study was not able to assess the environmental risk factors associated with neonatal sepsis due the study design and incomplete data.

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APPENDICES

APPENDIX I: PARENTAL INFORMED CONSENT FORM

Consent to participate in the study*:* *Read this information carefully before you decide whether you want to take part in this study.*

The purpose of this study is to determine the cause(s) of infection and risk factors associated with bacterial infections at Moi Teaching and Referral Hospital newborn unit. It is intended purely for research purpose only though we believe that any useful information obtained can be used or shared by the hospital and other policy formulators to improve healthcare service to these newborns.

Study Procedure: This involves filling out a data collection form detailing the mother and baby's biodata, as well as the presenting symptoms and signs of your baby regarding this current illness. Other information will also be gathered laboratory investigation results for analysis. All these data shall be completely anonymous and confidential since we will employ only serial numbers instead of names.

Risks: This study has no risks associated with it. It will not interrupt the treatment your baby will be put on. The baby will receive treatment as scheduled or prescribed by ward doctors based on the hospital and Ministry neonatal protocols.

Benefits: There are no financial or direct medical benefits to you or your child for participating in this study. It is our hope that the study will be potentially beneficial in terms of improved healthcare service delivery based on the recommendations out of study results.

Alternative Procedures: Participation in this study is voluntary. You have the right to decide to take part or decline the study.

Confidentiality: All data collection tools used will be identified by numbers or codes to protect any information that could be used to identify your baby. Results of this study may be published, but no names or other identifying information will be released. This research will be conducted in accordance with the Kenyan laws and regulations that protect rights of human research process. All records and other information obtained will be kept strictly confidential and your baby's protected health information will not be used without permission

Person to Contact: If you have queries, complaints or concerns regarding this study, you can contact the principal investigator from the Moi University, School of Medicine, department of Child Health and Paediatrics, Postgraduate programme.

Dr. BENARD M. ATEKA Mobile Tel. # 0722476420 or email: atekadr@gmail.com

Institutional Review Board: This research is approved by the Institutional Research and Ethics Committee (IREC) of Moi University/Moi Teaching and Referral Hospital. You may contact IREC in case of questions, complaints or concerns which you feel you cannot discuss with the investigator. Use the following contact: The Chairman IREC, Moi Teaching and Referral Hospital, PO BOX 3-30100, Eldoret, Kenya. Tel. 33471/2/3

Voluntary Participation: Refusal to participate will involve no penalty or loss of benefits to which your child is otherwise entitled. Furthermore, the decision to withdraw from this research at any stage after recruitment will not affect your relationship with the investigators or the staff.

Right of investigator to withdraw: The investigator reserves the right withdraw your baby from the research without your approval**.**

Costs and Compensation to the participants: Participation in this study is free of any charge. There will be no extra cost or compensation for taking part in this study.

Number of Participants: 141 babies in total will be recruited to participate in this study

Authorization for use of your protected health information: This study that does not entail the use of your baby's protected health information. We truly appreciate your help and thank you for your baby's participation.

CONSENT: By signing this consent form, I confirm that I have read the information herein and that I have been explained well regarding the study. I will be given a signed copy of this consent form for my retention. I voluntarily agree to take part in this study.

Name (parent)…… …Sign/thumbprint…..……...Date…….

Name of Investigator ……Signature……....Date……..

APPENDIX II: DATA COLLECTION TOOL

DEMOGRAPHIC DATA **Serial #……**

INFANT CHARACTERISTICS

1. Gender: Male Female
2. Date of birth_____ County of Residence: _____ village_____
3. Birth order _____
4. Place of birth (circle one): RMBH-LW RMBH Theatre other Health Facility at Home
   On the way to hospital (specify site)_____
5. Gestational age: by LMP_____Wks; by U/S_____Wks; by Ballard Scoring_____
6. Mode of delivery SVD____ SBD____ AVD____ EMCS_____ELCS____
7. Was it a difficult delivery? Yes ____ No_____
8. Birth weight in grams _____
9. Age at admission (hospitalization)_____hrs/days
10. Apgar Score at 1min_____5min _____10min _____ Cried immediately > birth Y or N
11. Diagnosis at admission
    _____
    Final

    diagnosis_____

    Evidence of fetal distress during labour: YES_____NO____
12. Age at earliest suspicion of sepsis (onset of symptoms)_____Days/Hrs
13. Central venous catheter Y N
14. Invasive medical or surgical procedures Y N
    Specify_____
15. Nasal catheterization Y N
16. CPAP use Y N
17. H2 Receptor blocker or PPI use_____
18. GIT pathology Y N specify_____

CULTURE REPORT

DATE	SPECIMEN	ORGANISMS	SENSITIVITY*

***** Use space overleaf

MATERNAL CHARACTERISTICS

1. Age: ____years
2. Education level (circle one): None Primary secondary tertiary
3. Socio-Economic status: Unemployed: Formal Employment Informal Employment
4. Parity: Para_____+_____ Number dead…….
5. Total ANC attendance _____ Gestational age at first ANC visit_____
6. ANC profile: VDRL_____ HIV_____ DATE HAART COMMENCED____
   HB_____
   Urinalysis report if available
   ……
7. Anti-malarial prophylaxis…… ……..…...
8. Folic acid given ……
9. Ferrous sulphate or other hematinic given ……
10. Did the mother receive intrapartum antibiotic prophylaxis (IPAP) YES NO
11. Antibiotic use during this pregnancy: Y__ or N___ name of the antibiotic_____
12. Any other drugs……
13. Antenatal Complications: List and specify time……
14. Duration of Labor 1st stage _____ 2nd stage _____
15. Rupture of membranes (hrs before delivery)_____
16. Number of vaginal examinations performed during labor……
17. Intrapartum pyrexia: Y__ N___ Highest body Temp_____ ^{o}C
18. Other illnesses……..
19. PV discharge: Yes __ or No___
    a. If yes:
        i. Foul Smelling
        ii. Not Foul Smelling
        iii. No Smell
20. UTI during this pregnancy Y ____ N _____ If yes, Specify date_____
21. Was this mother treated for UTI YES____ NO ____

APPENDIX III: ETHICAL APPROVAL

INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE (IREC)

MOI TEACHING AND REFERRAL HOSPITAL
P.O. BOX 3
ELDORET
Tel: 33471//2/3

MOI UNIVERSITY
SCHOOL OF MEDICINE
P.O. BOX 4606
ELDORET

Reference: IREC/2014/158
Approval Number: 0001264

15th September, 2014

Dr. Benard Mageto,
Moi University,
School of Medicine,
P.O. Box 4606-30100,
ELDORET-KENYA.

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
15 SEP 2014
APPROVED
P.O. BOX 4606-30100 ELDORET

Dear Dr. Mageto,

RE: FORMAL APPROVAL

The Institutional Research and Ethics Committee has reviewed your research proposal titled:-

"Causative Organisms, Antibiotic Sensitivity Pattern and Risk Factors Associated with Neonatal Sepsis at Moi Teaching and Referral Hospital."

Your proposal has been granted a Formal Approval Number: ***FAN: IREC 1264*** on 15th September, 2014. You are therefore permitted to begin your investigations.

Note that this approval is for 1 year; it will thus expire on 14th September, 2015. If it is necessary to continue with this research beyond the expiry date, a request for continuation should be made in writing to IREC Secretariat two months prior to the expiry date.

You are required to submit progress report(s) regularly as dictated by your proposal. Furthermore, you must notify the Committee of any proposal change (s) or amendment (s), serious or unexpected outcomes related to the conduct of the study, or study termination for any reason. The Committee expects to receive a final report at the end of the study.

Sincerely,

PROF. E. WERE
CHAIRMAN
INSTITUTIONAL RESEARCH AND ETHICS COMMITTEE

cc	Director	-	MTRH	Dean	-	SOP	Dean	- SOM
	Principal	-	CHS	Dean	-	SON	Dean	- SOD

APPENDIX IV: HOSPITAL APPROVAL (MTRH)

MOI TEACHING AND REFERRAL HOSPITAL

Telephone: 2033471/2/3/4
Fax: 61749
Email: director@mtrh.or.ke

P. O. Box 3
ELDORET

Ref: ELD/MTRH/R.6/VOL.II/2008

16th September, 2014

Dr.Benard Mageto,
Moi University,
College of Health Sciences,
School of Medicine.
P.O. Box 4606-30100,
ELDORET-KENYA.

RE: APPROVAL TO CONDUCT RESEARCH AT MTRH

Upon obtaining approval from the Institutional Research and Ethics Committee (IREC) to conduct your research proposal titled:

"Causative Organisms, Antibiotic Sensitivity Pattern and Risk Factors Associated with Neonatal Sepsis at Moi Teaching and Referral Hospital".

You are hereby permitted to commence your investigation at Moi Teaching and Referral Hospital.

DR.JOHN KIBOSIA
DIRECTOR
MOI TEACHING AND REFERRAL HOSPITAL

CC - Deputy Director (CS)
- Chief Nurse
- HOD,HRISM

INSTITUTIONAL RESEARCH & ETHICS COMMITTEE
16 SEP 2014
APPROVED
P.O. Box 4606-30100 ELDORET