Risk Factors associated with Early – onset Neonatal Sepsis Occurring within 24 hours after Birth in Mwingi Level 4 Hospital, Kitui County

By

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Declaration

I declare that this dissertation is my original work and has not been previously presented in this or any other university for a similar or any other degree award.

Signed ……  **…… Date…18th August 2021**

Simon M. Kithome, Reg. W64/7749/2019

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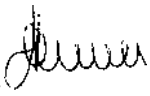
Signed……  ……Date…**22nd August 2021**

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DEDICATION

I would like to dedicate my work to my wife Virginia Wangari Mukora and my children; Hope Kendi, Emmanuel Mwenda and Victoria Muthoni for being very supportive and source of joy during the study period. All through, they have been my companion and they sacrificed their interests to help me achieve my goal.

Abbreviations

Acronym	Meaning
AOR	Adjusted Odds Ratio
ANC	Antenatal Care
C/S	Caesarean Section
CHMT	County Health management Team
COR	Crude Odds Ratio
CONS	Coagulase Negative Staphylococcus
CRP	C- Reactive Protein
CSF	Cerebral Spinal Fluid
E. coli	Escherichia coli
EONS	Early Onset Neonatal Sepsis
GA	Gestational age
GBS	Group Streptococcus
HIV	Human Immunodeficiency Virus
HRS	Hours
KMS	Kilometers
KNH	Kenyatta National Hospital
LONS	Late Onset Neonatal sepsis
NBU	New Born Unit
OR	Odds Ratio
PROM	Premature Rapture of Membrane
SDG	Sustainable Development Goal
SPSS	Statistical Package for the Social Science
SVD	Spontaneous Delivery
TID	Tropical and Infectious Diseases
UON	University of Nairobi
UTI	Urinary Tract Infection

Table of Contents

List of tables

List of figures

Abstract

Background: Neonatal mortality in most low income countries is due to infections, with the majority of deaths occurring as a result of early onset neonatal sepsis (EONS). EONS occurs within 72 hours of life; 85% occurring within the first 24 hours.

Objective: This study aimed to determine the risk factors associated with EONS and the association between hospital length of stay and antibiotic treatment regimen among neonates admitted in Mwingi Level 4 Hospital who developed sepsis within the first 24 hours of life in the year 2018.

Methodology: A retrospective case control hospital- based study covering a period of 1 year (2018). Cases were neonates born in Mwingi Level 4 Hospital who developed neonatal sepsis within 24 hours after birth, and controls were neonates born in Mwingi Level 4 Hospital who didn't develop the disease within 24 hours after birth. Systematic random sampling method was used to obtain the required sample size. Medical records of 340 neonates (85 cases and 255 controls) were studied and data collected using semi structured data collection tool.

Results: Majority of the neonates were males with 47 (55.3%) in cases and 142 (55.7%) in controls (Figure 2).The mean age of neonates was 22.7 hours (SD±3.74, n=340) ranging from 6 to 24 hours. Mean age of neonates with EONS was 23.1 hours (SD±3.19, n=85) while in controls was 22.6 hours (SD±3.90, n=340) ranging from10-24 and 6-24 hours respectively. Multivariable logistic regression analysis showed that the possible risk factor of EONS occurring within 24 hours after birth in this study was spontaneous vertex delivery [AOR= 2.041, 95% CI (1.24-3.36)] $p < 0.005$. Three variables showed an overall association with neonatal sepsis at the 5% level of significance though without statistical significance after adjusting the odds ratio. These were primiparous [AOR=1.50;95% CI (0.88-2.53)] $P< 0.045$, referrals from other health facilities [AOR=1.83; 95% CI (0.99-3.40)] $P< 0.004$, distance from residence to the health facility, [AOR= 1.78; 95% CI (0.95-3.33)] $P< 0.004$. Neonates treated with gentamicin and benzyl pencillin had 88% less likilihood of staying in the hospital for more than 5 days [OR =0.122 CI 95% (0.031, 0.478)] $p< 0.001$

Conclusion: This study showed that maternal risk factors are possible leading contributors to EONS occurring within 24 hours after birth in Mwingi Level 4 Hospital, these include spontaneous vertex delivery (SVD), primiparity, distance from residence to the health facility (the longer the distance the higher the risk), and referrals from other health facilities.

Use of benzyl penicillin and gentamicin combination as first line antibiotic regimen is associated with shorter hospital length of stay compared to the other antibiotic combination used.

CHAPTER ONE

1.0 Introduction

1.1 Background Information

Neonatal sepsis is a systemic inflammatory response syndrome in the presence of or as a suspected or proven infection in a newborn within the first 28 days of life (Gebremedhin, Berhe, & Gebrekirstos, 2016). Neonatal sepsis is an important cause of morbidity and mortality among newborns and especially among the low birth weight < 1500gms. Neonatal sepsis is caused by bacteria, fungi, viruses and protozoa but bacteria and viruses are the most common causes (Cortese et al., 2016). Neonatal mortality in most of the developing countries is due to infections. WHO estimates about 2.5 million neonatal deaths occur annually, and almost half the number is from Sub-Sahara African(SSA) countries (Hug, Sharrows, Zhong, & You, 2018). In Kenya 15.8 % of neonatal deaths are attributable to sepsis (Unicef, 2016).

Neonatal sepsis is divided into late onset sepsis and early onset sepsis. Late onset sepsis occurs after 72 hours after birth and in most cases is a result of environmental contamination after delivery; maybe nosocomial or community acquired (Tewabe et al., 2017).

Early onset neonatal sepsis occurs within 72 hrs of life with 85% occurring within 24 hrs of life, 5% within 24 hrs to 48 hrs and 10% occurring within 48 to 72 hrs, with most of the neonates being symptomatic as early as 6 hrs after birth (Javed, 2014, Tewabe et al., 2017, Jefferies, Society, & Committee, 2017). EONS mostly occurs as a result of vertical transmission prenatally or through contamination during the delivery process (Cortese et al., 2016). The commonest causative agents may vary from region to region and from one hospital to another. Group B streptococcus remains the leading causative agent of EONS globally, followed *Escherichia coli*, coagulase negative staphylococcus (CONS), *Streptococcus pneumonia*, *Listeria monocytogenes* (Cortese et al., 2016). EONS is a life threatening disease with high fatality and a risk factor for a bad outcome in neonates with sepsis (Javed, 2014).

In the previous decades since 2000, mortality and morbidity for neonatal sepsis has been declining significantly due to improved medical management though the current levels are still

high and requires intervention(Ranjeva, Warf, & Schiff, 2018). Appropriate prevention and control strategies are needed in order to achieve Sustainable Development Goals (SDG3) which states that every country to reduce neonatal mortality rate to 12 deaths per 1000 live births by the year 2030. Some of the factors associated with neonatal sepsis include; premature rupture of membrane, maternal infections among other factors which will be making important part of investigation in this study. Currently in Mwingi Level 4 Hospital, early neonatal deaths are notably high, 17deaths per 1000 live births as per District Health Information Systems Kitui County (DHIS 2018) with unknown prevalence because of gaps in reporting, hence making it necessary for a study to be conducted to determine risk factors associated with EONS in the hospital and initiate appropriate interventions.

CHAPTER TWO

2.0 Literature Review.

2.1 Epid emiology of EONS

Globally 26% of neonatal deaths are as a result of neonatal sepsis (Ranjeva et al., 2018). Of these close to 50% occur in South Sahara Africa (SSA) where 34% - 66% of deaths occur within the first 24 hrs of life, (S. C. V. Id et al., 2019). A study done in Australia on EONS showed that a proportion of babies having positive blood culture ranged from 1.9% to 5.1% within 72 hours after birth (K. B. Id, Foureur,Waal, Jones, & Putt, 2019). A study done in Italy showed that EONS occurs during the intra partum period with an incidence of 2 per 1000 live births and a mortality rate of 3% among term neonates and 16% in low birth weight neonates respectively, (Cortese et al., 2016). Another study carried out in Tanzania showed that the high burden of neonatal sepsis lies in low and middle income countries accounting for 98% of the perinatal deaths. Neonatal sepsis is estimated to affect about 9 out of 1000 live births. In Tanzania, neonatal sepsis causes 29% of the neonatal deaths which occur within the first week of life, (Masanja, Kibusi, & Mkhoi, 2019).

2.2 Etiology

2.2.1. Causative Agents

EONS mostly occurs as a result of vertical transmission prenatally or through contamination during the delivery process (Cortese et al., 2016). The commonest causative agents may vary from region to region and from one hospital to another. Group B streptococcus remains the most leading causative agent of EONS globally, followed by *E. coli*, CONS, *Streptococcus pneumoniae*, *L. monocytogenes* (Cortese et al., 2016). A study carried out in United Kingdom by Alison R. Bedford Russell (2015) was also in agreement with this order. Organisms that are associated with late onset neonatal sepsis (LONS), are *Staphylococcus aureus*, *E. coli*, *Klebsiella*, *Pseudomonas*, *Enterobacter*, *Candi da*, GBS, *Serratia*, *Acineto bacter* and anaerobes. (Simonsen, Anderson-Berry, Delair, & Dele Davies, 2014)

Studies done in Kenyatta National Hospital by E. Ng'ang'a (2013) and Aga Khan University Hospital by Kohli et al. revealed the major causative agents of EONS to be CoNS (*Staphylococcus epidermidis*) followed by gram negative bacteria, (Ng'ang'a, 2013, Kohli-

kochhar, Omuse, & Revathi, 2011). Yet another study done in Kisii Level 5 Hospital did not yield any positive blood culture (Muturi C., 2015).

2.3 Pathogenesis

In EONS neonates get infected before or during labour due to ascending infection through the birth canal. Aspiration of the infected amniotic fluid by the fetus while in utero or during birth process may result to pneumonia. In late onset neonatal sepsis (LONS), infection is acquired from the care giving environment and mostly affects the preterm neonates. Other predisposing factors of LONS are prolonged hospitalization, invasive procedures, mechanical ventilation and intravascular catheterization, (Cortese et al., 2016). Previous study has shown chorioamnionitis during third trimester and or intrapartum period strongly associates with EONS. Studies in Tanzania also found that HIV-exposed neonates had an increased risk than the unexposed group. Digital vaginal examinations exceeding three times during labor causes considerable effect on developing EONS. (Masanja et al., 2019)

2.4 Risk Factors Associated with EONS

Risk factors associated with neonatal sepsis have been studied in Africa and across the world and they are grouped into two main categories namely; maternal factors and neonatal factors.

Two recent studies have been conducted in Ghana at Trauma and Specialist Hospital Wanneba. (Adatara et al., 2019, Adatara et al., 2018).

Maternal factors: Include parity, prolonged rupture of membranes, maternal genital urinary tract infections or colonization by the EONS causative agents, mode of delivery, bleeding disorders, and age of the mother.

Neonatal factors: Include low birth weight, preterm birth, meconium aspiration, poor APGAR score, resuscitation at birth, place of birth, among others.

In a case control study done by Adatara et al. in 2018 at Wanneba Hospital maternal factors that were found to have significant association with EONS were: Parity, mode of delivery, bleeding disorders, prolonged and premature rupture of membranes. Neonatal factors found to have significant association included; APGAR score, resuscitation at birth, and age on admission. When the same type of study was done in 2019 in the same hospital but on neonates born to caesarean section mothers, he noted that low birth weight, prematurity and meconium aspiration

were the main factors for that scenario. In both studies 82.1% of cases had EONS (Adatara et al., 2018, Adatara et al., 2019). In another case control study done in Ethiopia, 76.8% of cases had EONS (Gebremedhin et al., 2016). Comparing the studies done in these two African countries, it is worth noting that in Ghana, maternal education level and antenatal care (ANC) utilization did not have any significant association contrary to Ethiopia where there was a significant association.

2.5 Clinical Presentation

Clinical signs and symptoms in early onset neonatal sepsis are subtle and appear within the first six hours of life with 80% -90% of EONS occurring within 24 hours after birth. In most cases signs and symptoms include thermal instability, presenting with hypo or hyperthermia, lethargy, poor feeding and respiratory impairment marked by intercostals retraction. EONS may also present with cardiac signs marked by cyanosis and bradycardia (Simonsen et al., 2014). Generally, signs and symptoms are more severe in gram negative infections than in gram positive infections (Simonsen et al., 2014).

2.6 Diagnosis

Early onset neonatal sepsis is diagnosed through clinical presentation, assessment of both maternal and neonatal risk factors which are good predictors, positive blood culture and hematological investigations. Important clinical signs suggestive of EONS in making diagnosis are lethargy, poor feeding, temperature instability (<35℃ or > 37.5℃), tachypnoea, convulsions and chest indrawing (Ng'ang'a, 2013).

An accurate diagnosis is a challenge, a test with 100% sensitivity rather than 100% specificity is required, and this allows the use of effective antibiotics or withholding the use of the same. The greatest sensitivity results from a combination of various diagnostic tests (Mishra, Jacobs, Doyle, & Garland, 2006).

Blood culture

Isolation of the EONS causing organism through the culture of blood, urine or cerebral spinal fluid (CSF) remains the gold standard diagnostic method for EONS. Isolation of the causative agents has got challenges in that it could result in false negative due to various factors like

inadequate volume of blood specimen among others. The result could also yield in false positives as a result of specimen contamination (Simonsen et al., 2014).

Complete white blood cell count

Other laboratory investigative measures include complete white blood cell count, which may be helpful if done within the first 24hrs. Low total white blood cell count of < 5000/µl and immature neutrophils total ratio (I:T) of 0.2 and above is associated with EONS (Jefferies et al., 2017).

Acute phase reactants

The major acute phase reactants used in diagnosis of EONS includes C - reactive protein (CRP) and procalcitonin. These are endogenous peptides produced by the liver as part of the immediate response to tissue damage resulting from infection or trauma (Turhan, Gürsoy, & Ovalı, 2015). CRP is produced 6hrs to 8hrs after the infection. CRP sensitivity ranges from 43% to 90% and its specificity ranges from 70% to 78% in EONS (Mishra et al., 2006). Procalcitonin starts to rise 4 hours after the infection. Its specificity and sensitivity ranges from 87% to 100% making it superior to the other acute phase reactants. It is also used in assessment of the progress of the treatment and as an outcome predictor (Mishra et al., 2006).

2.7 Treatment

Treating EONS depends on the etiology of the infection and whether culture and sensitivity has been done or not. If treatment is based on clinical presentation empirical treatment is commenced and is directed towards the most common EONS causative agents such as GBS, *E.coli*, and other common pathogens. A combination of ampicillin and gentamicin is commonly used. Another combination commonly used for the infections involving the meninges is ampicillin and cefotaxime (Simonsen et al., 2014). Pathogen directed treatment is commenced if there is a positive culture and sensitivity test has been done. Duration of treatment varies from 7 to 21 days(Cortese et al., 2016, Uon, 2015).

2.8 Prevention and Control

GBS screening tests for antenatal mothers at 35 to 37 weeks of gestation and commencement of appropriate intrapartum antibiotic prophylaxis. Early initiation of breastfeeding also has a major role in prevention of EONS (Cortese et al., 2016). Strict observation of the following: up to date

infection control policies and antibiotic stewardship is necessary to prevent drug resistance by EONS causative agents (Camacho-gonzalez et al., 2015) interventions on HIV prevention from mother to child transmission and adherence to antiretroviral therapy, low maternal viral loads and absence of opportunistic infections minimize the risks of EONS. (Masanja et al., 2019)

2.9 Statement of the Problem

Globally, neonatal mortality rate is 18 deaths per 1000 live births(Hug et al., 2018) , a clear indication that specific preventive interventions need to be initiated at various levels of healthcare. A study done in Turkey showed that EONS accounts for a high percentage of neonatal mortality and morbidity (Turhan et al., 2015). Other studies done in Ghana and Ethiopia showed that EONS affected the majority of those study populations at 82.1% and 76.8% respectively, (Gebremedhin et al., 2016). In Kenya, the neonatal mortality rate is 22/1000 live births 15.8% of the newborn deaths are due to sepsis while EONS accounts for 8% (Makokha & Bungoma, 2018)

Many scholars in Kenya have studied the causative agents of EONS and their sensitivity patterns, These studies shows that the prevalence of neonatal sepsis in Kenya is high (19.7%), (Ng'ang'a, 2013, Kohli-kochhar, Omuse, & Revathi, 2011, Muturi C., 2015) but there are limited studies that have been carried out to determine the risk factors associated with EONS if any.

2.10 Study Justification

There is a high morbidity and mortality rate among neonates within the first week of life in Mwingi Level 4 Hospital accounting for 17deaths per 1000 live (DHIS). It has been noted that the highest percentage of admissions in Newborn Unit (NBU) is as a result of EONS compared to other common conditions that lead to neonates' admissions in this hospital. The aim of this study was to determine the risk factors contributing to early onset neonatal sepsis in Mwingi Level 4 Hospital, and hence inform Kitui County health policy makers on possible preventive interventions. No study has been done in Mwingi or in the entire Kitui County to determine factors associated with EONS to the best of my knowledge, leaving a knowledge gap on this subject. Mwingi Level 4 Hospital serves a catchment area of over a100 - kilometers radius as the only facility offering comprehensive obstetric and neonatal care; the long hours needed to travel to the health facility may therefore be one of maternal risk factors for EONS. The study also aimed to describe the hospital length of stay among newborns admitted with early onset neonatal sepsis in Mwingi Level 4 Hospital newborn unit. The length of hospital stay among neonates with EONS in the Hospital, its possible association to antibiotic regimens has not been studied. The study findings will inform the treatment guideline for EONS in the hospital.

2.11 Research Questions

I) What are the maternal risk factors associated with early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital newborn unit (NBU)?

II) What are the neonatal risk factors associated with early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital new born unit?

III) Is the hospital length of stay among babies admitted with early onset neonatal sepsis 24 hours after birth in Mwingi Level 4 Hospital newborn unit associated with the antibiotic regimen choice?

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2.12.0 Objectives

2.12.1 General Objective

To determine risk factors for early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital

2.13.2 Specific Objectives

I) To determine maternal risk factors for early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital newborn unit.

II) To determine neonatal risk factors for early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital newborn unit.

III) To describe the association between hospital length of stay and antibiotic treatment regimen among babies admitted with early onset neonatal sepsis in Mwingi level 4 hospital newborn unit.

CHAPTER THREE

3.0 Methodology

3.1 Study Site

This was a hospital- based study that was conducted in Mwingi Level 4 Hospital, located 172 km East of Nairobi. It's the second largest hospital in Kitui County after Kitui Level 5 Hospital with a catchment population of 51338 and a bed capacity of 211 beds. The hospital has a maternity unit with a 30 bed capacity, and a newborn unit with 5 incubators. It handles approximately 2800 lives births and about 700 NBU admissions annually according to DHIS Kitui County 2018.

3.2 Study Design

This was an unmatched case control study. The study participants did not necessarily have same characteristics but were from the same population at risk of the exposures.

The diagnostic criteria for neonatal sepsis in this hospital involved the use of hematological findings that is low total white blood cell count of < 5000/µl along with the established Integrated Management of Neonatal and Childhood Illness (IMNCI) (Ministry of Health, 2018) clinical features of neonatal sepsis these were; lethargy, poor feeding, temperature instability (<35℃ or > 37.5℃), tachypnoea, convulsions and chest in drawing.

3.3 Study Population

The study was carried out among neonates who were born alive in Mwingi Level 4 Hospital in Kitui County from January 2018 to December 2018.

3.4 Sample Size Determination

Formula for calculating sample size

Sample size was calculated using OpenEpi online sample size calculator Version 3, for unmatched case control study (Kelsey, J.L; Whittemore, A.S; Evans, A.S; and Thompson, 1996)

$$n_1 = \left(\frac{r+1}{r}\right) \frac{(\overline{p})(1-\overline{p})(Z\beta + Z\alpha/2)^2}{(p1 - p2)^2}$$

$$\overline{p} = \frac{p1 + rp2}{r+1} = 0.3315$$

$n_1 = (\frac{3+1}{3})(\frac{0.3315 \times 0.6685 \times 7.84}{0.027556}) = 84.064$

Therefore: $n_1 = 85$

$n_2 = rn_1 = 3n1$

$n_2 = 255$

Total sample size $N = n_1 + n_2 = 340$

Where:

n_1 = sample size of the cases

n_2 = sample size of the controls

N = study sample size

$Z\alpha/2$ is the desired level of statistical significance = 1.96

r= ratio of controls to cases = 3.0

Z_β = desired power = 0.84

p1 = proportion of cases with exposure = 45.6%

p2 = proportion of controls with exposure = 29.0%

Least extreme Odds Ratio to be detected = 2.05

Estimates were derived from prevalences of risk factors for EONS in studies done in Ghana (Adatara et al., 2019, Mupepi, Sylvia C, Siakwa, Mate Kpikpitse, & Semuatu, 2014)) and another one done in Ethiopia (Gebremedhin et al., 2016). As shown in **table 1** below. Least extreme expected odds ratio 2.05. Prevalence of APGAR score of ≤ 7 in 1 minutes was selected because it had the largest sample size of 340 participants that is 85 cases and 255 controls (3:1) owing to the fact that it was hypothesized to represent the study population of Mwingi Level 4 Hospital.

Table 1: Summary of desired sample size for different EONS risk factors

Risk factors	Vaginal delivery	C/S delivery	Birth weight <2500gms	APGAR score ≤7 in 1 min	APGAR score ≤7 in 5 min	Gestational age < 37 weeks	PROM	Maternal infection UTI/STI
Exposure in cases	34%	65%	21.4%	45.6%	28.2%	26%	30.8%%	50.4%
Exposure in controls	59.2%	39.6%	5.6%	29%	14.1%	8.7%	3.8	81.1%
Cases	43	41	37	85	77	40	14	13
Controls (3:1)	127	122	109	255	230	119	41	39
Total sample size	170	163	146	340	307	159	55	52

3.5 Sampling procedure

Cases and controls were selected through systematic random sampling. A total of 2295 medical records for the controls were retrieved, a random starting point was selected then the rest of the study participants were selected using a fixed interval of 9^{th} calculated by dividing the study population by the sample size. (Taherdoost & Group, 2017). For cases only 115 medical records met the inclusion criteria from which a total of 85 medical records were selected randomly. Regarding description of hospital length of stay, since only cases were admitted in newborn unit, 85 participants' (all cases) medical records were studied to describe the hospital length of stay in regard to antibiotic choice.

Cases: Neonates born in Mwingi Level 4 Hospital who developed early-onset neonatal sepsis within 24hrs after birth and were admitted in newborn unit in the year 2018.

3.5.1 The Inclusion Criteria

a. Neonates born in Mwingi Level 4 Hospital in 2018 and were hospitalized with diagnosis of neonatal sepsis within 24 hours after birth

3.5.2 Exclusion Criteria

a. Incomplete records

Controls: Neonates born in Mwingi Level 4 Hospital and who did not develop early onset neonatal sepsis within 24 hrs after birth in the year 2018. Three controls were included for each case, to get a ratio of 3:1.

3.6.0 Data Management

3.6.1 Data collection and storage

A semi structured data collection tool was developed based on studied related literature on factors associated with early onset neonatal sepsis. The data collection tool consisted of socio demographic, neonatal and maternal characteristics.

Data collection was done through neonates' medical records review. Medical records were retrieved from medical department with assistance from the medical records personnel in the hospital. Data was collected using the data collection tool, entered into a password protected computer for storage and a hard copies kept under lock and key. A flash disk was used for back up. Qualitywas ensured by checking for consistency and completeness. Recording of data from cases and controls admitted in the newborn unit in the 2018 was done by four (4) research assistants who were three (3) nurses and one record officer under the supervision of the principal investigator.

Finally data was entered into IBM SPSS version 23 for cleaning and analysis.

3.6.2 Data Presentation

3.6.2.0 Variables

3.6.2.1 Independent Variables

a. Birth weight < 2500gms ≥2500gms
b. Gestational age < 28 , ≥37 weeks
c. APGAR score ≤7 in 1 min ≤7 in 5 min
d. Onset of labour – induction , spontaneous
e. Duration of labour , < 18 hrs ≥18hrs
f. Maternal infection , chorioamnionitis , HIV, UTI
g. Parity – prime gravida – multi parity
h. Premature rupture of membranes, <18 hrs, ≥18hrs
i. Distance from the hospital > 50 km, ≤ 50 km
j. Treatment options type of antibiotics used
k. Duration of stay in the hospital < 5 days ≤ 5day
l. Source of maternal admission referral from other health facilities, admission from home.

3.6.2.2 Dependent Variables

a. Early onset neonatal sepsis
b. Hospital length of stay < 5 days
c. Hospital length of stay >5 days

3.6. 3 Data Analysis

Univariate analysis was done showing frequency distribution, percentages, and proportions for the sociodemographic and clinical characteristics of the cases and controls as shown in **table 2** and 3. Bivariate and multivariate analysis was done by use of cross- tabulations to measure the association between independent and dependent variables as shown in **table 3, 4 and 5**, odds ratio (OR) and adjusted odds ratio (AOR) was used to estimate the strength of the association between exposure variables like PROM, APGAR score, maternal infection and EONS. Chi-square ($X^{2)}$ test statistic was used to quantify the strength of the association. P value was set at 0.05. and limits set at 95% confidence interval (CI). Data was analyzed using statistical package for social science (IBM SPSS version latest version)

3.7 Ethical Considerations

The proposal was submitted to KNH-UON Ethics and Research Committee for review. A waiver for informed consent was sought because the study involved secondary data only. Approval was sought from Kitui County Health Management Team. Permission was also sought from the hospital medical superintended and the officer in charge of medical records department. Confidentiality was maintained by keeping patients' medical records in a safe lockable cabinet. Cases and controls were identified using code numbers.

CHAPTER FOUR

4.0 RESULTS

4.1 Neonatal characteristic

The study included 340 neonates and their mothers; 85 (25%) neonates who had sepsis within 24 hours after birth (cases) and 255 (75%) neonates who had no sepsis (controls). Majority of the participants were males, 47 (55.3%) cases and 142 (55.7%) controls as shown in **figure1** below. The mean age of all participants was 22.74 hours (SD±3.74, n=340) ranging from 6 to 24 hours. Mean age for neonates in cases was 23.08 (SD±3.19, n=85) hours while for controls it was 22.62 (SD±3.90, n=340) hours ranging from10-24 and 6-24 hours respectively. There was no significant difference in neonatal age between the cases and controls (*p=0.324*).

A higher proportion of the neonates had a birth weight greater than 2.5kg 78 (91.8%) for cases and 238 (93.3%) for controls. Most of the participants had an APGAR score greater than 8 in the 5th minute among the cases 80 (94.1%) and controls 237 (92.9%)

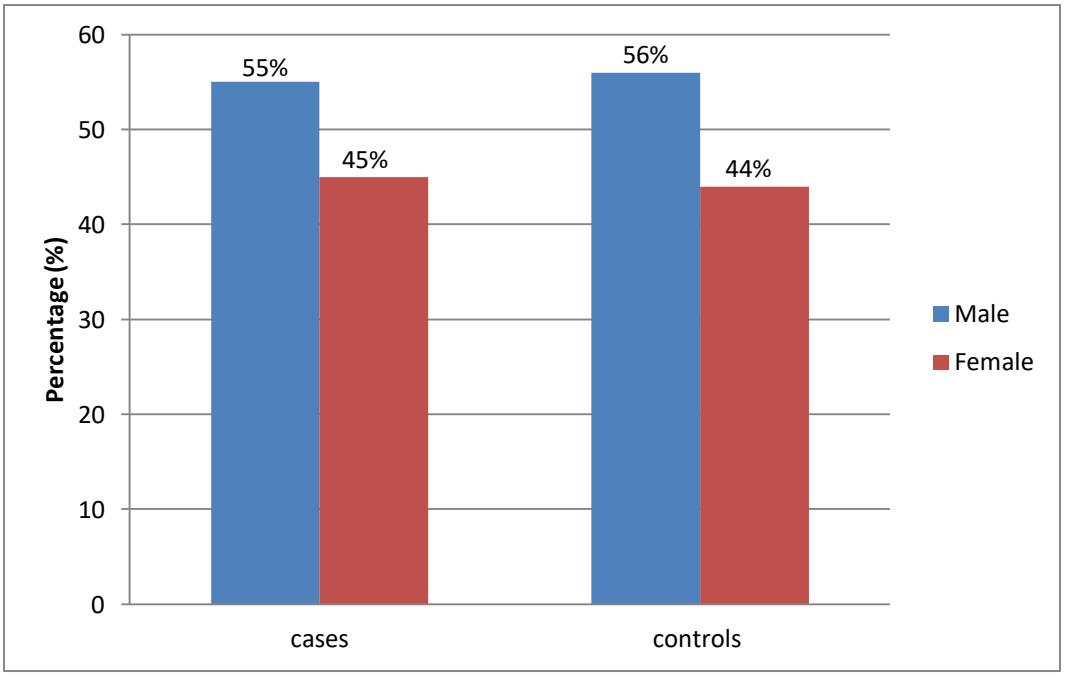

Figure1: Distribution of neonates based on sex

4.2 Maternal characteristics

In this study deliveries through caesarean section were 50 (58.3%) in cases and 105 (41.2%) in controls, and 35 (41.2%) and 150(58.8%) were delivered through spontaneous vertex delivery in cases and controls respectively.

The proportion of mothers who gave birth after 18 hours with ruptured membranes (PROM) was higher for the cases 75 (88.2%) than controls 219 (85.9%). However the difference lacked statistical significance.

4.3 Risk factors Associated with EONS occurring 24 hours after birth

After applying both bivariate and multivariable logistic regression, four variables showed an overall association as risk factors of neonatal sepsis at the 5% level of significance though only one had statistical significance after adjusting the odds ratio for confounders.

Association between Maternal risk factors and EONS

In this study it was noted that after adjusting for confounders, all variables studied except SVD, lacked statistical significance.

The study revealed that the odds of having neonates with sepsis within 24 hours after birth among mothers who delivered through SVD was 2.04 times higher as compared to birth through caesarean section; [AOR= 2.04, 95% CI (1.24-3.36)] $p < 0.005$

It was further noted that primiparous mothers had 1.50 times higher odds of having neonates with sepsis within 24 hours after birth as compared to multiparous mothers; [AOR=1.50;95% CI (0.88-2.53)] P< 0.045 although the difference lacked statistical significance.

In this study it was also noted that there was 83% likelihood of developing EONS within the first 24 hours of life among neonates born to mothers who had been referred while in labour from other health facilities, as compared to neonates born to mothers admitted in the hospital directly from home while in labour during the index pregnancy; [AOR =1.83; 95% CI (0.99-3.40)] P< 0.004

Similarly, neonates who were born to mothers who travelled more than 50 km from their residence to the hospital for delivery during the index pregnancy had 1.78 times higher odds of developing EONS as compared to those who travelled less than 50 km to the facility while in labour during the index pregnancy. [AOR= 1.78; 95% CI (0.95-3.33)] P< 0.004

Association between Neonatal risk factors and EONS

This study showed that there was no significant association between neonatal risk factors of EONS occurring in the first 24 hours after birth. However, the study revealed that the odds of developing EONS within 24 hours after birth in neonates with birth weight < 2500grams was 73% higher as compared to those who had normal birth weight >2500gms [AOR= 1.73; 95% CI (0.63-4.77)] P< 0.625, this association lacked statistical significance.

Table 2 Maternal and neonatal characteristics of cases and controls in Mwingi Level 4 Hospital

Variables		Cases n=85 (%)	Controls n=255 (%)	Total n=340 (%)
Gestational age	<37	12 (14.1)	41 (16.1)	53 (15.6)
	>37	73 (85.9)	214 (83.9)	287 (84.4)
Duration of labour (hours)	<18	58 (68.2)	193 (75.7)	251(73.8)
	>18	27 (31.8)	62 (24.3)	89 (26.2)
Onset of labour	Spontaneous	83 (97.6)	249 (97.6)	332 (97.6)
	Induction	2 (2.4)	6 (2.4)	8 (2.4)
Mode of delivery	SVD	35 (41.2)	150 (58.8)	185 (54.4)
	CS	50 (58.8)	105 (41.2)	155 (45.6)
Chorioamnionitis/UTI/STI	Yes	6 (7.1)	21 (8.2)	27 (7.9)
	No	79 (92.9)	234 (91.8)	313 (92.1)
Parity	Primigravida	49 (57.6)	115 (45.1)	164 (48.2)
	Multipara	36 (42.4)	140 (54.9)	176 (51.8)
Premature Rapture of membranes (in hours)	<18	75 (88.2)	219 (85.9)	294 (86.5)
	>18	10 (11.8)	36 (14.1)	46 (13.5)
Distance from Hospital to residence	>50	25 (29.4)	39 (15.3)	64 (18.8)
	<50	60 (70.6)	216 (84.7)	276 (81.2)
Referral in from other health facilities	Yes	27 (31.8)	44 (17.3)	71 (20.9)
	No	58 (68.2)	211 (82.7)	269 (79.1)
Neonatal age (hours)	<20	7 (8.2)	30 (11.8)	37 (10.9)
	>20	78 (91.8)	225 (88.2)	303 (89.1)
Gender	Male	47 (55.3)	142 (55.7)	189 (55.6)
	Female	38 (44.7)	113 (44.3)	151 (44.4)
Antibiotics	Yes	85 (100)	0(0)	85 (25.0)
	No	0 (0)	255 (100)	255 (75.0)
Duration of Hospital stay (Days)	<5	65 (76.5)	255 (100)	320 (94.1)
	>5	20 (23.5)	0 (0)	20 (5.9)
Treatment outcome	Recovered	84 (98.8)	0 (0)	84 (24.7)
	Referred	1 (1.2)	0 (0)	1 (0.3)
	died	0 (0)	0 (0)	0 (0)
APGAR	<7	5 (5.9)	18 (7.1)	23 (6.8)
	>7	80 (94.1)	237 (92.9)	317 (93.2)
Birth weight (grams)	<2500	7 (8.2)	17 (6.7)	24 (7.1)
	>2500	78 (91.8)	238 (93.3)	316 (92.9)

Table 3 Bivariate and multivariable logistic regression analysis of the study result

Variables		Cases n=85(%)	Controls n=255(%)	X^2	*p* value	COR (95%CI)	AOR (95%CI)
Gestational age	<37	12 (14.1)	41 (16.1)	0.186	*0.666*	0.86 (0.43-1.72)	0.91 (0.42-1.96)
	>37	73 (85.9)	214 (83.9)			1.0	1.0
Duration of labour (hours)	<18	58 (68.2)	193 (75.7)	1.831	*0.176*	1.0	1.0
	>18	27 (31.8)	62 (24.3)			1.45(0.85-2.48)	1.31 (0.68-2.52)
Onset of labour	Spontaneous	83 (97.6)	249 (97.6)	0.000	*>0.05*	1.0	1.0
	Induction	2 (2.4)	6 (2.4)			1.00 (0.20-5.05)	0.84 (0.15-4.71)
Mode of delivery	SVD	35 (41.2)	150 (58.8)	8.003	*0.005*	1.0	1.0
	CS	50 (58.8)	105 (41.2)			0.49 (0.30-0.81)	1.61 (0.92-2.82)
UTI/STI	Yes	6 (7.1)	21 (8.2)	0.121	*0.728*	0.85 (0.33-2.17)	1.19 (0.44-3.21)
	No	79 (92.9)	234 (91.8)			1.0	1.0
Parity	Primigravida	49 (57.6)	115 (45.1)	4.021	*0.045*	1.66 (1.00-2.72)	1.50 (0.88-2.53)
	Multipara	36 (42.4)	140 (54.9)			1.0	1.0
PROM (hours)	<18	75 (88.2)	219 (85.9)	0.302	*0.583*	1.0	1.0
	>18	10 (11.8)	36 (14.1)			0.81 (0.38-1.71)	0.58 (0.24-1.39)
Distance from Area of residence to Hospital	>50KM	25 (29.4)	39 (15.3)	8.315	*0.004*	2.31 (1.30-4.11)	1.78 (0.95-3.33)
	<50KM	60 (70.6)	216 (84.7)			1.0	1.0
Referral from other health facilities	Yes	27 (31.8)	44 (17.3)	8.124	*0.004*	2.23 (1.28-3.91)	1.83 (0.99-3.40)
	No	58 (68.2)	211 (82.7)			1.0	1.0
Neonatal age (hours)	<20	7 (8.2)	30 (11.8)	0.819	*0.366*	0.67 (0.28-1.60)	0.87 (0.35-2.15)
	>20	78 (91.8)	225 (88.2)			1.0	1.0
Gender	Male	47 (55.3)	142 (55.7)	0.004	*0.950*	1.0	1.0
	Female	38 (44.7)	113 (44.3)			1.02 (0.62-1.67)	0.92 (0.55-1.56)
APGAR	<7	5 (5.9)	18 (7.1)	0.140	*0.708*	0.82 (0.30-2.29)	0.55 (0.18-1.71)
	>7	80 (94.1)	237 (92.9)			1.0	1.0
Birth weight (grams)	<2500	7 (8.2)	17 (6.7)	0.239	*0.625*	1.26 (0.50-3.14)	1.73 (0.63-4.77)
	>2500	78 (91.8)	238 (93.3)			1.0	1.0

Table 4 Distribution of antibiotic profile in neonatal EONS cases

Antibiotics	**Hospital stay(days)**	**(n)**	**$\sum_n$ (%)**
Gentamicin	>5	0	1 (1.2%)
	<5	1	
Gentamicin, ceftriaxone	>5	1	1 (1.2%)
	<5	0	
Gentamicin , flucloxacillin	>5	2	3 (3.5%)
	<5	1	
Gentamicin, Benzyl penicillin	>5	10	74 (87.1%)
	<5	64	
Gentamicin, Benzyl penicillin, ceftriaxone	>5	3	5 (5.9%)
	< 5	2	
Gentamicin, Benzyl penicillin, ceftazidime	>5	1	1 (1.2%)
	<5	0	
Total		85	85(100%)

Table 5 Antibiotic choice and the hospital stay

Antibiotic regimen	**>5 days**	**<5days**	**Total**
Benzyl pencillin and gentamicin	13	61	74
Other treatment combinations	7	4	11
Total	20	65	85

Among neonates admitted with EONS, (87.1 %) were treated with gentamicin and Benzyl penicillin. Out of this, 17.6% had stayed in the hospital longer than 5days. Among the remainder, 12.9% who were treated with other antibiotic combinations, 63.6% had stayed in the hospital longer than 5 days. The hospital length of stay for more than 5 days in neonates treated with gentamicin and benzyl penicillin combination as first line antibiotic treatment had 88% less likelihood of occurrence as compared to the other antibiotic combinations; [OR =0.122 CI 95% (0.031, 0.478)] p< 0.001

CHAPTER FIVE

5.0 DISCUSSION

This study assessed various possible risk factors of EONS occurring within 24 hours after birth. One variable (spontaneous vertex deliver) showed an association with statistical significance and three variables (primiparity, distance from area of residence to hospital and referral from other health facilities) showed an association without statistical significance.

This study found that spontaneous vertex delivery had significant association with neonatal sepsis (AOR = 2.04). Further logistic regression analysis revealed that neonates who had been delivered through SVD were 2.041times more likely to be at risk of neonatal sepsis than those neonates who were delivered through caesarean section. The present findings are contrary to the findings of studies

done by other researchers in Ghana and Nepal (Adatara et al., 2019) (Budhathoki et al., 2020) respectively who found that caesarean sections were a risk factor for EONS. The difference could have been brought about by the fact that this study looked at EONS occurring within 24 hours after birth. The study supports the studies that showed that EONS mostly occurs as a result of vertical transmission prenatally or through contamination during delivery process (Cortese et al., 2016)

In this study it was further observed that the proportion of neonates born to first time mothers who developed EONS within 24 hours was higher in cases (57.7%) than in controls (45.1%). On bivariate and multivariable logistic regression analysis, it was revealed that primiparity had a higher likelihood of developing EONS occurring within the first 24 hours of life though without statistical significance, [AOR=1.50;95% CI (0.88-2.53)] P< *0.045*. In this respect, the study agrees with other studies done in Ghana. (Adatara et al., 2019)(Budhathoki et al., 2020) respectively. The possible reason for primiparity being a risk factor could be due to maternal complications related to first time delivery among them prolonged labour and delay in establishment of lactation within the first hour after delivery.

This study also revealed that neonates who were born to mothers who travelled for more than 50 km from their residence to the hospital were at higher risk of developing EONS within 24 hours after birth as compared to those who travelled less than 50km. On bivariate and multivariable logistic regression analysis, it was shown that distance to the health facility was associated with EONS within the first 24 hours of life, however, the association lacked statistical significance. [AOR= 1.78; 95% CI (0.95-3.33)] P< 0.004. Long distance to the health care facility affects healthcare utilization and consequently increases the risk of ill health in many spheres of life including neonatal health. This study is consistent with a study done in northern Vietnam which states that distance from residence to the healthcare facility is a risk factor for neonatal mortality of which EONS is a major contributor (Målqvist, Sohel, Do, Eriksson, & Persson, 2010)

Furthermore, it was revealed that neonates born to mothers who had been referred from other health facilities while in labour were at higher risk of developing neonatal sepsis within 24 hours of life as compared to neonates born to mothers who had been admitted directly from home to the hospital [AOR 1.83; 95% CI (0.99-3.40) P< 0.004 . Mothers referred from other health facilities while in labour may have undergone repeated vaginal examinations which could result in increased risk of ascending vaginal infections hence increased risk of EONS (Russell, 2015).

Similarly the study revealed that low birth weight <2500gms is a possible risk factor for EONS within the first 24 hours of life. The proportion of low birth weight <2500gms was higher in cases (8.2%) compared to (6.7%) in controls. On calculating the AOR it was noted that neonates with low birth weight had 73% higher likelihood of developing EONS within the first 24 hours of life. These findings agrees with a study done in Ghana, India and Ethiopia (Adatara et al., 2018) (Dhumal et al., 2018)(Belachew & Tewabe, 2020). The possible explanation for this is that most neonates born with weight <2500gms are premature and have immature immune system and in addition, are unable to breastfeed well increasing the likelihood of EONS.

In this study prolonged rupture of membrane for more than 18 hours and APGAR score of less than 7 in 5 minutes neither showed statistical significance nor association with EONS occurring 24 hours after birth. This was inconsistent with several other studies that revealed that PROM and low APGAR score as a significant risk factors, (Adatara et al., 2019; Gebremedhin et al., 2016; Wahono, 2018; Perera et al., 2018). Mupepi et al (2014) also observed no statistical significance from their study in in Ghan. These findings could be as a result of intrapartum interventions like administration of intrapartum antibiotics, minimized vaginal examinations which are normally initiated to reduce the risk of EONS.

On hospital length of stay among babies admitted with early onset neonatal sepsis occurring within 24 hours after birth in Mwingi Level 4 Hospital NBU, it was noted that benzyl pencillin and gentamcin combinations as first line antibiotic treatment resulted in a shorter hospital stay as compared to the other antibiotic combinations used at the Mwingi level 4 Hospittal (p= 0.001). This observation is not in agreement with a study done in Pumwani Maternity Hospital by Norah K. Maore, (2015) which observed an

association between a shorter duration of inpatient stay with other antibiotic regimen other than gentamycin and benzyl penicillin combination regimen. This study also was not consistent with another study done by Snselling et al. which portrayed ceftazidime as being more effective than benzyl penicillin and gentamycin combination in treatment of EONS, (Snelling, Hart, & Cooke, 1983). In another study carried out by Metsvaht, they showed no difference in effectiveness between ampicillin plus gentamicin and benzyl penicillin plus gentamicin combinations in treatment of EONS,(Metsvaht et al., 2010). The difference showed in this study could be as a result of over prescription of benzyl penicillin plus gentamicin by clinicians because these antibiotics in particular are cheaper and available as compared to other antibiotics which end up being used as second line treatment regimens.

6.0 CONCLUSION

In conclusion, this study identified SVD as a significant risk factor for EONS occurring within the first 24 hours of life. In addition this study showed that maternal risk factors are possible leading contributors to EONS occurring within 24 hours after birth in Mwingi Level 4 Hospital, which included primiparity, distance from the health facility (the longer the distance the higher the risk), and referrals from other health facilities.

Low birth weight was the only fetal factor shown to possibly contribute to EONS within 24 hours after birth.

The study also revealed that use of benzyl penicillin and gentamicin combination as a first line antibiotic regimen has a shorter hospital stay as compared to the other antibiotic combination used

7.0 STUDY LIMITATIONS

Since the study was done on hospitalized newborns, these results cannot be generalized to the entire population in the catchment area.

Limited laboratory diagnosis; diagnosis by different health providers could arise errors in the identification of cases and controls in the study.

8.0 RECOMMENDATION

Based on the study findings, decentralization of obstetric emergency services to other facilities within Mwingi bringing services closer to the people would minimize referrals and delays in services delivery, hence reduce incidences EONS.

Since the maternal risk factors are the possible leading contributors to EONS, it is recommended that preventive interventions be initiated during antenatal and intrapartum period. There is need for improved laboratory services that are able to carry out timely laboratory diagnosis of EONS through culture and sensitivity as this will lead to improved care and treatment for newborns with EONS

In future, studies on causative organisms for EONS should be in Mwingi Level 4 Hospital to help in specific management.

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Appendices

Appendix I:

1. Ethical approval

2. Request for a waiver of an informed consent

Appendix II:

1. Semi structured data collection tool

Data Collection Tool

Code.	**Age**	**Sex**	**Disease**	**No disease**	**Birth weights (gms)**		**Gestatational age (wks)**		**Apgar score**		**Onset of labour**	
					<2500	≥2500	<37	≤37	≤7 in 5min	≥8 in 5min	induction	spontaneous

Mode of delivery		Duration of labour		Maternal infection			Parity		Premature rapture of membranes		Distance from the hospital	
Svd	c/s	<18hrs	≥18hrs	chorioamnitis	HIV	UTI	prime gravida	multi parity	<18hrs	≥18hrs	>50km	≤50km

Treat options type of antibiotics use	Hospital length of stay		source maternal admission referral from other health facilities
	<5says	≤5days	