PREVALENCE OF SEPSIS AMONG NEONATES ADMITTED TO KISII LEVEL 5 HOSPITAL

A dissertation submitted in part fulfillment for the degree of Masters of Medicine in Paediatrics and Child Health, University of Nairobi.

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H58/ 68659/ 2011

DECLARATION

This dissertation is my original work and has not been presented for the award of a degree in any other university.

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DEDICATION

I thank Almighty God, whose grace , mercy and fortitude were granted to me afresh each day.

I thank my husband Alex, for his unwavering support and for challenging me to pursue my destiny.

To my daughter Celleste, your achievements are a daily inspiration to me. You are my delight.

I am grateful for the guidance, insight and direction I received from my supervisors Professor Onyango, Professor Musoke and Dr. Mungai.

To the neonates included in the study, I thank you for your participation. I wish those who survived a happy and healthy childhood as well as a productive adulthood. For those who passed away, you will be remembered in the lessons you taught us that will be used to save others.

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TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

TABLES

FIGURES

ABBREVIATIONS

MDG -	Millennium Development Goals
PMTCT-	Prevention of Mother to Child Transmission of HIV
TB-	Tuberculosis
UN-	United Nations
GBS-	Group B Streptococci
WHO-	World Health Organization
S. aureus-	*Staphylococcus aureus*
E. coli.-	*Escherichia coli*
L. monocytogenes-	*Listeria monocytogenes*
P. aeruginosa-	*Pseudomonas aeruginosa*
SOP-	Standard Operating Procedures
MCV-	Mean Corpuscular Volume
MCH-	Mean Corpuscular Haemoglobin
I :T ratio-	Immature to Total neutrophil ratio
NBU-	New Born Unit
CSF-	Cerebral Spinal Fluid
ANC-	Antenatal Clinic

MCH booklet- Maternal and Child Health booklet

KNH- Kenyatta National Hospital

IMCI- Integrated Management of Childhood Illnesses

KDHS- Kenya Demographic and Health Survey

HSS- Haematological Scoring System

SVD- Spontaneous Vertex Delivery

PMN- Polymorphonuclear

ABSTRACT

BACKGROUND

Neonatal sepsis is the systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection during the first 28 days of life [18].Neonatal sepsis is the third most common cause of death in the neonate, contributing 10- 20% of deaths in this age group, most of which occur in resource limited countries like Kenya. In Kenya, the current neonatal mortality rate is 31 per 1000 live births. This study sought to determine the burden of neonatal sepsis at Kisii level 5 hospital as well as the causative organisms and pattern of antibiotic susceptibility, so as to allow appropriate treatment of neonates with sepsis.

OBJECTIVES

To determine the prevalence of sepsis among neonates admitted to Kisii Level 5 hospital as well as the pattern of bacterial causes of sepsis and the socio-demographic and economic factors associated with neonatal sepsis.

METHODS

The baseline population was made up of neonates who displayed the clinical criteria that form part of the definition of suspected neonatal sepsis. A questionnaire was administered to consenting mothers and blood samples were taken for full haemogram and culture.

ANALYSIS

Data was entered into a Microsoft Access database with inbuilt consistency and validation checks and was cleaned and stored. Analysis was done using SPSS analytical package. Data was presented as tables and graphs. The prevalence of neonatal sepsis was calculated as a

proportion of total neonates admitted over the study period. Data on neonatal characteristics, maternal characteristics, delivery data and post delivery neonatal care was analyzed for association with neonatal sepsis using chi square test and Fischer test where values were less than 5.

RESULTS

After assessing 406 neonates, 80 neonates met the inclusion criteria for the study. The prevalence of clinical sepsis was 19.7%. All the blood cultures undertaken in the study were negative. There was therefore a significant reliance on the Haematological Score as described by Rodwell et al to make inferences about the laboratory results of the recruited neonates [(22)].

Fifty one percent of mothers of neonates with highly likely or possible sepsis were housewives and 67.8% had a secondary level of education. Eighty seven percent of mothers were aged between 20 years to 30 years. Neonatal sepsis was significantly associated with maternal dysuria. The mothers lived under more affluent conditions as indicated by 68.8% living in stone or brick built houses.

CONCLUSION

Neonatal sepsis contributes significant proportion of neonatal admissions to Kisii Level 5 Hospital. Careful clinical evaluation of each admitted neonate for danger signs of neonatal sepsis is required to facilitate prompt laboratory evaluation for confirm of the same and commencement of antimicrobial therapy.

RECOMMENDATIONS

All neonates admitted to Kisii Level 5 Hospital should be carefully evaluated for signs of neonatal sepsis so as to identify early those neonates requiring further laboratory evaluation and empiric treatment of neonatal sepsis.

A follow up study with a larger sample size should be done to evaluate the value of using more sensitive automated blood culture methods to establish definitively the prevalence of culture proven sepsis in neonates at Kisii Level 5 Hospital.

1.0 BACKGROUND.

Neonatal sepsis is an invasive bacterial infection occurring during the first four weeks of life. It is identified from suggestive clinical features such as fever and refusal to breastfeed and is confirmed by isolation of bacterial pathogens from blood or cerebral spinal fluid.

Neonatal death is a major cause of deaths in the under fives, contributing between 30-50% of deaths in this age group. Neonatal infections are the third most common cause of deaths in the neonate, contributing 10- 20% of the deaths in this age group and leading to about half a million deaths every year, the vast majority of which are in resource limited countries.

In Kenya, the infant mortality rate is 52 per 1000 live births and the under five mortality rate is 74 per 1000 live births. Neonatal deaths are reported to contribute to 60% of deaths in infants and 40% of deaths in the under fives [(1)].

It will be difficult to achieve the 4th Millennium Development Goal's target without addressing the morbidity and mortality in the neonate. Evidence of the magnitude of illness caused by infections along with the aetiology and associated factors would go a long way in enriching the interventions targeted at reducing deaths in this age group.

1.1 LITERATURE REVIEW

1.1.1 EPIDEMIOLOGY

A study done by Berkley et al from August 1998 to July 2002 at Kilifi District Hospital in Kenya involving young infants who were defined as less than 60 days old, the prevalence of community acquired culture proven sepsis was 12.8% [(2)]. In neonates less than 7 days old, 13.5% (11.5- 16%) had proven bacteremia and among those 7-60 days old, 12.1% (10.1- 14.4%) had proven bacteremia [(2)]. In a prospective cross- sectional study at Bugando Medical Centre in Mwanza, Tanzania from March to November 2009, 300 neonates were found to have sepsis by WHO criteria. The rate of positive neonatal blood cultures was 25- 54% [(3)]. In

Ethiopia, Shitaye et al in 2010 found that of the 302 neonates aged 0- 28 days with clinical sepsis who were recruited in their study, 44.7 % were culture positive [4]. Laving et al showed that the prevalence of meningitis in suspected sepsis as defined by CSF positive to gram staining, aerobic bacterial culture or latex particle agglutination assay was 17.9%. Blood cultures were positive in 53.3% of neonates with meningitis [5]. Ng'ang'a et al found that the prevalence of proven sepsis in term newborns in the postnatal wards of Kenyatta National Hospital was 12% [30] Kohli et al found in their retrospective clinical- laboratory study that the prevalence of confirmed blood stream infection in neonates at the Aga Khan University Hospital in Nairobi was 23%. [32]

1.1.2 CAUSATIVE ORGANISMS.

The organisms that commonly cause early onset neonatal sepsis (sepsis that manifests within the first 72 hours of life) include GBS, *H. influenza, L. monocytogenes and C. trachomatis*. [9]. Organisms that commonly cause late onset neonatal sepsis (sepsis that manifests after 72 hours of life) include CONS, *Klebsiella spp, Enterobacter, E. coli, Serratia marcescens, Pseudomonas spp and S. aureus.* [9].

Berkley et al, Opiyo et al and Downie et al all found that *S. aureus* and *E. coli* were the commonest isolates causing early death of young infants [2, 6, 7]. Shitaye et al, Opiyo et al and Downie et al also found that *Klebsiella species* was frequently isolated [6, 7, 4]. Additional bacterial causes included *Streptococcus pneumonia* and *Group A Streptococcus* [2].

Opiyo et al found that gram negative bacteria were a commoner cause of sepsis than gram positive bacteria [6]. Organisms common to both early onset neonatal sepsis and late onset neonatal sepsis were *Klebsiella, Pseudomonas, E. coli, S. aureus and Group B Streptococci* across all settings [6]. Laving et al found that the causative agents of neonatal meningitis included *E. coli* (46.7%), *GBS* (26.7%) and *Klebsiella* (13.3%) [5]. In 1988 Evans et al concluded that cultures from surface swabs e.g. pus from abscesses were of limited value in

predicting aetiology of sepsis in the neonate [8]. Ng'ang'a et al found that the commonest organisms isolated in the study were gram positive with coagulase negative *Staphylococci* forming 43% of the isolates [30] This finding was similar to that of Kohli et al who found that the predominant aetiological agents were gram positive organisms in both early and late onset sepsis with coagulase negative *Staphylococci* being the most commonly isolated bacteria. Among the gram negatives, *K. pneumonia* was the predominant pathogen [32]

1.1.3 CLINICAL SIGNS

The diagnosis of neonatal sepsis begins with identifying neonates who are at risk of developing neonatal sepsis. Puopolo et al found that maternal fever and prolonged rupture of membranes were strong individual predictors of infection. [35]. In a risk assessment by Mukhopadhya et al it was found that neonates born at 34 to 36 weeks had a 2-3 times higher incidence of early onset sepsis as compared to those born at 37 to 40 weeks. [36]. Chorioamnionitis was identified as a risk factor for early onset neonatal sepsis and was associated with intrapartum fever, uterine tenderness and foul smelling amniotic fluid. [36]. There was a steep increase in the risk of GBS in early onset sepsis when rupture of membranes exceeded 18 hours as this provided the opportunity for ascending colonization of placental and fetal tissues. [36]. Other intrapartum risk factors included disruption of amniotic membranes and multiple intrapartum vaginal examinations. [36]. Kristof et al found that maternal risk factors for neonatal sepsis included prolonged and premature rupture of membranes, septic or traumatic delivery, maternal carriage of GBS, maternal poverty, pre-eclampsia, cardiac disease and diabetes mellitus. [37].

The clinical syndrome of neonatal sepsis has a non- specific presentation. Some of the signs of possible neonatal sepsis include; abnormal neurological status (irritable, lethargic, poor feeding, floppy or unresponsive), abnormal temperatures (hypothermia $<36^{o}C$ or hyperthermia $>37.8^{o}C$) for more than 1 hour, apnoea (ceased breathing for15 seconds with

bradycardia and desaturation), bleeding tendency (petechiae and purpura), cardiovascular compromise with increased heart rate >160/min, poor peripheral perfusion (mottling, delayed capillary refill time more than 3sec), cyanosis, gastrointestinal system manifestations (severe abdominal distention, emesis, diarrhea), deep jaundice, pallor, respiratory distress (tachypnoea >60/min and increased work of breathing), and skin manifestations (septic spots and omphalitis).[9]

Late signs of sepsis appear with advanced infection indicating presence of subtle signs for some time previously or a particularly virulent organism.[9]They include; respiratory system signs (grunting and dyspnoea beyond 6-12 hours of age, hinting at pneumonia), abdominal manifestations (flank lividity, induration and periumbilical staining in intraperitoneal sepsis), central nervous system signs (high pitched cry, neck retraction, bulging fontanelle, and convulsions which indicate neonatal meningitis with cerebritis and cortical thrombophlebitis), haemorrhagic diasthesis (petechiae and bleeding from puncture sites or the gut) and sclerema.

Various studies have tried to find which of these clinical signs occur more commonly in neonatal sepsis. Inability to breastfeed and cyanosis were common signs of sepsis in the studies done by Kayange et al, Opiyo et al and English et al [3, 6,10]. Kayange et al found that signs that correlated with positive blood cultures apart from those above were lethargy, meconium stained liquor, prolonged rupture of membranes and convulsions. The predictors of death were positive blood cultures, gram negative sepsis and infection by methicillin resistant *Staphylococcus aureus* [3]. Opiyo et al found that respiratory symptoms such as grunting and tachypnoea and temperature more than 38^0C were also valuable in the estimation of risk of severe illness [6]. English et al found that a bulging anterior fontanelle and unconsciousness in addition to the signs mentioned above indicated a high risk of invasive bacterial disease and need for broad spectrum antibiotics [10].

Some studies went further to try and compile a more restrictive list of signs to facilitate case finding of young infants with severe disease and that best predicted need for hospital based care [11, 10]. The 8 signs found by Opiyo et al had 85% sensitivity and 75% specificity for neonates aged 0- 6 days and 74% sensitivity and 75% specificity for infants aged 7- 59 days [11]. The signs included a history of feeding difficulty, history of convulsions, axillary temperature equal to or greater than 37.5^{o}C or less than 35.5^{o}C, change in activity level, respiratory rate above 60/min, severe chest indrawing, grunting and cyanosis [11]. English et al found that for infants in the first week of life, difficulty in feeding, difficulty breathing, cough, abnormal behavior and indrawing had sensitivity of 94% and specificity of 40% for any one sign in finding young infants with severe disease [10]. For the infant aged 7- 59 a history of feeding difficulty, abnormal behavior, difficulty breathing, chest wall indrawing, cyanosis and bulging fontanelle had 97% sensitivity and 56% specificity for very severe illnesses when any single sign was present [10].

Laving et al in 2003 found that meningitis accounts for up to a third of neonatal septicaemia and that diagnosis is difficult due to non- specific symptoms [5]. Of those with neonatal meningitis, patients with feeding intolerance were 73.3% and those with lethargy were 60% [5]. Shitaye et al found that features that correlated strongly with culture proven sepsis were prematurity, low birth weight, abnormal white blood cell counts (high or low) and immature to total neutrophil ratio greater than 0.2 [4]. Ng'ang'a et al found that refusal to breastfeed and grunting were the commonest signs in neonates with proven sepsis. [30]

1.1.4 ANTIBIOTIC SENSITIVITY OF COMMONLY ISOLATED BACTERIAL PATHOGENS.

The current recommended empiric treatment of suspected neonatal sepsis by the WHO is ampicillin or penicillin and gentamicin for patients from 0-2 months of age. Second line

treatment consisted of flucloxacillin for *Staphylococcus aureus* infections and 3rd generation cephalosporins.

Kayange et al found that 49% of gram positive isolates were resistant to third generation cephalosporins, 28% of Staphylococcus aureus were methicillin resistant and most of the *Klebsiella species and E.coli* isolates were resistant to ampicillin and gentamicin with 49% of the same being resistant to 3rd generation cephalosporins [(3)]. The majority of gram negative organisms were sensitive to ciprofloxacin and meropenem [(3)]. These findings are similar to those of Downie et al who found that there was a high rate of resistance among enteric gram negative bacteria to gentamicin, chloramphenicol and 3rd generation cephalosporins [(7)].

In terms of antimicrobial susceptibility, community based studies such as Berkley et al 2005 showed 55% susceptibility for amoxicillin or ampicillin, 31% for benzylpenicillin alone, 88% for penicillin with gentamicin, 97% for ampicillin with gentamicin and 82% for penicillin with chloramphenical [(6)]. This supports the WHO Young Infant Study Group- 1999 study suggesting initial treatment of neonatal sepsis with ampicillin and gentamicin. In contrast, the community based study by Downie et al found that susceptibility to penicillin and gentamicin was only 57% and susceptibility to third generation cephalosporins was 56% [(7)]. The study concluded that there is need to search for appropriate 2nd line treatment and mentions that amikacin is effective against most multi resistant *Klebsiella species* with similar cost implications as gentamicin [(7)].

In mixed studies including both community and hospital based populations there was a high rate of resistance of gram negative organisms to first line drugs i.e. ampicillin (79.3%), amoxicillin (74.6%) and gentamicin (43.2%), but these results mainly reflect findings in specialized newborn units which may have higher in vitro resistance [(6)].

Gentamicin resistance in Kenya is estimated at 20% [6]. In Kenya Musoke et al demonstrated good gram negative sensitivity to gentamicin, amikacin, cefuroxime and 3rd generation cephalosporins (ceftriaxone, ceftazidime, and cefotaxime) and concluded that variations in susceptibility are geographic and temporal [6]. The varying levels of resistance were used as justification for local surveillance data to support empiric antibiotic prescription [6]. Third generation cephalosporins were found in one controlled trial to increase rates of resistance when used as first line treatment and were not more effective against common bacterial pathogens in the blood [7]. Local prevalence susceptibility results were stated as the most important factor for local empiric antibiotic regimes and that data from provinces and districts are essential for representative or balanced global data [7].

Laving et al found that most blood and CSF isolates were resistant to ampicillin and gentamicin with good in vitro sensitivity to amikacin, cefuroxime and 3rd generation cephalosporins [5]. Given the non specific presentation of neonatal meningitis as mentioned previously, lumbar puncture should be included whenever possible in the diagnostic work up to facilitate the proper selection of antimicrobial therapy. Rutare et al found that the prevalence of MRSA isolated in the nasopharyngeal swabs of paediatric patients admitted in the ICU and NICU of Kenyatta National Hospital in Nairobi Kenya was 22%. These isolates were most sensitive to antibiotics such as vancomycin, linezolid and amikacin. In the study by Kohli et al, in which all the neonates were born at a hospital, the prevalence of MRSA was 10.2% and none of the common isolates had more than 50% resistance to first line (ampicillin and gentamicin) or second line (amikacin and ceftriaxone) empirical treatments.

1.1.5 PATHOGENESIS.

Neonatal infection occurs due to compromise of the barriers to infection offered by the integrity of the placenta and membranes, high pathogenicity of the colonizing organism and incompetence of the neonatal defense mechanisms.

Exposure to microorganisms can be transplacental (where infective agents penetrate and damage the placenta), ascending (where vaginal organisms ascend into the uterine cavity and with rupture of membranes, the risk increases progressively with time) or intrapartum (through vaginal delivery which initiates colonization of the skin and mucosal surfaces through aspiration). There can also be postnatal exposure where infective organisms are acquired from the environment and other people [(9)].

Innate immunity shields the newborn from infection during the transition from the sterile intrauterine environment until the colonization of mucosal surfaces and includes protective barriers e.g. vernix caseoa which has antimicrobial peptides and fatty acids and expression of acute phase reactants and complement proteins[(34)]. The functional maturation of the innate immunity allows for colonization with commensal organisms while reducing potentially dangerous inflammatory responses [(34)].

All neonates exhibit physiologic immunodeficiency that is more marked in premature or stressed and sick infants and which accounts for their susceptibility to infection. [(33)]. Placentally transferred IgG offsets the deficiency partially but the transfer occurs late in gestation so that preterms have significantly lower levels. The protective effect of maternal immunoglobin depends on the mother having the appropriate antigen specific IgG antibody e.g. in GBS sepsis, lack of specific antibody is a risk factor. [(33)]

The new born infant has poor antibody responses to polysaccharide antigens, does not switch from making IgM to IgA and IgG readily, and does not produce tightly sticking antibodies.

[33]. T cells have diminished expression of CD40 ligand so that signaling to B cells via the CD 40 receptor for isotype switching is reduced. T cells also have a high CD4: CD8 ratio with less than 10% of the CD 45 RO memory isoform and more expression of the CD 45RA naïve isoform. Naïve T cells are harder to stimulate and have a response tilted towards a TH2 rather than a TH1 response, which are required for defense against intracellular bacterial pathogens such as *L. monocytogenes* and *Salmonella spp*. [33]. Neutrophil bone marrow reserves are easily exhausted and have reduced chemotaxis and cell deformity. The neutrophil numbers and function also deteriorate in the presence of infection. At term the levels and function of complement are two- thirds that in the adult and in preterms it is less than 50%. [33].

The nature of the colonizing organisms of the neonate is determined by flora in the birth canal and the environment. [9]. The predominant intestinal organisms acquired by normal babies *are E. coli, Klebsiella spp, Citrobacter, Bacteroides spp and Bifidobacteria spp.* Colonization of the upper respiratory tract occurs rapidly with CONS, *S. viridians and S. aureus* and colonization of the skin is predominated by CONS and *S. aureus* [9]. Infection after colonization is determined by the host and the microorganism in question. Bacterial invasion can be facilitated by abrasions, cuts and mucosal injury as well as cannulae and catheters as neonates have poor local inflammatory responses. [9]. Heavier colonization increases the risk of sepsis especially with microorganisms known to be pathogenic to babies such as GBS, *S. aureus,* CONS, *L. ,monocytogenes, H. influenza, E. coli, Pseudomonas spp and Klebsiella*, hence the effort to reduce density of colonization by providing umbilical cord care and bathing. [9]. There is also competition between bacteria that determines levels of colonization e.g. *Lactobacillus bifidus* in the gut of breastfed infants inhibits gram negative bacteria. (9).

1.1.6 DIAGNOSIS.

Blood cultures are the gold standard and definitive test for detection of bacteremia in newborn infants with suspected sepsis and are taken prior to therapy. Many infants who are septic however may have negative blood cultures. Abnormal white blood cell counts and immature to total neutrophil ratio are indirect tests for neonatal sepsis. Chacha et al higher rates of C- reactive protein (CRP) positivity were observed among neonates with confirmed neonatal sepsis than those with negative cultures [(12)]. It was noted that CRP and white blood cell counts had a combined sensitivity of 90.3% and are an inexpensive method of diagnosing neonatal septicaemia in developing countries [(12)]. In 1988, Rodwell et al used full haemogram parameters as a screening tool for neonatal sepsis [(17)]. The haematological scoring system formulated assigned a score of 1 for each of 7 parameters including: abnormal total leukocyte count, abnormal total neutrophil count, elevated immature polymorphonuclear (PMN) count, elevated immature to total PMN ratio, immature to mature PMN ratio equal to or more than 0.3, platelet counts equal to or less than 150, 000/mm^3 and pronounced degenerative changes in PMN [(17)]. With a score equal to or less than 2, the likelihood that sepsis was absent was 99%. The higher the score, the greater was the likelihood of sepsis [(17)]. The study concluded that the scoring system improved the diagnostic accuracy of the full haemogram as a screening tool for neonatal sepsis [(17)].

Other cultures can be under taken as part of septic screening. Gastric aspirates only contribute to diagnosis of neonatal sepsis if they are taken immediately after birth and before the first feed and are viewed as a sample of amniotic fluid and secretions of the birth canal. [(9)]. If the neonate is thought to be clinically infected, the antibiotic therapy should cover the organisms found on gastric aspirate culture. [(9)]. Thirty three percent of neonates show presence of GBS, enterococci and enterobacteriaceae on gram staining of gastric aspirate even though most do not become septic and therefore gastric aspirate microbiology alone is not a justification to

begin antibiotics. [9]. The specimen for urine culture should be collected by suprapubic aspirate as part of the assessment of neonates thought to be septicaemic. [9]. Presence of pus cells or organisms suggest a urinary tract infection. Organisms from the upper airway may cause septicaemia and lower respiratory tract infections. Tracheal secretion cultures should inform the choice of antibiotic cover in suspected pulmonary infection. [9]. Diagnosis of pulmonary infection should however not be based solely on the results of culture of respiratory secretions. [9]. The tips of vascular lines and thoracocenthesis tubes can be sent for culture after removal. The Macki roll technique is used to distinguish organisms causing sepsis from skin contaminants. [9]. Lumbar puncture should be part of the septic screen of ill neonates before starting antibiotics due to the high morbidity and mortality of neonatal bacterial meningitis. It is more likely to be positive in late onset sepsis rather than early onset sepsis. [9].

1.1.7 TREATMENT

Empiric therapy consists of combinations effective against gram positive (*GBS, L. monocytogenes*) and gram negatives (*E. coli*). The common combination is ampicillin or penicillin and gentamicin for a duration of 10 days. Cloxacillin is given in place of penicillin for extensive skin pustules or abscesses (*S. aureus*) [13].

2.0 STUDY JUSTIFICATION AND UTILITY

Of the 11 million under five deaths worldwide every year, 4 million occur in the first 28 days of life. Deaths in babies less than 28 days constitute 40% of under five deaths. Seventy percent of neonatal deaths occur in just Africa and South East Asia. The risk of dying is highest closest to birth and decreases over subsequent days and weeks (is 50% in the first 24 hours and a total of 75% in the first week) [(14)].

There is a general declining world trend in neonatal mortality from 1990 (4.4 million) to 2010 (3.1 million), but this progress is unequally distributed, with a 50% reduction in Europe and the West Pacific but only 19% in Africa i.e. the slowest progress is observed in the region with the highest mortality rate, which translates to a 1% reduction per year of neonatal mortality rates in the region with the highest rate [(15)].Ninety- nine percent of deaths in neonates less than 28 days old are in low and middle income countries, and a newborn born in a low income setting is eight times more likely to die than one born in a high income setting [(15)].

Twenty- five percent of neonatal deaths are due to neonatal infections and up to two-thirds of newborn deaths can be averted if known effective health measures are provided at birth and during the first week of life [(14)].

Kenya is one of the countries in Africa with the highest number of neonatal deaths [(16)]. There is a wide disparity in mortality rates across the country. In Kenya, the neonatal mortality rate according to the Kenya Demographic and Health Survey (KDHS) 2008-2009 is 31 per 1000 live births for the whole country, but is 39 per 1000 live births in Nyanza Province [(1)].

The United Nations Millennium Development Goals (MDGs) are a set of 8 goals that all 191 UN member states have agreed to try to achieve by the year 2015. They are derived from the UN Millennium Declaration signed in Sept 2000 that commits world leaders to combat poverty, hunger, disease, illiteracy and environmental degradation as well as discrimination against women. The 4th MDG is to reduce child mortality. The target of the 4th MDG is to

reduce by two thirds between 1990 and 2015 the under five mortality rate. Since 40 % of that mortality rate is attributable to neonatal deaths, these deaths and their causes must be addressed to allow the full realization of this target. The 3 main causes of neonatal mortality are severe infection (27%), birth asphyxia (27%) and prematurity (26%) according to the Child Survival and Development Strategy [16].

Over the last half decade the Department of Paediatrics and Child Health, University of Nairobi in collaboration with the Child Community Health Project, Washington Seattle University has rotated postgraduate students at Kisii Level 5 Hospital. The rotations have been done over a 6 week period aimed at exposing the students to the care and management of children and newborns at the facility and its catchment population. Various aspects of neonatal and child health such as malnutrition, immunization, PMTCT and TB screening have been reviewed during such rotations. The 13th cycle of the Community Child Health Project was a retrospective review of medical records from 2009 to 2012 at Kisii Level 5 Hospital during which it was found that the prevalence of neonatal sepsis was 15- 20% even when some of the records were incomplete and not all neonates were given a diagnosis, meaning that this percentage may well be an underestimation. Unhygienic cord care practices are prevalent in this community and hygienic delivery practices are not strictly adhered to. In cycle 15 conducted in October 2012 by Makotsi and Ravindran, neonatal sepsis was found to be more among neonates born at home. These infants born at home also had higher case fatalities. Most cases were noted to be omphalitis and meningitis. Limitations cited included lack of accurate diagnosis and no information on possible sources of infection. There was also no mention of the diagnostic work ups done on the neonates with suspected sepsis. If the prevalence and common microbial pattern of neonatal sepsis can be understood, this will allow for evidence based planning for timely and accurate interventions that will avert the mortality and morbidity associated with neonatal sepsis. This study attempted to investigate

what percentage of admissions were due to neonatal sepsis as well as the associated socioeconomic and demographic factors.

2.1 STUDY OBJECTIVES

2.1.1 PRIMARY OBJECTIVE

To determine the prevalence of sepsis among neonates admitted to Kisii Level 5 Hospital.

2.1.2 SECONDARY OBJECTIVES

a) To determine the pattern of bacterial causes of sepsis among neonates admitted to Kisii Level 5 Hospital.

b) To determine the economic and socio-demographic factors associated with sepsis in neonates admitted to Kisii Level 5 Hospital.

3.0 MATERIALS AND METHODS

3.1 STUDY DESIGN

To answer the objectives above, a descriptive cross- sectional study was carried out.

3.2 STUDY SITE

The study was carried out in the Newborn Unit and Paediatric Wards of the Kisii Level 5 Hospital, which is the largest government owned facility in Kisii County in Kenya. It has a catchment of 3 million people, with a Newborn Unit which has 8 cots and 2 working incubators and an average of 140 admissions every month. The paediatric ward admits infants older than 21 days and receives an average of 10 infants per month.

3.3 STUDY POPULATION

The study population comprised neonates less than 28 days old admitted to the Kisii Level 5 Newborn Unit and Paediatric wards whether they were born in the hospital or elsewhere.

3.4 SAMPLE SIZE DETERMINATION

Sample size was determined using the equation;

$$n = \frac{Z^2 P (1-P)}{d^2}$$

Where

n= sample size

Z= the z statistic for a level of confidence

P= expected prevalence or proportion

d= precision or margin of error

- So

Z= 1.96 (to correspond to 95% confidence interval).

P=0.13 (prevalence of 13%)

d= 0.075 (i.e. 7.5%).

- So

$$\frac{3.8416 \times 0.13 \times 0.87}{0.005625}$$

Sample size =77.2417707 = approximately 77 as a minimum sample size. The prevalence was taken from the study by Berkley et al at Kilifi District Hospital in Kenya, in which the prevalence of community acquired culture proven sepsis in neonates and young infants ranged from 10% to 16% [(2)]. Thirteen percent was selected as the median figure and used to calculate the sample size as shown above.

3.5 SCREENING CRITERIA

All infants aged less than 28 days seen at the hospital were identified. The objectives of the study were explained to the mothers and consent for inclusion into the study was sought. The neonates were consecutively enrolled into the study until the sample size of 80 neonates with sepsis was recruited.

3.6 INCLUSION CRITERIA

Included in the study were infants;

a. Aged 0 to 28 days.
b. Born at gestational age of 34 weeks and above
c. Birth weight equal to or greater than 1500gms.
d. Whose mothers give consent.

3.7 EXCLUSION CRITERIA

The following infants were excluded;

a. Infants aged above 28 days.

b. Preterms less than 34 weeks gestational age.

c. Weight less than 1500gm.

d. Consent not given.

3.8 STUDY PROCEDURE.

Over the study duration, a total of 406 neonates who were admitted in the new born unit and paediatric wards at Kisii Level 5 Hospital were screened to ensure that they met the inclusion criteria for enrollment into the study. This was done either immediately upon admission when the principle investigator was present at the time of admission or by examining the details of the inpatient file if the neonates were admitted at a time when the principle investigator was not present. Neonates who met the inclusion criteria were then examined for clinical signs of sepsis. Demographic, social and economic data was collected from consenting mothers. All this information was entered into a predesigned data collection form. Consecutive recruitment was done until the desired sample size was achieved. The principal researcher had a qualified clinical officer as a research assistant. He was oriented in the required study procedures at the onset of the study and was involved in the screening, questionnaire completion and sample collection. The research assistant was a qualified clinical officer with a diploma in clinical medicine and surgery.

3.8.1 Definition of clinical sepsis

Sepsis in the study participants was defined as an infant with any of the following danger signs for serious bacterial infection, according to the Pocket Book of Hospital Care for Children from the World Health Organization[30];

1. History of inability or refusal to breastfeed
2. History of convulsions
3. Drowsiness, lethargy or unconsciousness (young infant cannot remain alert after being gently shaken or when the examiner claps their hands).
4. Respiratory rate more than 60 breaths per minute on two separate counts.
5. Grunting
6. Nasal flaring
7. Severe lower chest wall indrawing
8. Fever $\geq 37.5^{o}C$ or hypothermia $<35.5^{o}C$ from axillary temperature.
9. Deep jaundice involving palms and soles of the feet.
10. Ten or more pustules or a big abscess
11. Umbilical redness extending to the periumbilical skin
12. Pus draining from the ear.
13. Central cyanosis.

Infants with clinical evidence of sepsis had blood taken for

a) Full blood count.
b) Culture and sensitivity.

3.8.2 Laboratory procedure.

The full haemogram and blood culture samples taken from the neonates in the study were processed at the Aga Khan Kisumu laboratory which has an annex in Kisii town. They have both internal and external quality control processes. They use RIQUAS (Randox International Quality Assessment Scheme) an international external quality control assessment and HUQAS (Human Quality Assessment Services) which is locally based and provides proficiency testing services for medical laboratories. The laboratory gave the principle investigator and the research assistant a tutorial on the laboratory's standard operating

procedures and on the procedures for sample collection and delivery to ensure that the samples received and processed were optimal.

3.8.3 Procedure for blood sampling

The blood sample was drawn via venepuncture. The blood volume used was approximately 4 ml. Skin preparation was done using 70% alcohol which was used to cover the area for 30 seconds and allowed to dry. Blood was then drawn, with 2mls inoculated into the bottle for blood culture and 2 ml into the vaccutainer for full blood count.

3.8.4 Preparation of thin blood films for immature to total ratio reading

The specimen used was EDTA whole blood specimen. A clean grease free and dry glass slide were used. A drop of blood was mixed on one end of the glass slide 1cm from the end. A glass spreader was put in front of the blood drop and the blood was allowed to spread along that spreader at 45^0 after which the spreader was moved forward fast. The smear had to have a smooth tail and the film was left to air dry before being read.

3.8.5 Blood culture processing

The blood sample for blood culture was taken before the administration of antibiotics to the patient. The blood culture method used was manual and not automated. Two milliliters of blood obtained from venepuncture was inoculated into a culture bottle containing brain heart infusion broth. This bottle was then transported to the laboratory within one hour for incubation. In the laboratory, the bottle was incubated at 37^0 and monitored for visible signs of bacterial growth. These include turbidity above the red cell layer, colonies growing on top of red cells, hemolysis and gas bubbles and clots. If these signs were seen, a subculture was done. The top of the culture bottle was leaned with 70% alcohol and a sterile needle inserted via the rubber liner of the cap of the culture bottle. One milliliter of the broth culture was withdrawn and transferred to blood agar (for anaerobic incubation for 48 hours), chocolate agar (incubation in carbon dioxide atmosphere for 48 hours) and MacConkey agar incubated

aerobically overnight). Positive growth would have proceeded for microorganism identification. If no growth is seen, incubation was prolonged to 5 days.

3.9 DATA MANAGEMENT AND ANALYSIS

Data was collected uniformly and a quality assured laboratory was used for sampling. A statistician was used for data analysis and reporting. Recorded data was stored safely by the principle investigator. A link log was used to code all personal details of the neonates. Data from the questionnaires was stored in the database and entered into a computer. Data analysis was done using SPSS, with cut off of 0.05 for significant associations.

The character of the neonate and mother were described using means and medians for continuous variables and frequency distributions or percentages for categorical variables, to clean data. The main outcome was calculated as a percentage of neonates with probable sepsis from the total number of neonates screened during the study period. Risk factors for positive culture were determined by conducting chi square test for categorical variables. For continuous variables, significant association were determined using t- test or the Mann-Whitney test.

3.10 MINIMIZING BIAS AND ERRORS.

The research assistant was oriented on filling the questionnaire and assessing the neonate for signs of suspected sepsis as well as the correct procedure for sample collection. There was careful entry and cross checking of a computerized data base from and against the administered questionnaire. The blood collection techniques prescribed by WHO were followed to avoid inaccurate culture results. Participants were assigned a study number and a separate link log was kept securely by the primary investigator.

3.11 STUDY LIMITATIONS

The incomplete filling or unavailability of the maternal and child health booklet made it difficult to fill some parts of the questionnaire and we had to rely on the recall of the mother. There was a long turnaround time for blood cultures (about 1 week). Financial constraints meant it was not possible to conduct all the laboratory tests that have high sensitivity and specificity for sepsis e.g. C- reactive protein and procalcitonin.

3.12 ETHICAL CONSIDERATIONS

The study, which is classified as research was, began only after receiving written approval from the KNH Research and Ethics Committee. Informed consent was obtained from the mothers. If the mother did not wish to participate in the study or withdraw, her rights were respected and the withdrawal will not negatively affect the care her child received. No inducements were offered. Information given was strictly used for research purposes only.

4.0 RESULTS

4.1 Prevalence of neonatal sepsis

During the three-month period between March and May 2014, a total of 406 neonates were admitted to Kisii Level 5 Hospital. Of the 406 neonates in the study population, a subset of 80 neonates had clinical sepsis and the prevalence of neonatal sepsis was therefore 19.7% (95% CI 15.9- 23.9).

All the 80 blood cultures carried out on the patients recruited into the study were negative. There was therefore a significant reliance on the Haematological Scoring System (HSS) as described by Rodwell et al to make diagnostic inferences about the neonates [17].

4.2 ANALYSIS OF NEONATAL AND MATERNAL DATA

4.2.1 The characteristics of the admitted neonates.

Table 1 below shows the characteristics of the neonates studied. The median age of the recruited neonates was 3 days. Males accounted for 58.8% of the admissions with a male to female ratio of 1.4: 1. Ninety five percent of the neonates were born in a health facility with only 5% being born at home. Fifty percent of neonates were admitted between 24 and 72 hours of birth and 25% of neonates were admitted from 8 to 28 days of life.

4.2.2 Status at birth.

Ninety one percent of neonates were born at term. The mean gestational age was 39.2 weeks. At birth 88.8% of neonates weighed between 2500 and 4000 gm. The median weight was 3.4kg. Eleven percent of the neonates weighed between 1500 and 2499 gm.

Table 1: Characteristics of babies with clinical neonatal sepsis.

CHARACTERISTIC	FREQUENCY N= 80	PERCENT (%)
Sex		
Male	47	58.80
Female	33	41.20
Place of delivery		
Kisii Level 5 Hospital	61	76.30
Other health facility	15	18.70
Home	4	5.00
Neonates age		
<24 hrs	7	8.80
24-72 hrs	40	50.00
4-7 days	13	16.20
8-28 days	20	25.0
Gestation		
34 to 36 weeks	6	7.50
37 completed weeks	73	91.30
More than 42 weeks	1	1.20
Birth weight		
1500 - 1999 gm	3	3.75
2000 - 2499 gm	6	7.50
2500- 4000 gm	71	88.75

4.2.3 Maternal characteristics.

The maternal characteristics are summarized in Table 2. The maternal age ranged from 16 to 35 years with the mean maternal age being 23.6 years (SD 1.24). Eighty seven percent of the mothers fell between the ages of 20 and 30 years. There were only 6 (7.5%) teenage mothers who fell between the ages of 16 and 19 years of age. All the teenage mothers delivered their babies in a hospital. Of the 6 neonates born to teenage mothers, 4 (67%) developed symptoms of sepsis within 72 hours, 3 (50%) were born at a gestational age of 34 to 36 weeks and 3 (50%) were of low birth weight. Seventy four mothers (92.5%) were married. Sixty seven percent of the mothers had attained some level of secondary school education with only 3.8% having attained primary school as their highest level of education. All the mothers had some level of formal education.

Table 2: Maternal characteristics of babies admitted with clinical neonatal sepsis.

CHARACTERISTIC	FREQUENCY N= 80	PERCENT (%)
Maternal age		
16-19 years	6	7.50
20-24 years	47	58.75
25-29 years	23	28.75
30-35 years	4	5.0
Maternal marital status		
Single	6	7.50
Married	74	92.50
Highest level of education		
Primary education	3	3.80
Secondary education	54	67.50
College or university education	23	28.70
Maternal occupation		
Formal employment	10	12.50
Self employed	13	16.30
Subsistence farmer	16	20.00
Housewife	41	51.20
Material used to build home		
Stone/ brick	55	68.80
Mud	24	30.00
Other	1	1.20
Water source		
Treated tap water	38	47.50
Well	25	31.20
River	15	18.80
Borehole	1	1.25
Rain water	1	1.25

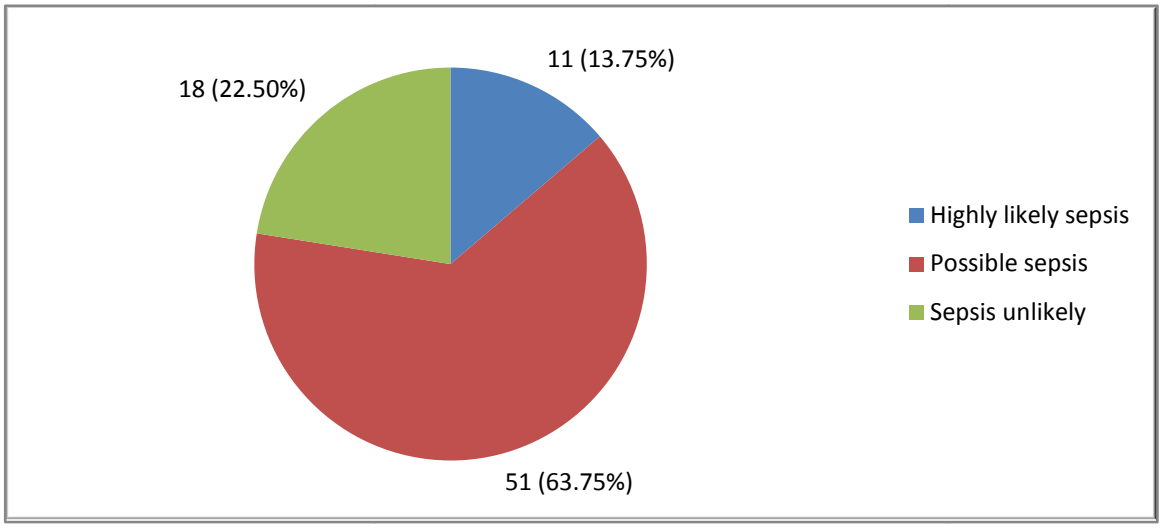
Majority of mothers (51.2%) were housewives. Twenty percent engaged in subsistence farming, 16.3% being self- employed and only 12.5% in formal employment. Most mothers (n = 55, 68.8%) lived in stone/ brick walled houses and had a treated tap water source in their residence (n = 38, 47.5%). Mothers who used un-improved sources of water that are susceptible to contamination i.e. wells, rivers and rain water were 51.25%.

4.3 ANALYSIS OF DATA FROM NEONATES WITH CLINICAL SEPSIS.

4.3.1 Classification of neonatal sepsis using the hematological scoring system

Figure 1 represents the classification of sepsis among the 80 patients with clinical signs of sepsis based on the HSS. Eleven (13.8%, 95% CI 7.1- 23.3) neonates had scores indicating a highly likely sepsis diagnosis, 51 (63.8%, 95% CI 52.2 to 74.2) had scores compatible with a diagnosis of possible sepsis and 18 (22.5%, 95% CI 13.9- 33.2) were unlikely to have sepsis. The haematologic scoring system was initially described in 1988 by Rodwell and Leslie. [17]. It uses a set of cut off values based on neonatal age in hours and days to assign scores to seven parameters that can be derived from a full haemogram. The parameters include an abnormal total white blood cell count, abnormal total polymorphonuclear count, increased I: T ratio, increased I: M ratio, reduced platelet count and degenerative changes in neutrophils on peripheral blood film. This is done to increase the value of the full haemogram as a screening tool. The total score is then interpreted using a standard scoring system to determine the likelihood of neonatal sepsis. A score of less than 2 means that sepsis is unlikely, a score of 3- 4 means that sepsis is possible and a score equal to or greater than 5 means that sepsis is highly likely.

Figure 1: Classification of the babies admitted with clinical neonatal sepsis based on the Hematological Score



4.3.2 Clinical features of babies admitted with clinical neonatal sepsis.

Table 3 summarizes the frequency of the clinical features of sepsis among the admitted neonates. The most common clinical features were fever (n = 51, 63.8%), refusal to feed (n = 39, 48.8%), and chest indrawing (n = 24, 30%). Tachypnoea (respiratory rate > 60 breaths per minute on two separate counts) was documented in 22 (27.9%) of neonates and skin pustules or abscess occurred in 18 (22.5%) neonates. Clinical features t edness extending to periumbilical skin, pus draining from ears and marked abdominal distention with each of these features occurring in only a single neonate for each sign.

Table 3: Clinical features of neonates admitted with clinical neonatal sepsis

CLINICAL FEATURE	FREQUENCY	PERCENT (%)
Fever/ hypothermia	51	63.8
Refusal to breastfeed	39	48.8
Chest indrawing	24	30.0
Abnormal respiratory rate above60/min, below 20/ min or apnea more than15 seconds.	22	27.9
Skin pustule/ abscess	18	22.5
Nasal flaring	10	12.5
History of convulsions	8	10.0
Grunting	8	10.0
Drowsy/ lethargic	7	8.8
Others*	4	5.0

* Includes one case each for; deep jaundice involving palms and soles of the feet, Umbilical redness extending to the periumbilical skin or draining pus, Pus draining from ear(s) and Marked abdominal distention.

4.3.3 Analysis of neonatal sepsis against general neonatal characteristics.

Comparisons of the proportions of neonates with neonatal sepsis according to demographic characteristics are shown in Table 4. There were no statistically significant associations between neonatal demographic characteristics (including, gender, birth weight, place of delivery, or gestation) and neonatal sepsis.

Table 4: Association between neonatal sepsis and neonatal demographic characteristics

CHARACTERISTIC	UNLIKELY-SEPSIS (N = 18)	POSSIBLE SEPSIS (N = 51)	HIGHLY LIKELY – SEPSIS (N =11)	UNLIKELY VS POSSIBLE P VALUE	OR (CI)	UNLIKELY VS HIGHLY LIKELY P VALUE	OR (CI)
Neonatal age							
<24 hrs	0(0.0)	5(9.8)	2(18.2)	0.563*	NA	0.200*	NA
24-72 hrs	8(44.4)	27(52.9)	5(45.5)	NA	1.0	NA	1.0
4-7 days	3(16.7)	9(17.6)	1(9.1)	1.000*	0.9 (0.2- 6.3)	1.000*	0.5 (0.01 -9.4)
8-28 days	7(38.9)	10(19.6)	3(27.3)	0.171	0.4 (0.1- 1.8)	1.000*	0.7 (0.1-5.3)
Birth weight							
1500 - 1999 gm	1(5.6)	2(3.9)	0(0.0)	NA	1.0	NA	NA
2000 - 2499 gm	2(11.1)	4(7.8)	0(0.0)	1.000*	1.0 (0.01-34.1)	NA	NA
2500- 4000 gm	14(77.8)	45(88.2)	11(100.0)	1.000*	1.6 (0.03-32.8)	1.000*	NA
Place of delivery							
Kisii Level 5 Hospital	12(66.7)	40(78.4)	9(81.8)	NA	1.0	NA	1.0
Other health facility	3(16.7)	10(19.6)	2(18.2)	1.000*	1.0 (0.2-6.6)	1.000*	0.9 (0.1-9.6)
Home	3(16.7)	1(2.0)	0(0.0)	0.055*	0.1 (0.002-1.4)	0.266*	NA
Gestation							
34 to 36 weeks	2(11.1)	4(7.8)	0(0.0)	NA	1.0	NA	NA
37 completed weeks	16(88.9)	46(90.2)	11(100.0)	0.652*	1.4 (0.1-11.1)	0.512*	NA
More than 42 weeks	0(0.0)	1(2.0)	0(0.0)	1.000*	NA	NA	NA
Sex							
Male	10(55.6)	33(64.7)	4(36.4)	NA	1.0	NA	1.0
Female	8(44.4)	18(35.3)	7(63.6)	0.491	0.7 (0.3-2.3)	0.491	2.2 (0.4-13.8)

* Fischer's exact test.

4.3.4 Association between neonatal sepsis and maternal characteristics.

Table 5: Association between neonatal sepsis and maternal characteristics.

CHARACTERISTIC	UNLIKELY-SEPSIS (N = 18)	POSSIBLE SEPSIS (N = 51)	HIGHLY LIKELY –SEPSIS (N =11)	UNLIKELY VS POSSIBLE P VALUE	OR (C)	UNLIKELY VS HIGHLY LIKELY P VALUE	OR (CI)
Maternal age							
16-19 years	2(11.1)	3(5.9)	1(9.1)	NA	1.0	NA	1.0
20-24 years	10(55.6)	30(58.8)	7(63.6)	0.598*	0.2 (0.1-19.9)	1.000*	1.4 (0.1-94.2)
25-29 years	6(33.3)	18(35.3)	3(27.3)	0.597*	2.0 (0.1-21.8)	1.000*	1.0 (0.04-78.4)
30-35 years	0(0.0)	5(9.8)	2(18.2)	0.444*	NA	0.400*	NA
Dysuria	1(5.6)	7(13.7)	5(45.5)	0.670*	2.7 (0.3-128.9)	0.018*	8.2 (0.7-407.9)
Recent febrile illness	1(5.6)	2(3.9)	1(9.1)	1.000*	0.7 (0.03-43.3)	1.000*	1.7 (0.02-141.2)
Maternal marital status							
Married	16(88.9)	47(92.2)	11(100.0)	0.647*	1.5 (0.1-11.3)	0.512*	NA
Highest level of education							
Primary	2(11.1)	1(2.0)	0(0.0)	NA	1.0	NA	NA
Secondary	9(50.0)	34(66.7)	11(100.0)	0.138*	7.6 (0.3-458)	0.476*	NA
Tertiary	7(38.9)	16(31.4)	0(0.0)	0.268*	4.6 (0.2-286)	NA	NA
Maternal occupation							
Formal employment	4(22.2)	6(12.0)	0(0.0)	NA	1.0	NA	NA
Self employed	4(22.2)	7(14.0)	2(18.2)	1.000*	1.2 (0.1-9.5)	0.467*	1.0
Subsistence farmer	4(22.2)	12(24.0)	0(0.0)	0.664*	2.0 (0.3-14.9)	NA	NA
Housewife	6(33.3)	25(50.0)	9(81.8)	0.222*	2.8 (0.4-16.5)	0.087*	3 (0.3-41.1)
Water source							
Treated tap water	6(33.3)	23(45.1)	9(81.8)	NA	1.0	NA	1.0
Well	7(38.9)	19(37.3)	1(9.1)	0.087	0.7 (0.3-3)	0.074*	0.1 (0.001-1.2)
River	5(27.8)	9(17.6)	1(9.1)	0.290	0.5 (0.1-2.5)	0.149*	0.1 (0.003-1.8)

* Fischer exact test

Table 5 shows the association between maternal factors and neonatal sepsis. Among the maternal characteristics, the factor that was significantly associated with neonatal sepsis was dysuria. The total number of subjects adds up to 45 as presence or absence of dysuria was not stated for 35 mothers. Neonates who were classified as highly likely to have sepsis were 8.2 times more likely to have a mother who reported a history of dysuria than a neonate who was classified as unlikely to have sepsis. (p= 0.018).

4.4 ANALYSIS OF DELIVERY AND POST- DELIVERY NEONATAL CARE DATA

4.4.1 Analysis of delivery data

From the delivery data shown in table 6, most women had rupture of membranes for less than 18 hours (96.3%) and had no meconium staining of liquor (82.5%). Also, most women did not have a fever during labour (91.3%). Majority of the women (82.5%) delivered by spontaneous vaginal delivery.

Table 6: Some important intra- partum factors

	Frequency	Percent
Duration of rupture		
More than 18 hrs	3	3.8
Less than 18 hrs	77	96.3
Meconium stained liquor		
Yes	14	17.5
No	66	82.5
Mode of delivery		
Caesarian section	14	17.5
Spontaneous vertex delivery	66	82.5
High fever during labor		
Yes	6	7.5
No	73	91.3
Not documented.	1	1.3

As shown in table 7, there was no significant association between neonatal sepsis and the mode of delivery, duration of rupture of membranes, hi the mode of delivery, duration of rupture of membranes, maternal fever during labour or presence of meconium stained liquor. Most women had a duration of rupture of membranes that was less than 18 hours and most women did not have meconium staining of liquor.

Table 7: Delivery data and neonatal sepsis in admissions at Kisii Level 5 Hospital.

CHARACTERISTIC	UNLIKELY-SEPSIS (N = 18)	POSSIBLE SEPSIS (N = 51)	HIGHLY LIKELY – SEPSIS (N =11)	UNLIKELY VS POSSIBLE P VALUE	OR (CI)	UNLIKELY VS HIGHLY LIKELY P VALUE	OR (CI)
Mode of delivery							
Caesarian section	3(16.7)	8(15.7)	3(27.3)	NA	1.0	NA	1.0
SVD	15(83.3)	43(84.3)	8(72.7)	1.000*	1.1 (0.2-5.3)	0.646*	0.5 (0.1-5.1)
Duration of rupture							
More than 18 hrs	0(0.0)	2(3.9)	1(9.1)	NA	NA	NA	NA
Less than 18 hrs	18(100.0)	49(96.1)	10(90.9)	1.000*	NA	0.379*	NA
Fever during labor							
Yes	0(0.0)	6(11.8)	0(0.0)	NA	NA	NA	NA
No	18(100.0)	44(86.3)	11(100.0)	0.016*	NA	NA	NA
Unclear	0(0.0)	1(2.0)	0(0.0)	NA	NA	NA	NA
Meconium stained liquor							
Yes	4(22.2)	9(17.6)	1(9.1)	NA	1.0	NA	1.0
No	14(77.8)	42(82.4)	10(90.9)	0.730*	1.3 (0.3-3.8)	0.622*	2.9 (0.2-154)

There were no significant associations between neonatal sepsis and mode of delivery, duration of membrane rupture, fever or meconium stained liquor.

4.4.2 Analysis of post delivery neonatal care

Table 8 below highlights some aspects of post delivery care on the neonates in the study. Ninety two percent of mothers received postnatal counseling on the importance of breastfeeding and on danger signs in the neonate. For cord care, most mothers left the cord to air dry. Water was used by 13.7% of mothers and only 6.25% applied traditional substances like cow dung or saliva.

Table 8: Post delivery neonatal care data.

ASPECT OF CARE	FREQUENCY (N)	PERCENT (%)
Received post natal counseling on breastfeeding	74	92.5
Received post natal counseling on neonatal danger signs	74	92.5
Type of cord care provided.		
Air dried	59	73.75
Spirit	1	1.25
Chlorhexidine	4	5
Water	11	13.75
Cow dung or saliva	5	6.25
Baby given prelacteal feed.	1	1.25
Hand washing before breastfeeding		
Yes always	56	70
Sometimes	23	28.75
No	1	1.25
Hand washing after changing diapers		
Yes always	60	75
Sometimes	20	25
Hand washing before handling infant		
Yes always	5	6.25
Sometimes	37	46.25
No	38	47.50
Breast feeding initiated within 1 hour of birth	41	51.20

Only 70% of mothers consistently washed their hands before breast feeding and only 75% remembered to consistently wash their hands after changing dirty diapers. Only one neonate had been exposed or handled by an adult who was known to be unwell (the neonates mother was on management for TB). Only 51.2% of mothers initiated breast feeding within one hour of delivery.

Table 9: Post delivery neonatal care data and sepsis

ASPECT OF POSTNATAL CARE	UNLIKELY-SEPSIS (N = 18)	POSSIBLE SEPSIS (N = 51)	HIGHLY LIKELY –SEPSIS (N =11)	UNLIKELY VS POSSIBLE SEPSIS P VALUE	OR (CI)	UNLIKELY VS HIGHLY LIKELY SEPSIS P VALUE	OR (CI)
Cord care							
Nothing applied	9(50.0)	40(78.4)	10(90.9)	NA	1.0	NA	1.0
Spirit	0(0.0)	1(2.0)	0(0.0)	1.000*	NA	NA	NA
Chlorhexidine	2(11.1)	2(3.9)	0(0.0)	0.187*	0.2 (0.01-3.6)	0.476*	NA
Water	4(22.2)	6(11.8)	1(9.1)	0.204*	0.3 (0.1-2.0)	0.327*	0.3 (0.004-3)
Cow dung or saliva	3(16.7)	2(3.9)	0(0.0)	0.067*	0.2 (0.01-1.6)	0.221*	NA
Post natal counseling on neonatal danger signs							
Yes	15(83.3)	49(96.1)	10(90.9)	NA	1.0	NA	1.0
No	3(16.7)	2(3.9)	1(9.1)	0.107*	0.2 (0.02-2)	1.000*	0.5 (0.01-7.5)
Exposure to sick sibling/ adult							
Yes	0(0.0)	1(2.0)	0(0.0)	NA	NA	NA	NA
No	18(100.0)	50(98.0)	11(100.0)	NA	NA	NA	NA
Hand washing after changing diaper							
Yes	13(72.2)	39(76.5)	8(72.7)	NA	1.0	NA	1.0
No	5(27.8)	12(23.5)	3(27.3)	0.719	0.8 (0.2-3.5)	1.000*	1.0 (0.1-6.8)
Hand washing before breastfeeding							
Yes always	13(72.2)	36(70.6)	7(63.6)	NA	1.0	NA	1.0
Sometimes	4(22.2)	15(29.4)	4(36.4)	0.761*	1.4 (0.3-6.6)	0.671*	1.9 (0.3-13.4)
Hand washing before handling infant							
Yes always	0(0.0)	3(5.9)	2(18.2)	0.562*	NA	0.135*	NA
Sometimes	10(55.6)	24(47.1)	3(27.3)	0.535	1.0	0.249*	1.0
No	8(44.4)	24(47.1)	6(54.5)	0.535	1.3 (0.4-4.3)	0.420*	2.5 (0.4-9.9)
No prelacteal feeding	17(94.4)	51(100.0)	11(100.0)	0.261*	1.3 (0.4-3.4)	NA	2.2 (0.4-14.7)
Post natal counseling on breastfeeding							
Yes	15(83.3)	49(96.1)	10(90.9)	NA	1.0	NA	1.0
No	3(16.7)	2(3.9)	1(9.1)	0.107*	0.2 (0.02-2)	1.000*	0.5 (0.01-7.5)
Breastfeeding initiated within 1 hour							
No	10(29.4)	19(55.9)	5(14.7)	NA	1.0	NA	1.0
Yes	8(18.6)	30(69.8)	5(11.6)	0.176	2 (0.6-6.8)	0.778	1.3 (0.2-7.7)

As shown in table 9, there were no significant associations between post delivery neonatal care and neonatal sepsis.

4.5 OUTCOMES OF THE BABIES WITH NEONATAL SEPSIS

4.5.1 Deaths.

There were 12 (15%) deaths in the neonates as shown in table 10. There was no significant association between neonatal sepsis diagnosis and mortality. Of the patients with unlikely sepsis diagnosis 11.1% died. The mortality rate in highly likely sepsis was 27.2%.

Table 10: Hospitalization outcome according to neonatal sepsis diagnosis.

	Outcome			OR (95% CI)	P VALUE
	Died	**Alive**	**Total**		
Unlikely-sepsis	2 (11.1%)	16 (88.9%)	18 (100%)	1.00	
Possible sepsis	7 (13.7%)	44 (86.3%	51 (100%)	0.79 (0.07-4.76)	1.000*
Highly likely -sepsis	3 (27.2%)	8 (72.7%)	11 (100%)	3.0 (0.27-41.2)	0.339*

The mortality rate in the three neonatal sepsis categorization increased with increasing risk of sepsis (unlikely sepsis 11.1% mortality; possible sepsis 13.7% and highly likely sepsis at 27.2%). The outcome of hospitalization was however not significantly associated with neonatal sepsis.

4.5.2 Duration of hospital stay.

Table 11: Median length of hospitalization according to sepsis diagnosis

	Unlikely-sepsis	Possible sepsis	Highly likely - sepsis	Total	P value
Median	6	4	4	5	0.134
IQR	4 to 9	3 to 7	2 to 6	3 to 7	NA

Overall, the median duration of stay in hospital was 5 days (IQR 3 to 7) as deduced from table 11. The median ranges for hospital stay ranged from 4 to 6 days and was not significantly different for neonates with the different sepsis diagnosis. The median length of stay did not show a significant association with sepsis. (Kruskall Wallis P value = 0.134). No neonates were transferred to other facilities. Those who were categorized as unlikely sepsis may have stayed longer due to other conditions unrelated to sepsis.

5.0 DISCUSSION

Neonatal sepsis is the systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection during the first 28 days of life [18].

The study revealed that the prevalence of clinical neonatal sepsis at Kisii Level 5 Hospital was 19.7%. This was in keeping with the retrospective review of medical records at the hospital from 2009 to 2012 undertaken in the 13th cycle of the Community Child Health Project where the prevalence of clinical neonatal sepsis was estimated to be 15- 20%. After application of the hematological scoring system, it was found that 12.6% of neonates had possible sepsis and 2.7% had highly likely sepsis. In the study by Berkley et al done from 1998 to the year 2002 at Kilifi in Kenya on young infants the prevalence of community acquired culture proven sepsis was 12.8% [2]. The limitations of my study included the smaller sample size and shorter time span over which the study was conducted.

In the study, 58.8% of neonates with sepsis were male. There was however no statistical significance found between sex and sepsis. Hassan et al found that the frequency rate of sepsis was more in males than females and that the difference was statistically significant [19].

The commonest clinical features of neonatal sepsis were fever or hypothermia, refusal to breastfeed, chest wall indrawing and tachypnoea (respiratory rate above 60 breaths/ minute). According to Opiyo et al, refusal to breastfeed and tachypnoea were among some of the clinical features most valuable in estimation of risk of severe illness in neonates [6]. Chest wall indrawing was considered as part of a more restrictive set of signs of illness for infants aged 7 to 59 days in a study by English et al [10].

In the study by Onyedibe et al, neonates born at home had the highest percentage of culture proven sepsis [27]. Even though there was no significant association in this study between place of delivery and sepsis, this lack of association may have been due to the small sample

size used. It was found that 95% of mothers delivered in a hospital. Other studies found that a significant number of neonates born in health facilities developed sepsis [18, 19]. This was because most mothers labored for prolonged periods at home and presented to hospital late. In this study however, 96.3% of mothers had a duration of membrane rupture that was less than 18 hours by the time they arrived in hospital. This could indicate a need to improve on standards of care offered in health facilities during delivery to avoid sepsis and to find mothers whose neonates are at risk of developing sepsis early.

The diagnosis of neonatal sepsis is important because sepsis presents a serious threat to the neonate and it is urgent to know if the baby has sepsis to allow for institution of treatment as soon as possible. The usefulness of a clinical test e.g. blood culture or full haemogram depends on the clinical condition of the neonate [20]. The situation where diagnostic testing is most useful is when the clinical picture leaves the clinician in doubt and the results of such tests should be evaluated in light of the clinical condition of the baby [20]. The blood cultures undertaken in this study were all negative. The positivity of blood cultures in the study by Berkley et al was 12.8% [2]. Blood cultures are not free from error and can be falsely sterile as has been demonstrated in some postmortem cultures. The possible reasons for the low yield of blood cultures include insufficient sample volumes, intermittent or low density bacteremia and suppression of bacterial growth by antibiotic administration [20]. A single blood culture of sufficient volume is required in all cases of suspected neonatal sepsis. One milliliter of blood should be the minimum when pediatric culture bottles are used for detection of low level bacteremia of 4 CFU/ml and less. Blood cultures obtained in adequate volumes are twice as likely to give a positive result. The standard blood volume inoculated into the culture media in the study was at least 2ml. The lower limit recommended for paediatric bottles is 1ml [21]. The culture bottles available for the study were standard bottles, not particularly paediatric. There are a number of factors that could have contributed to the negative findings in the

study. The bactericidal activity of blood i.e. innate immunity (complement, phagocytic white blood cells, and lysozyme) as well as presence of antibiotics in the blood can reduce the viability of organisms [21]. Liquid cultures dilute bactericidal activity. The volumes for media used in paediatric bottles should be 20- 40 ml. The blood should be 10- 20% of the total medium volume [21]. The volumes liquid broth used in the study ranged from 20 to 30ml and the bottles were not particularly paediatric culture bottles. The blood to broth ratio was therefore not strictly adhered to. Usually one culture sample is taken before antibiotics are initiated. Reduced sampling in neonates is done because of small circulating volumes of blood [21]. The optimal site for sampling is a peripheral venous or arterial vessel as false positives cultures can be gotten from indwelling vascular devices [21]. Different blood culture technologies are available. Manual systems, such as the one used in the study involves incubation of liquid culture media with frequent inspection and microscopy with blind plating onto solid medium culture to see if any growth had occurred. Modern closed computer based systems assess changes in carbon dioxide every 10- 15 minutes as an indicator of bacterial growth [21]. The Aga Khan laboratories in Kisii planned to phase out the manual system in favour of a computerized system which is felt to be more sensitive and accurate in detecting presence of bacteria in blood samples. There was also a move to replace liquid cultures with biphasic media which would have a special resin to bind antibiotics present in blood to reduce inhibition to growth of bacteria. Since the study utilized the manual method as well as liquid medium, it is possible that the system was not sensitive enough to detect lower level colony count bacteremia. It has been found that 25% of infants with sepsis have low colony count bacteremia and two- thirds of those under two months of age have counts less than 10 CFU/ml [22]. This would apply to the study subjects who were neonates.

Even though blood cultures are more sensitive (82%) and specific (96%) indicators of presence of potentially fatal bacterial infection, negative cultures can occur in the presence of significant bacterial illness [23]. In a study by Seale et al, 17 % of neonates with fatal illness associated with bacterial infection had negative pre- mortem blood cultures [23].

The full haemograms that were performed simultaneously with blood cultures were used to make inferences about the neonates in the study. Total white blood cell counts have little value in the diagnosis of early onset neonatal sepsis and have a poor positive predictive accuracy, which has lead to the analysis of subcomponents of white blood cells and neutrophil indices e.g. absolute neutrophil counts, absolute band counts and I: T ratio to help identify infected infants [22]. A single I: T ratio has a poor positive predictive accuracy of 25%, but a high negative predictive accuracy of 99% [22] . The timing of doing a white blood cell count is important as counts obtained 6-12 hours after birth are more likely to be abnormal because altered numbers and ratios of mature and immature neutrophils need an established inflammatory respond [22]. Low platelet counts are non-specific and a late indicator of sepsis. They also remain low for days to weeks and cannot be used to gauge response to antibiotics [22]. The haematological scoring system which combines multiple laboratory values is a useful diagnostic aid. Such screening laboratory tests are best used to determine high risk healthy appearing neonates who don't need antibiotics or in whom antibiotic treatments can be stopped [22].

Even though blood cultures give a definitive diagnosis, they are time consuming with a turnaround time of 48- 72 hours, are low yielding (from 8- 73%) and the test's reliability depends on the laboratory it was conducted in [24]. A study carried out by Makkar et al evaluated the performance of the Hematological Scoring System (HSS) of Rodwell et al 1988 for the purpose of early detection of sepsis in high risk infants and to improve the diagnostic accuracy of full haemogram as a screen test [24]. It was found that 83.3% of patients with

culture proven sepsis had haematological scores above five, which shows that the HSS has a good correlation with culture positive sepsis [24].

The HSS has the advantage of being applicable to all infants even when receiving antibiotic therapy and being the single test that is easily available in most hospitals [25]. The elevation of the I: T ratio is the most reliable indicator of sepsis [24, 25].

In this study, dysuria was used as an indicator of presence of urinary tract infection in the mother. There was a significant association between dysuria and sepsis. This is in keeping with the study by Woldu et al [18] in which a significant number of neonates born to mothers with urinary tract infections developed sepsis.

Onyedibe et al investigated the impact of socioeconomic factors on neonatal sepsis in Jos, Nigeria. They found that 71.1% of neonates in their study were born at term [27]. In this study 91.3% of the neonates had a gestational age of 37 completed weeks. In the study by Onyedibe et al, the highest number of neonates with sepsis had mothers who had attained a primary education, with the second highest frequency of mothers with neonates who had sepsis having no formal education [27]. They identified low socioeconomic status as a risk factor for sepsis. In this study all the mothers had received some level of formal education and 68.8% lived in stone houses. This may have been due to the small sample size used in this study as the study in Jos had a sample size of 218 neonates [27].

6.0 CONCLUSION

The prevalence of sepsis among neonates admitted to Kisii Level 5 Hospital was 19.7%. It is therefore necessary to carry out careful clinical evaluation for the danger signs of neonatal sepsis in each admitted neonate to facilitate prompt laboratory evaluation and timely commencement of antimicrobial therapy. The pattern of bacterial causes of neonatal sepsis could not be determined as all the cultures done turned out negative. The maternal age of admitted neonates ranged from 16 to 35 years with 87% of mothers falling between the ages of 20 years to 30 years. Fifty one percent of mothers were housewives, 74% were married, and 67% had a secondary school level of education. The mothers lived under more affluent conditions as indicated by 68.8% living in stone or brick built houses and 47.5% having treated tap water in their houses. Neonates with sepsis were more likely to have been born to mothers with dysuria.

6.1 RECOMMENDATIONS.

- It is important that each neonate be evaluated for the danger signs associated with neonatal sepsis and if these signs are found, empiric treatment should be started as early as possible after blood samples have been taken in adequate volumes for blood culture and full haemogram.
- A follow up study should be done with a larger sample size to evaluate the value of utilizing the more sensitive automated method of detecting bacterial growth as the method used for this study was manual.

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APPENDICES

Appendix I: QUESTIONNAIRE

Instructions to the interviewer

- The respondent to the questionnaire should be the biological mother of the neonate.
- For questions with alternatives, fill in the number corresponding to the appropriate response.

- **STUDY NUMBER …….**
- **DATE OF INTERIVIEW …….**
- **HOSPITAL INPATIENT NUMBER ……**

A) MATERNAL DATA

I) SOCIO-DEMOGRAPHIC AND ECONOMIC DATA

1. Age of the mother (in years) …….
2. Marital status ……..(1- Single 2- Married 3-Divorced or separated 4-Widowed)
3. Maternal level of education ……
4. (1-No formal education 2- Primary education 3- Secondary education 4- College or university education).
5. Maternal occupation ……..
6. (1-Formal employment 2- Self employed 3- Subsistence farmer 4- Housewife).
7. Family home..... (1- owed 2- rented)
8. Material used to build home..... (1-stone/ bricks 2- mud 3- iron sheet 4- other, specify).

9. Water source..... (1- tap 2- well 3- borehole 4- river 5- water vendor)
10. Income bracket.....

    (a- [less than 3,000] b -[3,000- 5,999] c- [6,000- 8,999] d- [9,000- 11,999] e- [12,000- 14,999] f- [more 15,000].
11. Any NHIF cover..... (1- yes 2- no).
12. Any money saved monthly..... (1- yes 2- no)

II) PRENATAL DATA

1. LMP ……
2. Parity ……..
3. How many living children do you have
4. Any deaths of an older child……1-yes, in the first month of life, 2- yes, after the first month of life, 3- no).
5. When was your last delivery (day, month year).....
6. Contraception used prior to this pregnancy ……(1-yes, specify, 2- no).
7. Any febrile illness within 2 weeks before delivery ……(1- yes 2- no)
8. Any antibiotic treatment given during delivery or two weeks prior to delivery …….(1- yes 2- no)
9. Any dysuria during pregnancy …….....(1- yes 2- no)
10. Was ANC attended……(1- no 2- yes)

11. Is MCH booklet available …….(1- no 2- yes)

12. How many times was ANC attended ……..

13. Details of ANC profile

PARAMETER	HIV	VDRL	HAEMOGLOBIN	URINALYSIS
DATE				
FINDINGS				

III) DELIVERY DATA

1. Date of delivery ……
2. Duration of rupture of membranes ……(1- more than 18 hours 2- less than 18 hours)
3. Presence of foul smelling liquor ……..(1- yes 2- no)
4. Presence of meconium stained liquor ……(1- yes 2- no)
5. Drainage of liquor prior to onset of labour pain……(1-yes 2- no)
6. Mode of delivery…….(1- caesarian section 2- spontaneous vaginal delivery 3- vacuum assisted delivery)
7. Place of delivery …….(1- Kisii level five 2- another health facility 3- at home)
8. Resuscitation needed for neonate (suction) ……(1- yes 2- no)
9. High fevers >37.9o C before or during labour ……(1- yes 2- no 3- unclear)
10. Number of vaginal examinations …….

B. NEONATE DATA

1. Gestational age (weeks) ……(1 [34 to36 weeks and 6 days] 2- [37 completed weeks] 3- [more than 42 weeks]).
2. Birth weight (kg)…….(1- [1500- 2000gm] 2-[2000- 2500gm] 3-[more than 2500gm]). Indicate specific weight.
3. Current weight (kg)…….
4. Presenting complaint..... ....
5. Age at diagnosis of sepsis (in days).....
6. Duration of presenting complaint (days).....
7. Premedication given before hospital arrival.....(1- yes, specify kind and duration, 2- no)
8. Birth order of child.....
9. Birth interval between neonate and immediate older sibling.....months.
10. Sex ……..(1- male 2- female)
11. Immunization status up to date for age.....(1-yes, MCH booklet 2- yes, mother's account, 3-no).
12. Any postnatal counseling on breast feeding (technique/ importance).....(1- yes, 2- no).
13. Any postnatal counseling on danger signs in the neonate.....(1- yes, 2- no).
14. Cord care after delivery ……..

    (1- left dry 2- spirit 3-chlorhexidine 4- traditional substance -specify)
15. Number of times cord was cleaned daily.....

16. Eyes cleaned with.....(1- not specifically cleaned, 2- water, 3- breast milk, 4- antiseptic solution 5- other, specify).
17. Eyes cleaned with.....(1- same cloth/ piece of cotton 2- separate cloths/ pieces of cotton 3- along with whole face 4- others, specify).
18. Skin care/ bathing began at what age.....
19. Skin care/ bathing done with.....(1- water only 2- soap and water 3- others, specify).
20. Emollient applied to the skin.....(1- none, 2- commercial baby product 3- commercial product not for babies, 4- traditional substance, specify).
21. Any prelacteal feed given……(yes (specify what used) 2- no)
22. Hours before first breast feed.....
23. Is current breastfeeding exclusive ……(1- yes 2- no)
24. Breast feeding schedule..... (1- on demand, 2 hour based schedule, 3- other, specify.
25. Is replacement feeding used.....(1- yes (state why), 2- no).
26. Hand washing before breast feeding.....(1 yes, always, 2- sometimes, 3- no).
27. Hand washing after changing diapers.....(1- yes, always, 2- sometimes, 3- no).
28. Hand washing before handling the neonate (mother and others)..... (1 yes, always, 2- sometimes, 3- no).
29. Exposure to sick adult/ sibling/ care giver one week prior to presenting complaint .....(1- no, 2 yes [A- respiratory symptoms, B- GIT symptoms] 3- adult discharged from hospital < 2 weeks ago.

- Presence of any one of the following signs

FEATURES	YES	NO	ANY ADDITIONS
1) Inability or refusal to breastfeed.			
2) History of convulsions.			
3) Drowsy, lethargic or unconscious			
4) RR> 60/ min on two separate counts			
5) Grunting			
6) Nasal flaring			
7) Severe lower chest wall indrawing			
8) Fever >37.5^{o}C or hypothermia< 35.5^{o}C			
9) Deep jaundice involving palms and soles of the feet			
10) Ten or more skin pustules or big abscesses.			
11) Umbilical redness extending to the periumbilical skin			
12) Pus draining form ear(s)			

C) LABORATORY RESULTS

1. FULL HAEMAOGRAM REPORT

- Date taken…….
- WBC counts……..
- neutrophil counts
    - absolute…….
    - percentage ……
- Hemoglobin level (g/dl)…….
- MCV……..
- MCH…….
- Platelet counts……
- I: T ratio……

2. BLOOD CULTURE REPORT

- Date taken.....
- Date reported.....
- Growth obtained.....(1- yes 2- no)
    - Organism(s) grown.....

      .....
    - Sensitivity

      pattern.....

      .....

    ……

THE HAEMATOLOGICAL SCORING SYSTEM.

The following cut offs were used to interpret the full haemogram;

Table 3: Cut off values for interpreting full haemaogram results using the HSS.

CRITERIA	CUT OFFS	SCORE
Total WBC (x 10^9/l)	<5 at any age	1
	≥ 25 at birth	1
	≥ 30 at 12- 24 hours age	1
	≥ 21 at 2 days and older	1
Total PMN (x 1000/mm^3)	1.8- 6.5 at birth	Score 1 if above or below range
	7- 12 at 3- 24 hours old	Score 1 if above or below range.
	4- 9 at 25- 48 hours old	Score 1 if above or below range.
	2- 7 at > 48 hours old	Score 1 if above or below range.
	No mature cells seen	2
Immature PMN (x1000/mm3)	> 1.44 at birth	1
	> 1.28 at 24 hours	1
	> 1.12 at 36 hours	1
	> 0.8 at 48 hours	1
	> 0.6 at age above 48 hours	1
I:T ratio	< 0.2	0
	> 0.2	1
I:M ratio	< 0.3	0
	> 0.3	1
Degenerative changes	Toxic granules and vacuolations	1
Platelet counts	< 150,000 cells/mm^3	1

The cut offs in table 3 were obtained from the studies by Narasimha et al [28] and Makkar et al [24]. They were also deduced from normograms from the Paediatric Hematology text by Arceci [29]. Total scores of less than 2 meant sepsis was unlikely, scores of 3-4 meant sepsis was possible and scores equal to or above 5 meant that sepsis was highly likely. The range of score is 0 to 8.

Appendix II: CONSENT FORM

Research question

The prevalence of sepsis among young infants less than 60 days old attended to in Kisii level 5 hospital.

Investigator.

Dr. Celia Muturi,

Department of Paediatrics, University of Nairobi.

Contact- 0720 800 237.

Supervisors

- Professor Francis Onyang'o, Department of Paediatrics, University of Nairobi.
- Dr. Lucy Mungai, Department of Paediatrics , University of Nairobi.

Introduction

Sepsis is one of the leading causes of death in neonates. The signs of sepsis are non- specific and a high index of suspicion is required to identify sick children with sepsis to facilitate early treatment and laboratory confirmation of sensitivity patterns.

Benefits

Early identification of infants with sepsis and initiation of prompt and appropriate antibiotic treatment. There will be no monetary compensation for participation in this study.

Risks

A blood sample will be required from the baby which will cause some discomfort.

Investigator's note

The consent form will give you a summary of the study with its benefits and risks to facilitate you making an informed decision on you and your baby's participation, which is completely voluntary. If you choose to participate, you may withdraw at any time without consequence. The results obtained will be treated with confidentiality. A link log will be used to code the participants of the study which will be kept safely.

Parent/ guardian note

I have read the above information or it has been read to me. I have had an opportunity to ask questions, which have been answered satisfactorily. If I need further clarification I can contact Dr. Muturi on her number. I consent voluntarily to participate as a subject in this study and understand that I can withdraw at anytime without affecting my continuing medical care. I understand that I will receive no monetary benefit for my participation

I, Mr., Mrs., Miss.....the parent of .....agree to the above and give my consent

I understand the purpose of the study and conditions of participation.

Sign..... Date.....

(**Witness if mother or guardian cannot read**)

I certify that.....received all the information about the study, that they understood it and freely gave their consent to participate.

Witness signature..... Date.....

Appendix III: IDHINI

Swali la utafiti

Idadi ya watoto chini ya umri ya siku sitini wanao hudumiwa Kisii level 5 ambao wanaonyesha ishara ya maradhi yanayosababishwa na viini vya bacteria katika damu.

Mpelelezi

Dr. Celia Muturi, Idara ya Madaktari wa Watoto, Chuo Kikuu Cha Nairobi

Mawasiliano; 0720 800 237

Wasimamizi

- Professa Francis Onyang'o, Idara ya Madaktari wa Watoto, Chuo Kikuu cha Nairobi.
- Daktari Lucy Mungai, Idara ya Madaktari was Watoto, Chuo Kikuu cha Nairobi.

Utangulizi

Maradhi yanayosababishwa na bacteria kwa damu husababisha maafa ya watoto wengi. Dalili za maradhi haya zinahitaji makini kugunduliwa ili matibabu yanayofaa yaanzishwe kwa wakati unaofaa na vipimo vya damu kudhibitisha aina ya viini kufanywa.

Faida

Matokeo ya utafiti huu yatasaidia hospitali kutambua watoto wagonjwa mapema na kuwaanzisha madawa yanayofaa mapema ilikuokoa maisha yao na kuwaepusha matokeo mbovu ya maradhi. Ninaelewa ya kwamba sitapewa malipo yoyote ya pesa kushiriki katika utafiti huu.

Madhara

Vipimo vya damu vitahitajika kutambua aina ya viini na kitendo ya kutoa hiyo damu itasababisha uchungu kiasi kwa motto. Kutakuwa na uangalifu kuhakikisha kwamba hatutatoa damu zaidi ya kiwango kinachohitajika.

Mkaguzi

Idhini hiii inaeleza jinsi utafiti huu utafanywa na faida pamoja na madhara zinazohusika. Hii ni kukusaidia kufanya uamuzi sahihi kabla ya kushiriki katika utafiti huu. Kushirika kwako in

hiari kabisa. Unaweza kuamua kutoshiriki na kujiondoa wakati wowote bila madhara. Matokeo ya utafiti yatashugulikiwa kwa siri. Hakuna malipo ya aina yoyote kushiriki kwa utafiti huu.

Majina ya watoto watakaoshiriki katika utafiti huu hayatawekwa wazi. Yatahifadhiwa katika kitabu ambamo nambari zitatumika kuwashiria washiriki badala ya kutumia majina yao rasmi.

Mzazi

Nimesoma habari hii au nimeelezewa na nimeelewa. Nimepewa nafasi kuuliza maswali na yamejibiwa kwa njia inayoridhisha. Nikihitaji maelezo zaidi ninaweza kuwasiliana na Dr Muturi kwa simu. Mimi nimekubali kwa hiari kushiriki kama somo katika utafiti huu na kuelewa kuwa ninahaki kutoka wakati wotote bila kuathirika.

MimiBwana/Binti/Bi.....mzazi wa.....

nimekubali yaliyoelezewa na kutoa uamuzi kwa niaba ya motto wangu kushiriki katika utafiti huu, kama ilivyoelezwa na.....

Ishara..... Tarehe.....

(Ushahidi ni wa lazima kama mzazi hawezi kusoma)

Nimethibitisha kwamba.....ameelewa kwa upana kuhusu utafiti huu na ameelewa na kupeana ruhusu ya motto wake kushiriki kwenye utafiti huu.

Shahidi..... Sahihi.....

Tarehe.....

Appendix IV: TIME TABLE

SUBMISSION FOR ETHICAL APPROVAL	NOV 2013
SEEK PERMISSION FOR STUDY	FEB 2014
DATA COLLECTION	MAR- MAY 2014
DATA ANALYSIS	JUNE 2014
THESIS WRITING	JULY 2014
THESIS SUBMISSION	AUG 2014

Appendix V: BUDGET

ITEMS	AMOUNT
SUPPLIES(STATIONERY)	KSH 2,780
PRINTING, PHOTOCOPY, PROPOSAL BOOKLET AND POSTER	KSH 38,000
TRANSPORT, COMMUNICATION AND ACCOMODATION.	KSH 118,000
RESEARCH ASSISTANT	KSH 45,000
LABORATORY PROCEDURES	KSH 285,000
STATISTICIAN	KSH 10,000

Appendix VI: KNH/UON-ERC LETTER OF APPROVAL

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KENYATTA NATIONAL HOSPITAL
APPROVED
24 FEB 2014
P O BOX 20723-00202 KNH-UON ERC

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: www.uonbi.ac.ke

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/43 Link:www.uonbi.ac.ke/activities/KNHUoN 24th February 2014

Dr. Celia K. Muturi
Dept.of Paediatrics & Child Health
School of Medicine
University of Nairobi

Dear Dr. Muturi

Research proposal: Prevalence of sepsis among young infants admitted to Kisii Level 5 Hospital (P592/11/2013)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 24th February 2014 to 23rd February 2015.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and severe adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study
This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.uonbi.ac.ke/activities/KNHUoN.**

Yours sincerely

PROF. M.L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. Prof.A.N. Guantai, Chairperson, KNH/UoN-ERC
The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Medicine,UoN
The Chairman, Dept.of Paediatrics & Child Health, UoN
The Assistant Director, Health Information, KNH
Supervisors: Prof. F.E.Onyango, Dr. L. N. Mungai Wainaina