MATERNAL FACTORS PREDISPOSING TO EARLY-ONSET NEONATAL SEPSIS AT KENYATTA NATIONAL HOSPITAL MATERNITY UNIT

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A research dissertation, submitted to the University of Nairobi, Department of Obstetrics and Gynaecology in partial fulfilment of the requirements, for the award of Master of Medicine in Obstetrics and Gynaecology

DECLARATION

This dissertation is my original work and has not been presented elsewhere, to the best of my knowledge. References to work done by others have been clearly indicated.

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CERTIFICATE OF AUTHENTICITY

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LIST OF ABBREVIATIONS

ACOG..... American College of Obstetricians and Gynaecologists

CI.....Confidence Interval

CSF.....Cerebrospinal Fluid

GBS..... Group B *Streptococcus*

EONS.....Early Onset Neonatal Sepsis

HVS.....High Vaginal Swab

IAP.....Intrapartum Antibiotic Prophylaxis

KNH.....Kenyatta National Hospital

LNMP..... Last Normal Menstrual Period

MSAF..... Meconium stained Amniotic Fluid

PROM.....Prelabour Rupture of Membranes

TSI.....Triple Sugar Iron

UNICEF..... United Nations Children's Fund

UTI..... Urinary Tract Infection

LIST OF FIGURES AND TABLES

DEDICATION

To my wife Nancy, my daughters Nyaighendia and Moraa for their perseverance.

To my parents David Nyamota and Dorcas Magoma for nurturing and support.

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ABSTRACT

Background: Neonatal sepsis, defined as sepsis within the first 28 days of life, is a major risk factor for neonatal mortality and accounts for about 1 million deaths annually. Early onset neonatal sepsis is acquired from the mother during passage through a colonised genital tract during birth. The incidence of early onset neonatal sepsis (sepsis in neonates less than 7 days old) differs in the general population and is estimated to be between 1-10 cases per 1000 live births. A study done in Kilifi, Kenya documented a prevalence of early neonatal sepsis of 13.5%.

Objective: To determine maternal factors predisposing to occurrence of early onset neonatal sepsis among mothers of 3 day old neonates admitted at the KNH New Born Unit (NBU).

Study design: This was a hospital based case- control study.

Methodology: Cases were defined as mothers of 3 day old neonates admitted in the Kenyatta National Hospital New Born Unit with a diagnosis of early onset neonatal sepsis and controls were mothers of 3 day old neonates admitted in the KNH maternity unit without a diagnosis of neonatal sepsis. Data for this study was collected using structured questionnaires, inpatient progress notes from mothers and neonates' files and laboratory microbiology results of vaginal swabs and urine cultures from the mothers. An access database was designed for data entry and SPSS version 15.0 was used for data analysis.

Setting: The study was conducted at the Kenyatta National Hospital's maternity unit.

Results: During the study period a total of 100 mothers met the eligibility criteria and were enrolled in the study. Of these 50 mothers comprised the cases and the other 50 made up the control group. Factors found to predispose to early onset neonatal sepsis were PROM (p value=0.002) and maternal genital colonisation (P-value< 0.001). maternal bacteriuria (P-value< 0.001), Commonest isolates were *E.coli, Acinetobacter*, and *Candida.* Socio-demographic and obstetric factors that were statistically significant between cases and controls were employment (p value=0.019), onset of labour (p value=0.026), meconium staining of liquor (p value=0.026) and mode of delivery (p value=0.021).

Conclusion: Maternal genito-urinary colonisation , bacteriuria and PROM predispose of early onset neonatal sepsis in the maternity unit of KNH.

CHAPTER 1: INTRODUCTION

1.1Background and Literature review

Millennium development goals four and five recognize maternal and child health as major prerequisites for international development (1). Sub-Saharan Africa is heavily burdened by unfulfilled needs in provision of quality medical care and little progress has been made in achieving millennium development goal four: a reduction in child mortality rate by two thirds by 2015 (2-3). Developing countries bears the biggest burden of neonatal mortality in comparison to developed countries. In 2004, UNICEF estimated the neonatal mortality rate (under 28 days) per 1,000 live births to be: 28 globally, 3 in industrialized countries, 31 in developing countries and 41 in Sub-Saharan Africa(4). According to the Kenya Demographic Health Survey 2009, the neonatal mortality rate was 31 deaths per 1,000 live births and the perinatal mortality rate was 37 deaths per 1,000 live births(5). At the Kenyatta National Hospital during the month of January 2011, the neonatal mortality rate was 85 deaths per 1,000 live births and the perinatal mortality rate was 129 deaths per 1,000 live births.

The world health organization estimates that 4 million neonatal deaths occur worldwide each year. More than a third of these are due to severe infections. Neonatal sepsis, defined as sepsis within the first 28 days of life, is a major risk factor for neonatal mortality and accounts for about 1 million deaths annually and early onset neonatal sepsis is defined as sepsis occurring within the first 7 days of life (6-8). The incidence of early onset neonatal sepsis differs in the general population and is estimated to be between 1-10 cases per 1000 live births(9). A study done in Kilifi, Kenya found 5.46 cases of neonatal bacteraemia per 1000 live births and a prevalence of early neonatal sepsis of 13.5% (10).

As opposed to the characteristic complication of systemic inflammatory response in adults, the definition of sepsis in neonates is contentious. Neonatal sepsis is often characterized by a fulminant course. This is because neonates have a relatively immature immune system. They have a very thin skin which is easily damaged. Their cellular immunity is similarly underdeveloped. The B cell's ability to respond to exogenous antigen by producing antibody is reduced. Phagocytotic activity of polymorphonuclear leucocytes is decreased due to reduced chemotaxis. It is therefore not possible to apply the same criteria for diagnosis as for adults. The international consensus conference held in 2002 agreed that neonatal sepsis is a syndrome resulting from metabolic and haemodynamic impairment brought about by infection. Diagnosis is based on either a positive culture from an otherwise sterile specimen (e.g. blood, CSF) or the inexplicable manifestation of multisystem clinical symptoms without a positive culture (7-8, 11).

Early onset neonatal sepsis is sepsis in neonates less than 7 days old. Late onset sepsis appears after day 8 of life (7, 12). Neonates who develop early onset sepsis invariably have history of one or more risk factors for infection acquired from the mother during parturition. Maternal and obstetric risk factors have been implicated in early onset neonatal sepsis. Infections that arise in the first week of life are transmitted vertically as a result of exposure to microorganisms in the maternal genital tract as opposed to late onset sepsis which is acquired from the environment (7, 13-15).

Intrauterine infection of the foetus results from bacteria ascending from a colonized vagina. The most important risk factors for early onset neonatal septicaemia in term pregnancies include; prolonged rupture of membranes for more than 18 hours, clinical signs of chorioamnionitis (maternal fever, unexplained uterine tenderness, purulent liquor), *Streptococcus agalactiae* bacteriuria during pregnancy ,a history of previous neonate with invasive Group B streptococcus

(GBS) disease, prolonged internal intrapartum monitoring and frequent vaginal examinations (9, 11, 13, 15-18). Bacterial vaginosis has been associated with adverse outcomes in pregnancy such as chorioamnionitis, premature rupture of membranes, amniotic fluid infection, preterm labour and delivery, urinary tract infection and post partum endometritis. It therefore contributes to early onset neonatal sepsis. This warrants early treatment for women found to be symptomatic(19). Other non specific risk factors that have been alluded to include: primiparity and early maternal age. They appear to play a role because they prolong labour thereby increasing the danger of ascending infection (6).

In the last three decades *Streptococcus agalactiae,* commonly known as group B *Streptococcus* (GBS), has been found to be responsible for high rates of morbidity and mortality in the neonatal period in industrialized countries (9, 21). Numerous studies have been focused in the prevention of group B Streptococcal infection during pregnancy and parturition. Clinical trials have led to the adoption of antimicrobial prophylaxis (16, 21-22). A risk based approach approved by the American College of Obstetricians and Gynaecologists (ACOG), the Infectious Diseases Society for Obstetrics and Gynaecology and the American Academy of Paediatrics recommend intrapartum antibiotic prophylaxis (IAP) for all preterm deliveries. As for deliveries beyond 37 weeks gestation, there are two schools of thought. One school advocates for treatment of all mothers at term with a positive culture for GBS, while the other recommends treatment based on risk factors identified as PROM for more than 18 hours or documented fever in labour. Penicillin or Ampicillin is recommended for intrapartum prophylaxis. For patients with a history of a non-life- threatening allergy to Penicillin, Cefazolin is an alternative. However, in patients with a life threatening allergy, Clindamycin or Vancomycin should be given (25).

In developed countries chemoprophylaxis is widely employed and has greatly improved perinatal outcomes. This preventive strategy was developed based on obstetric risk factors identified in these countries. The presence of maternal risk factors warrants screening of asymptomatic neonates. Current research is geared towards the development of vaccines against the common pathogens such as group B streptococcus (27-28).

A wide spectrum of pathogens is responsible for early onset neonatal sepsis in Kenya. Studies have isolated *Streptococcus agalactiae* as the most common gram positive bacteria and *Escherichia coli* as most common gram negative bacteria causing early onset neonatal sepsis (10, 20, 26).

1.2 Justification

The Millennium Development Goal number four for child survival cannot be achieved without substantial reduction in infection-specific neonatal mortality. Early onset neonatal sepsis has been recognized to significantly contribute to neonatal mortality. It is estimated that between 5-75% of neonates with early onset neonatal sepsis die within the first week of life. This is in contrast to an estimated neonatal mortality of between 10-20% attributable to late onset sepsis (2, 9). Since early onset neonatal sepsis is transmitted vertically from the mother during the intrapartum period then obstetric interventions can be employed in combating it. In some countries resources have been mobilized toward early diagnosis in mothers with risk factors and the treatment of early onset sepsis. Timely obstetric interventions have proved successful in these cases (2, 9, 20)

The burden, aetiology and risk factors (particularly maternal) responsible for early onset neonatal sepsis at KNH have not been extensively studied, hence this study was aimed at determining maternal factors that predispose to the occurrence of early onset neonatal sepsis

among mothers of 3 day old neonates admitted at the KNH New Born Unit (NBU). Findings from this study will guide strengthening and development of guidelines aimed at reducing early onset neonatal sepsis.

1.3 Research question

Does premature rupture of membranes and maternal genito-urinary colonization predispose to early onset neonatal sepsis in Kenyatta National Hospital?

1.4 Null Hypothesis

There is no correlation between maternal factors and early onset neonatal sepsis.

1.5 Objectives

1.5.1 Broad Objectives

To determine maternal factors predisposing to occurrence of early onset neonatal sepsis among mothers of 3 day old neonates admitted at the KNH New Born Unit (NBU).

1.5.2 Specific Objectives

1. To determine the association between prolonged rupture of membranes and occurrence of early onset neonatal sepsis.
2. To determine the association between maternal high vaginal swab, and urine culture result and the occurrence of early onset neonatal sepsis.
3. To determine the association between postpartum endometritis and the occurrence of early onset neonatal sepsis.
4. To determine the correlation between the occurrence of early onset neonatal sepsis with maternal socio-demographic, obstetric variables and intrapartum events.
5. To determine the bacteriologic profile of maternal genitourinary colonization in cases of early onset neonatal sepsis.

1.6 Conceptual frame work

Fig 1 Conceptual framework

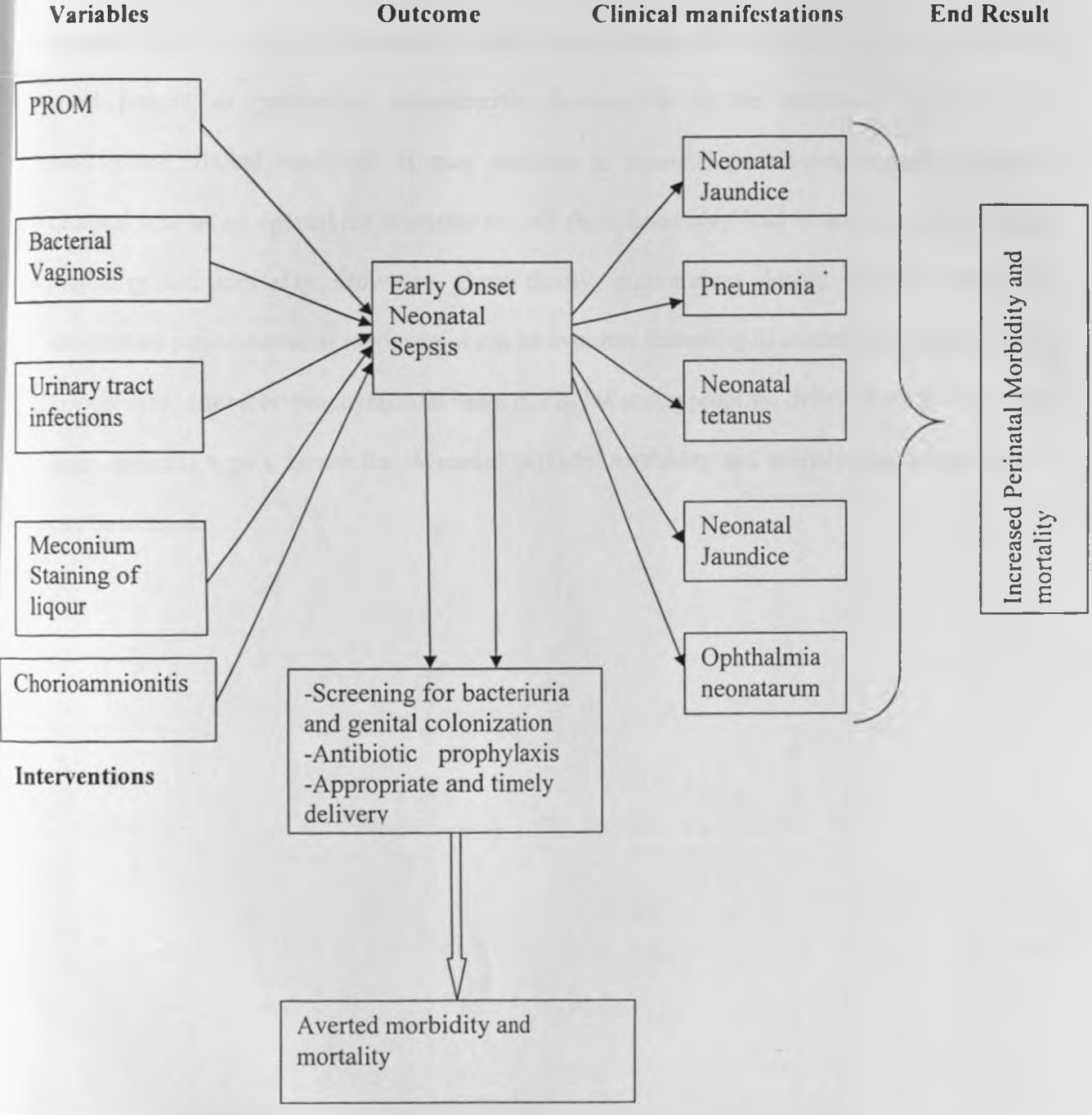


Figure 1 shows risk factors postulated to lead to early sepsis in neonates. Premature rupture of membranes, urinary tract infection, bacterial vaginosis, asymptomatic maternal genitourinary colonization and Meconium staining of liquor during parturition may predispose to early neonatal sepsis. PROM will sometimes lead to chorioamnionitis. In the postpartum period this could present as postpartum endometritis .Septicaemia in the neonates manifests as a multisystem clinical syndrome. It may manifest as neonatal pneumonia, neonatal jaundice, neonatal tetanus or ophthalmia neonatarum. All these invariably lead to an increased perinatal morbidity and mortality. However given timely interventions during the ante natal and intrapartum period neonatal septicaemia can be avoided. Screening of mothers for genito-urinary colonization, antibiotic prophylaxis in cases of PROM and appropriate delivery can prevent early onset neonatal sepsis. Hence the increased perinatal morbidity and mortality associated with it can be averted.

CHAPTER 2: METHODS

2.1 Study Site and Setting

This study was carried out at KNH maternity unit. The unit comprises of antenatal/postnatal wards, the labour ward, mothers' hostel and the NBU. KNH serves the population within and around the city and it is the national referral hospital. It also serves as the university teaching hospital for the College of Health Sciences of the University of Nairobi and the Kenya Medical Training College. The maternity unit caters for about 8000 deliveries annually. The antenatal/postnatal wards are three in number each with a 32 bed capacity. Each of these wards falls under one of the three firms which are headed by a senior consultant Obstetrician and Gynaecologist, who together with a team of senior registrars, registrars, interns and other paramedical staff run the wards. The KNH maternity unit serves mothers of diverse income and socio-economic groups.

Kenyatta National hospital has fully functional laboratories. In addition to this the Department of Obstetrics and Gynaecology of the University of Nairobi has a research laboratory. After delivery all newborns are reviewed by the paediatrics registrar who makes a decision whether or not to admit the newborn to NBU. In addition to direct admissions of new borns to NBU from KNH labour ward, babies born before arrival to the hospital are also reviewed and admitted to NBU if necessary. The diagnosis of neonatal sepsis is made by clinicians in the NBU and recorded in the admission book.

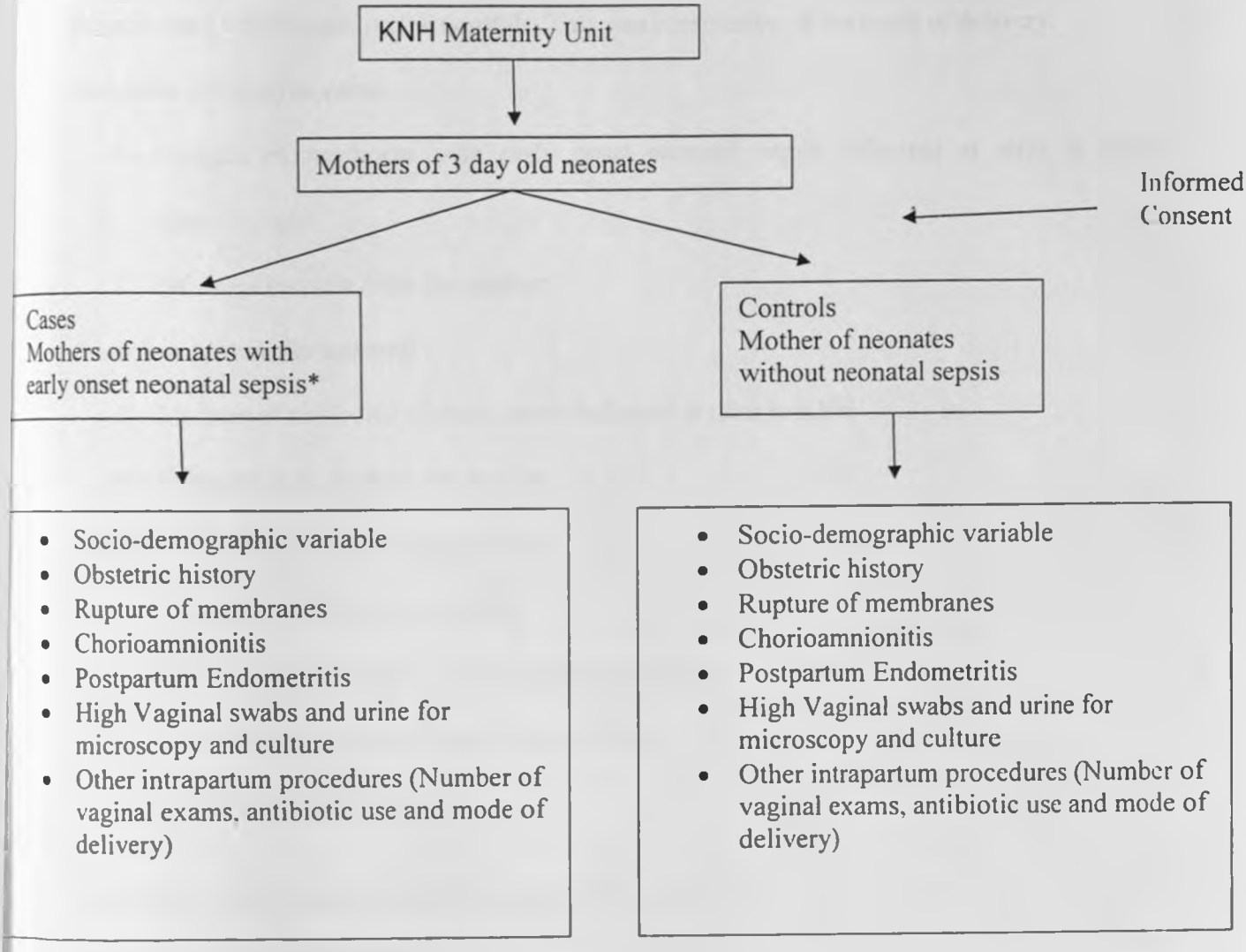
This site was suitable for this study because of the availability of the NBU in the facility where all cases of early onset neonatal sepsis are admitted. This would ensure an adequate number of participants due to the volume of admissions into the unit. The availability of a functional laboratory would also ensure that specimens were delivered promptly.

2.2 Study Design

This was a hospital based unmatched case-control study. This design was suitable as the study aimed at finding associations between maternal factors predisposing to early onset neonatal sepsis and the development of septicaemia in the neonates. The retrospective nature of this study meant that a case-control design would be ideal as neonates with early onset sepsis and those without were identified before looking back to their mothers to determine which factors predispose the newborns to septicaemia. The results from this study provide an estimate of strength of association between maternal risk factors and the occurrence of early onset sepsis in their neonates.

The enrolment algorithm is shown in figure 2

ıre 2 Enrolment Algorithm



* Diagnosis of neonatal sepsis was made according to the KNH NBU protocol by paediatricians caring for the neonates.

2.3 Study Population

The study participants were mothers of three day old babies admitted in the KNH maternity unit. Mothers of newborns admitted with early onset sepsis in the newborn unit who met the eligibility criteria constituted the cases. The mothers of three day old newborns without sepsis admitted in the postnatal wards made up the controls. This was irrespective of the mode of delivery.

Inclusion criteria for cases

1. Mothers of newborns with early onset neonatal sepsis delivered at term in KNH maternity unit
2. Informed consent from the mother

Inclusion criteria for controls

1. Mothers of newborns without sepsis delivered at term in KNH
2. Informed consent from the mother

Exclusion criteria for cases and controls

1. Mothers with preterm babies
2. Mothers of neonates with congenital anomalies
3. Mothers of neonates born before arrival
4. HIV-infected mothers

2.4 Sample Size Calculation and Sampling Procedure

2.4.1 Sample size calculation

In calculating the sample size OpenEpi epidemiologic calculator's software was used from the Centres for disease Control Website (29). A prevalence of early neonatal sepsis of 13.5% from a study done in Kilifi Kenya was used (10).

Using Fleiss with continuity correction formula a minimum total sample size of 100 (50 cases and 50 controls) was arrived at to achieve a 95% confidence interval and a power of 80%.

2.4.2 Sampling Procedure

Convenience sampling was used. All the eligible cases were enrolled during the study period until the desired sample size of 50 cases and 50 controls was arrived at. This sampling procedure minimized selection bias by consecutively enrolling any mother who meets the eligibility criteria.

2.5 Data collection and Management Methods

Two Clinical Officers working in the postnatal wards were engaged in data collection in this study. They were trained by the Principal Investigator on data collection. Neonates with early onset neonatal sepsis were identified in the NBU. Their mothers were then followed up in the postnatal wards or the mothers' hostel. If they met the eligibility criteria they were enrolled into the study after informed consent. Mothers of newborns without sepsis who were still in the wards on the third postnatal (or post operative day following caesarean delivery) were also recruited into the study. The study instrument comprised of a structured questionnaire and data abstraction form. The structured questionnaire was administered to collect maternal socio-demographic characteristics. The structured data abstraction form was used for to extract information on intrapartum events. The complete questionnaire and data abstraction form is attached as appendix II.

Clean catch midstream urine and high vaginal swab samples were then obtained from the participants and conveyed to the laboratory for processing.

All identifiers were removed from the forms and data was coded. An access database was designed for data entry. The obtained data was entered into the data base by the principal investigator and the biostatistician. All patient paper records were kept in locked cabinets and electronic records within the database were password protected. Only the biostatistician and Principal Investigator had access to them.

2.5.1 Definitions

- Early onset neonatal sepsis was defined as a case if a bacterial pathogen is isolated from a normally sterile site (blood or CSF) from a neonate in the first 72 hours of life or clinical suspicion in a symptomatic newborn (poor feeding, lethargy, irritability, fever, hypotension, respiratory distress).
- Gestational age was determined by the LNMP as given by the mother or by obstetric ultrasound anthropometric measurements before twenty weeks gestation.
- Preterm delivery was defined as delivery at any gestational age before thirty seven completed weeks.
- Premature rupture of membranes was defined as drainage of liquor before onset of labour.
- Chorioamnionitis was diagnosed in the presence of acceptable clinical signs such as an intrapartum fever (37.8°C) with two or more of the following: foetal tachycardia, uterine tenderness, malodorous vaginal discharge or maternal leucocytosis (> 15,000 leucocytes/ μL).
- Post partum endometritis was diagnosed when at least two of the following signs were present; fever ≥38□, foul smelling lochia, uterine tenderness or poor uterine involution.
- Prolonged premature rupture of membranes (PROM) was defined as PROM more than eighteen hours.
- Inborns are the babies born in KNH while outborns are babies referred to KNH or those born before arrival to hospital.

2.5.2 Laboratory procedures

After obtaining informed consent from the mothers, urine and high vaginal swab specimens were obtained. A clean catch midstream urine sample, from each mother, was collected into sterile bottles. These samples were diluted with normal saline and plated on CLED agar (Oxoid ,UK). Urine samples with ten or more bacteria per millimetre were cultured on MacConkey agar and incubated at 37° C for 24 hours. Bacteria resembling Gram negative rods were inoculated onto TSI agar before final speciation is done. High vaginal swabs were taken near the fornices with plain swabs then put in Stuart transport media and conveyed to the laboratory .They were plated onto blood agar as soon as possible and then onto a modified Thayer – Martin medium. After 24 hours of incubation, colonies were identified by morphology, gram stain and biochemical methods.

2.6 Ethical Considerations

This proposal was submitted to the Kenyatta National Hospital/University of Nairobi Institutional Research and Ethics Committee for approval.

There was little perceived risk to the patients in this study. Neonates were managed according to the KNH protocol and did not participate in this study only their progress notes were reviewed. Consent to collect high vaginal swab and urine a sample was sought from the mothers. A treatment prescription was given to the mothers whose samples were found to grow organisms. The study did not however buy these medications for them.

Confidentiality was maintained by the research assistants who were be trained by the Principal Investigator on ethical issues before the start of the study. All patient paper records were kept in locked cabinets and electronic records within the database were password protected, and only data entry personnel, clinicians overseeing the database, and researchers involved on this project

had access. In addition, patient names and identifiers were removed from all data tables and records prior to data analysis. Written informed consent (appendix IV) was obtained. Patients were free to leave the study any time they felt uncomfortable without any penalties or loss of any benefits to which they are entitled to them in the hospital.

Patients participated in the study at no cost and no incentives in form of money or otherwise were offered to the participants. Laboratory charges were paid by the study. While there is no direct benefit expected for the neonate, establishing maternal risk factors associated with early neonatal sepsis will help in developing and strengthening guidelines for preventing early neonatal sepsis and will form a basis for future studies.

2.7 Limitations of the study

Recall bias, misclassification and missing data are the main limitations in this study. Recall bias was minimized because data was collected within the first 3 days postpartum. Misclassification was minimized by using case definitions described under data collection and management section. Some missing data was a big challenge because of the retrospective nature of data collection using patient progress notes especially in documenting intrapartum events. The sample size was also a challenge as it was not sufficiently powered. It was not practicable to screen for GBS in the study due to lack of appropriate media.

2.8 Data Analysis and Presentation of Results

Only de-identified data was analyzed using SPSS version 15.0.

Primary Outcome results: The correlation between the occurrence of early onset neonatal sepsis with maternal socio-demographic, obstetric variables and other intrapartum factors (number of vaginal exams, intrapartum antibiotic use and mode of delivery) were determined. Analysis was carried out to compute chi square and p-values to test for the level of statistical significance.

Secondary Outcome results: Association between prolonged rupture of membranes, maternal high vaginal swab and urine culture result and postpartum endometritis and the occurrence of early onset neonatal sepsis were determined. Statistical significance was determined by use of p-values, confidence intervals and odds ratios.

Results are presented in form of tables and pie charts.

CHAPTER 3: RESULTS

This study was carried out between 14th April and 13th May 2011. During the study period a total of 100 mothers met the eligibility criteria and were enrolled in the study. Of these 50 mothers comprised the cases and the other 50 made up the control group.

3.1 Primary outcome analysis

Table 1 Socio-demographic characteristics of the participants by Cases and Controls

Variable	Characteristics	Cases (N)	Controls (N)	Chi-Square	P-Value
Age	20-24 Years	14	13	1.544	0.819
	25-29 Years	17	13		
	30-34Years	12	13		
	35-39 Years	6	9		
	40-44 Years	1	2		
Marital status	Married	40	44	3.276	0.194
	Separated	0	1		
	Single	10	5		
Employment	Yes	28	39	5.473	0.019
	No	22	11		
Form of Employment	Salaried	7	20	9.604	0.008
	Self Employed	22	19		
Level of Education	College/University	13	16	3.489	0.175
	Primary	12	5		
	Secondary	25	29		

The socio-demographic characteristics of the cases and control groups are presented in table 1. Analysis of the socio-demographic variables revealed that employment and the form of employment had an association with the development of EONS .On the contrary age, marital status and level of education were not significant risk factors for the development of early onset neonatal sepsis (p value > 0.05).

Table 2 Obstetric and intrapartum variables by Cases and Controls

Variable	Characteristics	Cases (N)	Controls (N)	Chi-Square	P-Value
Parity	Para 1	29	18	6.855	0.077
	Para 2	3	9		
	Para 3	2	1		
	Primigravida	16	22		
PROM	Yes	23	7	14.906	0.002
	No	25	34		
	Not Indicated	2	6		
Number of Vaginal Examinations	<3	26	22	0.641	0.423
	>3	24	28		
Mode of delivery	Elective Caesarean	2	11	7.709	0.021
	Emergency Caesarean	26	18		
	Spontaneous Vertex	22	21		
Onset of labour	Induced	18	12	5.383	0.0268
	Spontaneous	31	39		
Liquor appearance	Clear	33	43	5.482	0.0268
	Meconium Stained	17	7		
Meconium stained amniotic fluid	1	4	3	7.03	0.071
	2	10	4		
	3	3	0		

Obstetric and intrapartum variables that showed statistically significant differences between the cases and controls were onset of labour, liquor appearance and mode of delivery. There was a strong association between presence PROM and neonatal septicaemia. Other factors not found to be significant (p value > 0.05) were parity, the number of vaginal examinations, and the grade of MSAF.

3.2Secondary outcome analysis

Analysis of results determined associations between PROM, maternal genital colonization, bacteriuria, and postpartum endometritis (as shown in tables 1 to 4.) and occurrence of neonatal sepsis.

Table 3 Duration of PROM by Cases and Controls

Duration Of PROM	Cases (n=23)	Controls(n=7)	Odds Ratio	P-Value
≤18 Hrs	15 (65%)	6 (86%)	0.31	0.3
> 18 Hrs	8 (35%)	1 (14%)		

Table 3 presents the duration of PROM in the cases and controls. In the cases, 65% had PROM for 18 hours or less while 35% had it for more than 18hours.There was prolonged PROM in 14% of the controls. There was no difference in the duration of PROM between the cases and controls.

Table 4 Microbiological culture results of High Vaginal Swabs by Cases and Controls

Culture Result	Cases (n=50)	Controls (n=50)	Odds Ratio	P-Value
Growth obtained	18 (36%)	2 (4%)	13.5	<0.001
No Growth	32 (64%)	48 (96%)		

Table 4 presents microbiological culture results of high vaginal swabs of the cases and controls. Among the cases 36 % had a positive growth as compared to 2% in the control group.There was a statistically significant difference between the case and controls. This meant that there is a strong association between maternal genital tract colonization and early onset neonatal sepsis.

Table 5 Microbiological culture results of Urine Cultures by Cases and Controls

Culture Result	Cases (n=50)	Controls (n=50)	Odds Ratio	P-Value
Growth obtained	18 (36%)	2 (4%)	13.5	<0.001
No Growth	32 (64%)	48 (96%)		

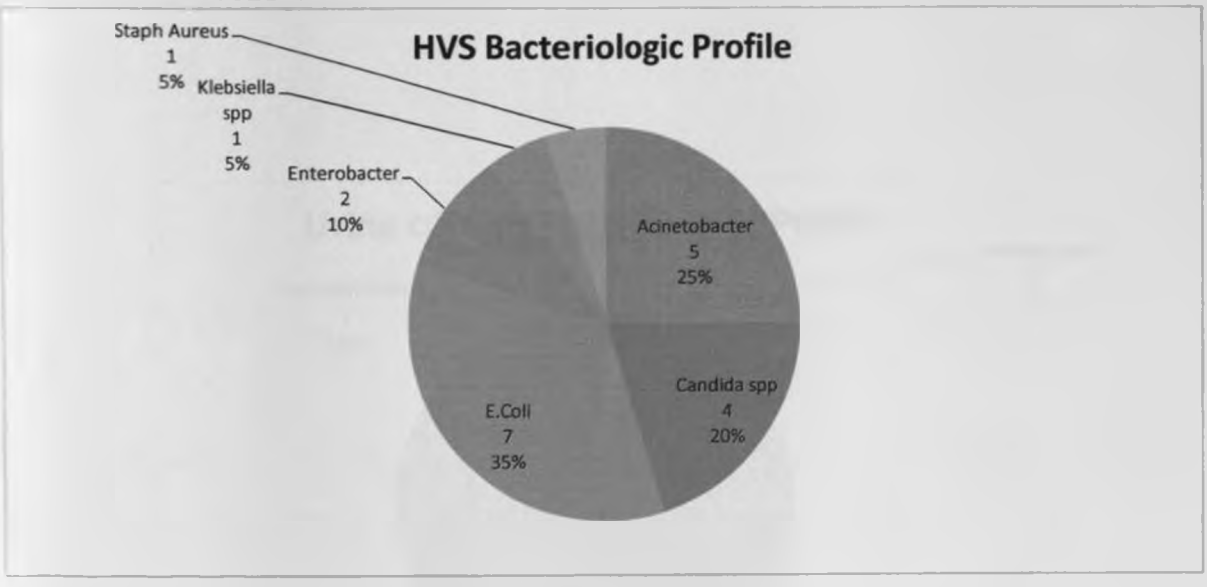
Table 5 presents urine presents microbiological culture results. Of the fifty participants in the cases group 36% had a positive growth while 2% had bacteriuria in the control group.Analysis shows that there was a statistically significant difference between the cases and controls. Therefore maternal bacteriuria predisposes to sepsis in neonates.

Table 6 Presence of Postpartum endometritis in Cases and Controls

Presence of Postpartum endometritis	Cases (n=50)	Controls (n=50)	Odds Ratio	P-Value
Postpartum endometritis	11 (22%)	10 (20%)	1.6	0.8
No Postpartum endometritis	39 (78%)	40 (80%)		

Table 6 shows the presence of post partum endometritis in the cases and controls. In 22% of the cases there was postpartum endometritis as opposed to 20% of the controls. There was no significant statistical difference between the two groups.

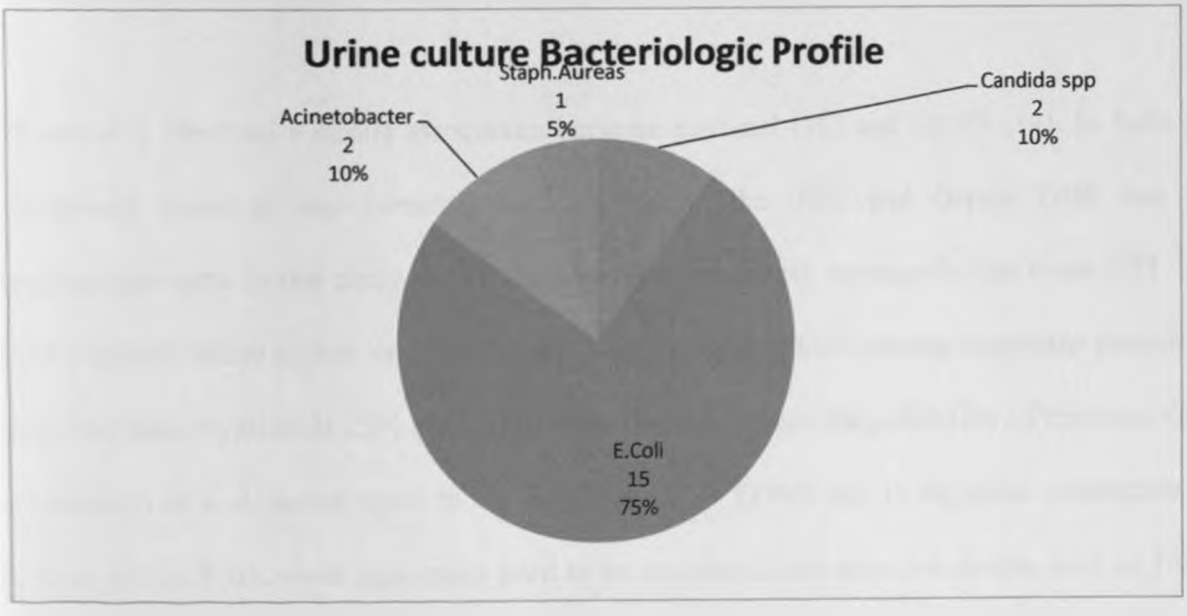
Fig 3 Bacteriologic Profile of High Vaginal Swab of Participants with a positive culture (n=20)



Pie chart shows the bacteria cultures of high vaginal swabs obtained from the participants. Out of the one hundred participants in this study, twenty had a positive culture. Of these two were in the control group.

E.coli constituted 35% followed by *Acinetobacter* 25%, *Candida spp* 20% and *Enterobacter* 10%. *Klebsiella* and *S.aureus* were each isolated from 5% of these participants.

Fig 4 Bacteriologic Profile of Urine Culture of Participants with a positive growth (n=20)



Pie chart shows the bacteria isolated from urine sample of the participants. Twenty out of the hundred mothers yielded a positive culture. *E.coli* was the most common isolate in fifteen mothers. This comprised 75% of the positive cultures. This was followed by *Acinetobacter* and *Candida spp* each at 10%. *S.aureus* was isolated from one mother. Among the twenty mothers with a positive urine culture, two were in the control group.

CHAPTER 4: DISCUSSION

Results from this study show a strong association between early onset neonatal sepsis and maternal genital colonization and bacteriuria. This is in tandem with studies done in India Greece and USA (6, 12, 14, 16). The presence of PROM actually predisposes to infection of the neonates, however the duration of PROM and postpartum endometritis were not found to play a role in the occurrence of early onset neonatal sepsis in our setting. This was in contrast to other studies which identified these risk factors as important predictors in the development of sepsis among neonates in the first 72 hours (6-7, 13, 17).

Bhutta et al observed a strong association between maternal UTI and EONS (14). In India the commonest organism was *pseudomonas*, whereas in the USA and Greece GBS was the predominant agent In our study not all mothers with bacteriuria necessarily had overt UTI. The most common isolate in this study was *E.coli.* A prevalence of GBS among expectant mothers in KNH has been reported as 25% (28). This study did not explore the possibility of maternal GBS colonization as a causative agent in the development of EONS due to logistical constraints. In order to culture GBS, swab specimens need to be inoculated into selective media, such as Todd-Hewitt, and supplemented with colistin and nalidixic acid subculturing on to blood agar plates 18 to 24 hours later. This was difficult to carry out in our study given the limited budget. This is a possible area for future research.

Mothers with PROM are twice more likely to deliver babies with EONS in KNH. In our study 23 out of 50 neonates with sepsis were born of mothers with PROM. This compared with results

from Nepal where the prevalence of septicaemia among neonates of mothers with PROM was at 46% (10).

Analysis of socio-demographic variables found that the form of employment was associated with the development of EONS. This is probably due to the ability to access medical care. Mothers with a steady income are empowered and are likely to seek medical attention promptly. Surprisingly the level of education was found not to play a significant role between the cases and controls. Additionally there was no association between age and marital status with an increased risk of EONS. Seaward et al, in their study, found that variables not associated with neonatal septicaemia included parity, number of vaginal examinations, mode of delivery and MSAF (17).These findings were similar to the results of this study.

In many countries strategies have been formulated to prevent early onset sepsis in neonates based on results of studies done in these countries assessing maternal risk factors. Some of these findings cannot be extrapolated to our settings because of differences in socio-demographics and the kind of micro organisms likely to cause these infections.

Conclusions

From the results of this study it can be concluded that:

1. Maternal genito-urinary colonisation and bacteriuria predispose to early onset neonatal sepsis in the maternity unit of KNH.
2. Among the intrapartum events the presence of PROM is associated with sepsis.
3. The duration of rupture of membranes is not directly related to the development of neonatal septicaemia.
4. Meconium stained liquor predisposes to early onset neonatal infection.

Recommendations

1. Mothers should be routinely screened for bacteriuria and genital colonization and be treated to prevent their newborns from acquiring neonatal sepsis during parturition.
2. Neonates born of mothers with Meconium stained liquor should be followed up closely immediately after birth because they are predisposed to infection.
3. More research should be carried out in this area especially the role of GBS in EONS. Many countries have linked GBS to sepsis in neonates. Studies should also be done to determine the most efficacious treatment for maternal genital colonisation in our setting.

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Appendix I: Questionnaire

Study Title: Maternal Factors predisposing to Early-Onset Neonatal Sepsis at Kenyatta National Hospital Maternity Unit.

A) Data Abstraction form (Neonates File) *Serial Number* ----------

1) Early onset neonatal sepsis Yes ☐ No ☐

(If Yes mother is a case; if No mother is a control)

2) If yes to number 1, how was the diagnosis of early onset neonatal sepsis made?

Culture result ☐

Clinical diagnosis ☐

Other ☐

3) Sex Male ☐ Female ☐ **Weight** ----------

B) Data Abstraction form (Mothers File)

Serial Number ---------- *(same serial number as for neonate above)*

1) Classification Case ☐ Control ☐

2) Parity before delivery

Primigravida ☐ Para 2 ☐ Para 3 ☐ Para 4 ☐ >para 4 ☐

3) Did the patient have PROM? Yes ☐ No ☐ Not indicated ☐

4) If yes to number 3 what was the duration of PROM?

Less than 18 hours ☐ More than 18hours ☐

5) Was the patient managed for chorioaminionitis? Yes ☐ No ☐

6) Number of vaginal exams during labour

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐ More than 10 ☐

7) Was the mother given antibiotics during labour?

Yes ☐

No ☐

8) What was the mode of delivery?

Spontaneous vertex delivery ☐

Assisted vaginal delivery ☐

Emergency caesarean ☐

Elective caesarean ☐

9) Onset of labour

Spontaneous ☐

Induced ☐

10) Liquor appearance

Clear ☐

Meconium stained ☐

12) If meconium stained for 10 above which grade

1☐ 2☐ 3☐

13) Did the liquor have a foul smell?

Yes ☐

No ☐

Not indicated ☐

14) Was there foul smelling lochia after delivery?

Yes ☐

No ☐

C) Questionnaire to the mother

1) How old are you? ----------

2) What is your marital status?

Married ☐ Single ☐ Widowed ☐ Divorced ☐ Separated ☐

3) Are you employed? Yes ☐ No ☐

4) If yes to 3 above what form of employment?

Self employed □ salaried employment ☐

5) What is your level of education?

Primary ☐ Secondary ☐ College/university ☐ None ☐

D) Laboratory test (Mother)

1) High vaginal swab culture result

No growth obtained ☐

Growth obtained:

☐ specify----------

2) Urine culture result

No growth obtained ☐

Growth obtained:

☐ specify----------

Appendix II: Budget

ITEM	QUANTITY	UNIT COST (KSH)	TOTAL COST(KSH)
PROPOSAL DEVELOPMENT			
Printing paper	3 Reams	360	1,080
Printing	240 Sheets	5	1,200
Binding- soft Cover	6 Copies	100	600
Sub-Total			**2,880**
PERSONNEL			
Clinical Officers	2	5,000 per month	20,000
Biostatistician	1	30,000	30,000
Sub-Total			**50,000**
TRAINING OF RESEARCH ASSISTANTS			
Note books	10	50	500
Ball Point pens	12	15	180
Pocket files	10	50	500
Stapler	1	200	200
Staples	1 Pack	200	200
Paper Punch	1	400	400
Permanent Marker pens	1 Pack	400	400
Sub-Total			**2,380**
DATA COLLECTION			
Printing Paper	10 Reams	360	3,600
Printing	40 sheets	5	200
Photocopying	4,000 Sheets	2	8,000
File folders	400	30	12,000
Gloves	5 Boxes	170	850
Wire loop and handle	1	750	750
Petridishes	50	200	10,000
HVS swabs	120	25	3000
Urine containers	120	10	1200
Polypots	300	3	1500
Disposable Cuscos speculums	120	50	6000
CLED agar	500g	5000	5000
MacConkey agar	500g	5200	5200
TSI agar	500g	4500	4500
Sub-Total			**61,800**
FINAL REPORT			
Printing Paper	2 Reams	360	720
Printing	1000 Sheets	5	5,000
Binding- Hard Cover	6 Copies	500	3,000
Sub-Total			**8,720**
Total			**125.330**
Contingencies(10% of total)			**12,533**
Grand Total			**137863**

Appendix III: Informed Consent

This consent form was read and explained to each prospective participant. Two copies of the consent form were signed (thumbprint); one copy to be kept by the research team and another copy to be given to participant.

Purpose of the study

We are interested in finding out the association between maternal risk factors and early onset neonatal sepsis (infection) at Kenyatta National Hospital. This work will help in prevention of infection among newborns in future.

Procedures in the study

Only mothers will participate in this study. No neonate will participate in this study. Mothers with 3 day old neonates with early onset neonatal sepsis and those without early onset neonatal sepsis will be enrolled in the study. If you accept to take part in this study the following will be asked of you:

1) After signing or putting your thumbprint on this consent form, we will take some baseline information from you. This information will be kept in confidence by the trial team.
2) We will ask for urine and a high vaginal swab sample which will be taken to the laboratory (the study will pay for laboratory charges).
3) The result of the sample will be communicated to you and a treatment prescription will be offered if deemed necessary. This study will however **NOT BUY MEDICATION FOR YOU.**

Your involvement in this study is entirely voluntary and if you decide not to take part, it will not affect the medical treatment you or your family gets in any way. If you decide to join the study, you are free to leave the study at any time without explanation. All information you provide or that is taken from your medical records will be treated under complete confidentiality.

Consent

This explanation of the study was given by

Name: ----------Date: ----------

Name of participant: ----------

I agree to take part in this study and I understand that participation is voluntary and will not affect any medical treatment entitled to my child, family and I in any way and all information will be kept confidential.

Signature: ----------Date: ----------

Signature of Witness: ---------- Date: ----------

Appendix IV: Institutional Ethical Research Approval

KENYATTA NATIONAL HOSPITAL
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P.O. Box 20723, Nairobi.
Tel: 726300-9
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Ref: KNH-ERC/ A/88

14th April 2011

Dr. George Kwame Orwenyo
Dept. of Obs/Gynae
School of Medicine
University of Nairobi

Dear Dr. Orwenyo

RESEARCH PROPOSAL: "MATERNAL FACTORS PREDISPOSING TO EARLY-ONSET NEONATAL SEPSIS AT KENYATTA NATIONAL HOSPITAL MATERNITY UNIT" (P5/01/2011)

This is to inform you that the KNH/UON-Ethics & Research Committee has reviewed and approved your above revised research proposal for the period 14th April 2011 – 13th April 2012.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimens must also be obtained from KNH/UON-Ethics & Research Committee for each batch.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of the data base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely,

PROF A N GUANTAI
SECRETARY. KNH/UON-ERC

c.c. The Deputy Director CS, KNH
The HOD, Records, KNH
Dean, School of Medicine, UON
The Chairman, Dept. of Obs/Gynae, UON
Supervisors: Prof. James B.O. Oyieke, Dept. of Obs/Gynae, UON
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