CHAPTER 1: BACKGROUND

Neonatal sepsis is one of the most common cause of neonatal morbidity and mortality. It is estimated to cause 26% of all neonatal deaths worldwide (Lawn *et al*, 2005).It's Incidence varies from country to country but is much higher in developing countries (Kaistha *et al,* 2009) where it is responsible for about 30-50% of the total of neonatal deaths (Bang *et al,* 1999).It is one of the most common reasons for admission to neonatal units in developing countries (Shitaye *et al*)

Neonatal sepsis refers to generalised bacterial infection documented by a positive blood culture in the first 28 days of life. It encompasses various systemic infections of the new born such as septicaemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections. Superficial infections like conjunctivitis and oral thrush are not usually included under neonatal sepsis (Report of the national neonatal perinatal database, National neonatology forum 2002-2003)

Sepsis can be classified into 2 types according to the age of onset; early onset sepsis and late onset sepsis. Early onset sepsis presents within the first 72 hours of life and in severe cases the neonate may be symptomatic at birth. The source of infection for early onset sepsis is usually the maternal genital tract (Singh *et al*, 1994). Late onset sepsis presents after 72 hours of age. It is usually nosocomial as a complication of neonatal intensive care or community acquired. This classification is important as it helps in determining the most probable organism and mode of transmission. This guides empiric treatment (Forfar and Arneil's textbook of paediatrics, 6th edition)

The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region even within the same hospital. This is due to the changing pattern of antibiotic use and changes in lifestyle (Shrestha *et al, 2013*).The local epidemiology of

neonatal sepsis should be constantly updated to detect changes in the pattern of causative organisms and their susceptibility to various antibiotics. Early diagnosis and proper management of neonatal sepsis by rational antimicrobial therapy and supportive care can reduce mortality. Blood culture is the gold standard for diagnosis of sepsis but blood culture reports are usually available after 48 to 72 hours. There is need to Identify the common bacteria causing such infections in every hospital and their susceptibility patterns in order to provide necessary information for timely intervention (Shrestha *et al* 2013).

Since the discovery of antimicrobial agents, microorganisms have developed resistance to them though mechanisms such as mutations and increased enzyme production. Resistance to commonly used antibiotics is an important problem worldwide.

CHAPTER TWO: LITERATURE REVIEW

2.1 Introduction

The number of neonatal patients at risk of acquiring nosocomial infections is increasing because of the improved survival of very low birth weight infants and their need for invasive monitoring and supportive care (Adams- Chapman *et al,* 2002)

The World Health organisation(WHO) reported in 2005 that over 70% of deaths in children under age five occur within the first year of life and 40% occur within the first month (WHO, World Health Report 2005. Make every mother and child count. Geneva: WHO; 2005.p.2005)

Neonatal infections currently cause 1.6 million deaths annually in developing countries. Sepsis and meningitis are responsible for most of these deaths. (Vergnano *et al,* 2005)

According to the World Health Organisation (WHO) Global health Observatory Data repository the neonatal mortality rate in Africa in 2012 was 32 per 1000 live births and 27 per 1000 live births in Asia. In the same report the Americas recorded a neonatal mortality rate of 8 per 1000 live births.

In the Kenya Demographic and Health Survey (KDHS) of 2008/2009 the neonatal mortality rate stood at 31 per 1000 live births.

2.2 Causative bacteria

The causative organisms include a wide variety of gram positive and gram negative organisms. These include *staphylococcus aureus*, coagulase negative *staphylococcus (*CONS*),Escherichia coli (Ecoli)*, *Listeria monocytogenes*, *Klebsiella pneumoniae*, Group B

*streptococcus(*GBS*)*, *Acinetobacter*, *Serratia*, *Pseudomona*s, *Haemophilus influenzae*, *Enterobacter, Candida* and anaerobes.

In many hospitals gram positive organisms cause upto 70% of nosocomial infections in neonates (Patel *et al,* 2010)with coagulase negative Staphylococci accounting for more than half of these(Van der Zwet WC *et al,* 2005). In developing countries gram negative organisms may be far more prevalent as neonatal pathogens (Couto *et al* 2007).GBS is generally rare or not seen at all although maternal recto-vaginal carriage rates of GBS may be similar to those recorded in developed countries. In most of the African studies the incidence of GBS is low with the exception of South Africa. In Asia GBS is also reported to be extremely rare. Neonatal surveillance in developed countries generally identifies GBS and *Ecoli* as the dominant early onset sepsis pathogens and CONS as the dominant late onset sepsis pathogen followed by GBS and staphylococcus aureus. (Vergnano *et al,* 2005).

A retrospective study done in a neonatal intensive care unit in Australia by Sanghvi *et al* over a 5 year period showed that CONS (38.8%), GBS (20.1 %)and gram negative bacilli (GNB)(20.1%), were the common causes of sepsis. (Sanghvi *et al,*1996)

A retrospective review of 390 neonatal blood cultures carried out by Iregbu *et al* in the department of Clinical Microbiology and Parasitology of a tertiary hospital in Nigeria in the year 2006 showed gram positive cocci (GPC) and GNB in almost equal proportion. Predominantly *Klebsiella pneumoniae*(86% of GNB) and *Staphylococcus aureus* (81% of GPC) (Iregbu *et al,*2006).

In a prospective study done in a Kenya by Musoke *et al* over a 5 month period in the year 2000 the predominant organisms were gram negative(73.6 percent of isolates) with *klebsiella* species topping the list at 31 percent.(Musoke *et al*,2000).

2.3 Risk Factors

Some of risk factors for neonatal sepsis include; prematurity or low birth weight, preterm labour, premature or prolonged rupture of membranes, maternal chorioamnionitis, foetal hypoxia, traumatic delivery, male gender and low socio-economic status.

2.4 Clinical features.

Neonates with sepsis may have nonspecific signs and symptoms and the initial manifestations may have limited symptomatology. Some of the features include temperature instability, hypotension, tachycardia, bradycardia, apnoea, respiratory distress, grunting, cyanosis, irritability, lethargy, seizures, feeding intolerance, abdominal distension and jaundice (Nelson Textbook of Paediatrics, 17th edition, 2004)

2.5 Diagnosis of neonatal sepsis

Neonatal sepsis is clinically diagnosed by a combination of clinical signs, nonspecific laboratory tests and microbiologically confirmed by detection of bacteria in blood by culture (Marchant *et al,* 2013)

Blood culture is the gold standard for diagnosis of septicaemia.

2.6 Antimicrobial management

There cannot be a single recommendation for the antibiotic regimen of neonatal sepsis for all settings. The choice of antibiotics depends on the prevailing flora in the given unit and their antimicrobial sensitivity. The decision to start antibiotics is based on clinical features and or positive septic screen. (Sankar *et al*, 2008)

The antibiotic combination prescribed in most units is a penicillin (Benzyl penicillin, ampicillin or cloxacillin) together with an aminoglycoside most commonly gentamicin (Vergnano *et al,* 2005)

2.7 Antibiotic resistance

Resistance to antibiotics is a global problem. Reports of multiresistant bacteria causing neonatal sepsis in developing countries are increasing and this may be explained by the wide availability of over the counter antibiotics and the inappropriate use of broad-spectrum antibiotics in the community. (Jyothi *et al,* 2013). At risk are unwell babies or premature babies, those needing additional support such as ventilation, intravenous fluid or blood products and those babies who stay in hospital for more than 48 hours (Al Rabea AA *et al*, 1998).Spread of resistant organisms in hospitals is a recognised problem although babies admitted from the community may also carry resistant pathogens (Bhutta, 1996)

It is difficult to compare antibiotic resistance between countries because the epidemiology of neonatal sepsis is extremely variable (Vergnano *et al*, 2005). Methicillin resistant staphylococci, Extended spectrum beta lactamase (ESBL) and multidrug resistant gram negative organisms represent the principal concern for clinicians who have to fight against infections (Paolucci *et al,* 2012). Most gram negative bacteria are now resistant to ampicillin and cloxacillin and many are becoming resistant to gentamicin (Vergnano *et al*, 2005).

A retrospective study carried out by Iregbu *et al* in the Department of Clinical Microbiology and Parasitology of a tertiary hospital in Nigeria in the year 2006 showed that 89% of staphylococcus aureus were sensitive to amoxicillin- clavulanic acid while 85%, 45%, 71% and 64% were sensitive to cefuroxime, ciprofloxacin, chloramphenicol and erythromycin respectively. The only three isolates tested against tetracycline were all susceptible to the drug. The resistance to penicillin was 90%.Resistance to ceftazidime, ceftriaxone and

gentamicin were 71% ,64% and 60% respectively. The resistance of the isolated *Klebsiella pneumoniae* to ceftazidime, ceftriaxone and cefotaxime was 85%, 87.5% and 94% respectively. Resistance to amoxicillin and ampicillin-sulbactam was 100%, and 85% for amoxicillin-clavulanic acid. All (100%) of the *Klebsiella pneumoniae* isolates tested against imipenem were susceptible while 75% were susceptible to amikacin. (Iregbu *et al,* 2006)

A study done over a 5 month period in the year 2000 in a neonatal unit of a referral hospital in Kenya by Musoke *et al* showed that resistance to gentamicin was 20%, chloramphenicol 23.6 %, and amoxicillin /ampicillin 66.3%, ceftazidime 19.1 %, and cefuroxime 21.3% (Musoke *et al*,2000).

Infection with antibiotic resistant organisms results in delay in starting effective antibiotic therapy, fewer possible treatment options and increased morbidity and mortality with prolonged hospital stay and greater costs of hospitalisation (Patel *et al*, 2010). The slow pace in the development of newer drugs and rapidity in resistance development are major areas of concern. (Shah *et al,* 2012)

2.8 Supportive management.

The following supportive measures are recommended in the management of neonatal sepsis; nursing in a thermo neutral environment to avoid hypo or hyperthermia, maintaining oxygen in the normal range, intravenous fluids if hemodynamically unstable and corticosteroids for adrenal insufficiency. Hyperbilirubinaemia should be monitored and treated with phototherapy and or exchange transfusion.

2.9 Prevention of neonatal sepsis

Strategies to reduce rates of infection includes clean and safe deliveries, adherence to universal precautions in all patient contact, strict postnatal cleanliness, early and exclusive breastfeeding avoiding nursery overcrowding and limiting nurse to patient ratios(Haque *et al,*2003, Simiyu 2003). Other measures include strict compliance to hand washing, decreasing the number of venepunctures and heel pricks and providing education to nursery personnel (Bang *et al,* 1999)

2.10 Complications

The short term complications of neonatal sepsis include respiratory failure, pulmonary hypertension, cardiac failure, shock, renal failure, liver dysfunction and cerebral oedema. Some of the long term complications include; developmental delays, sensory and neurological dysfunction.

CHAPTER THREE: RESEARCH DEFINITION

3.1 Justification

Neonatal sepsis is a leading cause of morbidity and mortality in both developing and developed countries. It is a life threatening emergency and delays in diagnosis and treatment with appropriate antibiotics may have devastating consequences.

The pattern of causative organisms constantly changes and the emergence of resistant bacteria has compounded the problem further. Knowledge of the aetiologic agents is important and helps to reduce associated mortality in neonatal septicaemia. Longitudinal surveillance should be carried out at regular intervals to describe the varied pathogens causing neonatal sepsis as well as their changing antibiotic susceptibility pattern.

The result of this study is expected to guide therapy of neonatal sepsis at KNH.

3.2 Study questions

1. Which are the bacteria commonly causing neonatal sepsis at Kenyatta National hospital and what is their susceptibility to commonly used antibiotics?

2. What are some of the risk factors for neonatal sepsis at Kenyatta National Hospital?

3.3 Objectives

Broad objective

To determine the bacterial aetiological agents of neonatal sepsis, risks associated with acquisition and the susceptibility of these organisms to commonly used antimicrobial agents at Kenyatta National Hospital.

Specific objectives

1.To determine the bacterial agents causing neonatal sepsis at Kenyatta National Hospital.

2.To describe the antibiotic susceptibility pattern of bacteria causing neonatal sepsis at Kenyatta National Hospital.

3.To determine some of the associated risk factors for neonatal sepsis at Kenyatta National Hospital.

CHAPTER FOUR: RESEARCH METHODOLOGY

4.1 Study site

The study was conducted at the Kenyatta National Hospital Medical Microbiology laboratory and records department. KNH is located in Nairobi, the politico-administrative and economic capital of Kenya. It caters for over 80,000 in-patients and over 500,000 out-patients annually. About 75% of the patients treated as outpatients and inpatients are residents of Nairobi through self-referral or referral from the public and private health facilities.

Neonates are reviewed in the Paediatric Filter Clinic (PFC). Those requiring admission are admitted to the New Born Unit (NBU) or to the general paediatric wards because of the limited space in the NBU. Others neonates are received from KNH labour ward and maternity theatre.

4.2 Study design

It was a retrospective cross sectional study involving review of patients' laboratory records and files.

4.3 Sampling method

Convenience selection of positive blood culture reports was employed. Risk factors for acquisition of sepsis were assessed through patients' files at the medical records department.

4.4 Study population

Neonates admitted in KNH between the periods 1st January 2013 to 31st December 2013 with reports showing bacterial growth from blood culture specimen.

4.5 Inclusion criteria

Positive blood culture reports of children less than or aged 28 days for the period 1st January 2013 to 31st December 2013.

4.6 Exclusion criteria

1. Reports of negative blood culture
2. Reports of patients > 28 days

4.7 Sample size determination

The standard statistical approach to determination of sample size for a descriptive cross sectional survey such as this one requires specification of the proportion (prevalence) of neonatal sepsis; the desired level of confidence desired for the proportion estimate and a tolerance error margin or width of the confidence interval (a measure precision of the estimate) so that the necessary sample size is then calculable for a given precision level.

The fisher's formula was hence used to estimate the sample size.

A study at Kenyatta National Hospital found that 16.7 % of the neonatal blood cultures yielded bacterial pathogens (Musoke *et al*, 2000). Using this study a prevalence of 16.7% was used to calculate sample size

$N=Z^2P\ (1-P)/\partial^2$

N=minimum sample size

Z=constant, standard normal deviation (1.96 for 95% confidence interval)

P=expected prevalence

∂=accepted margin of error

Z=1.96

P=0.167

1-P=0.83

∂=0.05

$N=1.96^{2(}0.167\times0.833)/0.05^{2=}213.76$

N=214+10%=226

The minimum sample size will be 226 positive blood culture reports.

4.8 Data collection procedures. Permission to extract data from the hospital registries and laboratory records was obtained from Kenyatta National Hospital Head of laboratory Medicine and the Head of the Medical Records department.

It involved going through Laboratory records of neonates with bacterial growth from blood specimens obtained from January to December 2013. Risk factors were abstracted by the investigator from medical files of patients with positive blood cultures. The medical files were traced using the patient numbers on the blood culture reports.

A data collection form was used to collect data.

4.9 Data management and analysis.

Data was entered into password protected microsoft access and analysis done using Statistical Package for Social sciences (SPSS) version 21.

4.10 Ethical consideration

Approval was sought from the Kenyatta National Hospital/University of Nairobi-Ethics Review Committee (KNH/UoN-ERC).For confidentiality the patients' laboratory records and medical files were used in the confines of the KNH microbiology laboratory and the medical records department.

The patients names were not included in the collection form. Only the investigator had access to the laboratory records and medical files for the purposes of the study.

Raw data in form of filled forms, data stored in password protected computer, backup copies in hard drives and compact disc will be destroyed at the end of the study.

4.11 Study limitations.

Incompletely filled patient laboratory and medical records. A number of files had incomplete information with important variables missing.

Growth of contaminants due to improper aseptic techniques during blood specimen collection.

4.12 Dissemination plan

The results of the study will be disseminated to the Paediatrics department of KNH, KNH Microbiology Laboratory, University of Nairobi library and UNITID library.

CHAPTER 5: RESULTS

In the year 2013 there were 325 positive blood culture reports for neonates. 226 of them were randomly selected.

		N	%
Sex	Female	116	51.3%
	Male	110	48.7%
	Total	226	100.0%

Table 1 - Gender distribution of the study population

116(51.3%) of the isolates were from female patients and 110(48.7%) from male patients. However the difference was not statistically significant (p value 0.309).

As illustrated in Table 2 below, most of the patients were from low income and low middle income regions of Nairobi, Kangemi(7.8%), Embakasi(6.7%), Dandora(6.1%), Kariobangi (6.1%) Githurai(5.6%).

Residence in Nairobi	N	%		Residence in Nairobi	n	%
Baba Dogo	1	0.6%		Komarock	2	1.1%
Buruburu	1	0.6%		Mathare	1	0.6%
Dagoretti	3	1.7%		Mbagathi	1	0.6%
Dandora	11	6.1%		Mlango Kubwa	1	0.6%
Donholm	1	0.6%		Mlolongo	4	2.2%
Eastleigh	8	4.5%		Mwiki	1	0.6%
Embakasi	12	6.7%		Ngong	4	2.2%
Fedha	1	0.6%		Ngumba	1	0.6%
Gikomba	1	0.6%		Nyayo Highrise	1	0.6%
Githurai	10	5.6%		Ongata Rongai	3	1.7%
Hardy	1	0.6%		Pipeline	7	3.9%
Highrise	2	1.1%		Prisoner	1	0.6%
Huruma	5	2.8%		Pumwani	1	0.6%
Imara Daima	1	0.6%		River Road	1	0.6%
Kahawa West	1	0.6%		Rongai	3	1.7%
Kangema	1	0.6%		Satellite	3	1.7%
Kangemi	14	7.8%		Shauri Moyo	1	0.6%
Kariobangi	11	6.1%		South B	1	0.6%
Kasarani	6	3.4%		Tena	2	1.1%
Kawangware	5	2.8%		Umoja	4	2.2%
Kayole	11	6.1%		Utawala	6	3.4%
Kibera	8	4.5%		Uthiru	4	2.2%
Kinoo	5	2.8%		Zimmerman	6	3.4%
Komarock	2	1.1%				

Table 2 - **Residence in Nairobi.**

Organisms isolated from blood culture

As illustrated in figure 1 below there was a preponderance of gram negative organisms 116(51.3%) over gram positive organisms 96(42.5%).

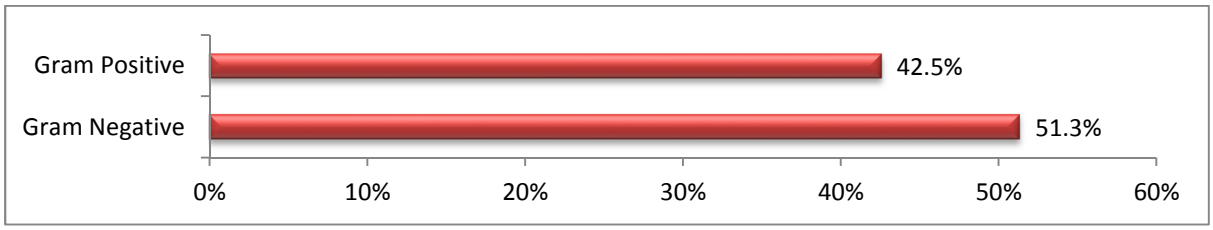

Figure 1 - **Distribution of isolated organisms**.

Coagulase negative staphylococcus was the most isolated organism (30.1%), followed by *Enterobacter spp* (19.9%), *Citrobacter spp*(12.8%) and *Klebsiella spp*(11%) spp. Other less frequently isolated organisms were *Enterococcus spp*(8.8%), *Escherichia coli*(7.1%), *Staphylococcus aureus*(3.5%), *Proteus spp*(0.9%)

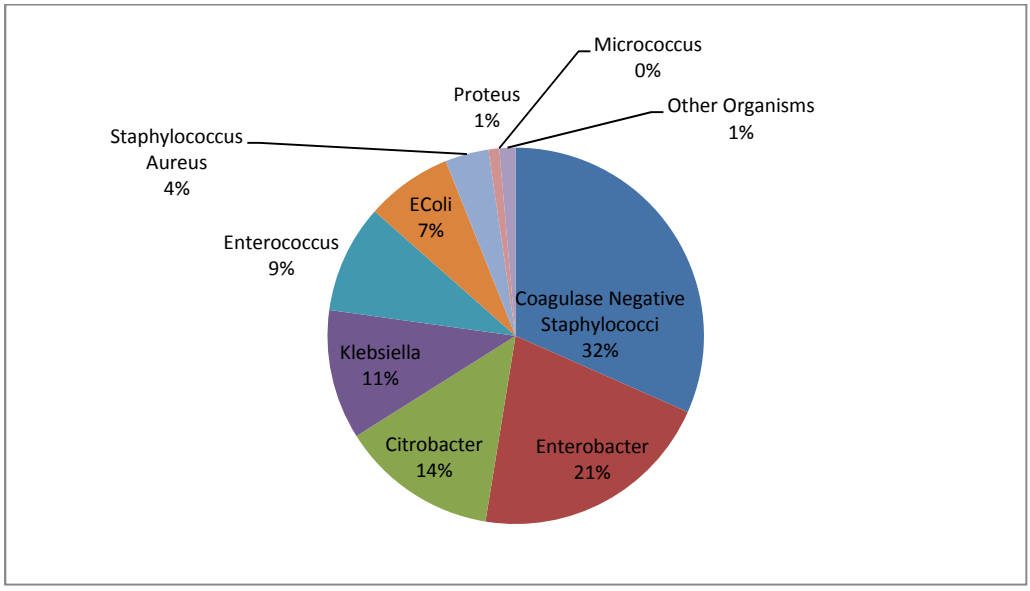

Figure 2 - **Frequency of isolated organisms.**

Antibiotic susceptibility patterns

The first line treatment of neonatal sepsis in Kenyatta hospital is a combination of penicillin and gentamicin. As shown in table 3, out of the 4 organisms tested against penicillin 3 of them showed resistance and 1 organism was susceptible. The resistance to gentamicin was (65.6%). Resistance to other antibiotics was also high ceftriaxone (75.2%), cefuroxime (72.6%), ampicillin (82.9%), ceftazidime (67.1%).

The was high sensitivity to vancomycin (100%), meropenem (90.8%), amikacin (87%), piperacillin tazobactam (89.7%), teicoplanin (93.5%), levofloxacin (83.8%)

There was also high sensitivity to amikacin (87.0%), piperacillin tazobactam (89.7%) imipenem (93.3%, meropenem (90.8%)

	Sensitive		Resistant	
	N	%	N	%
AMOXY_CLAV	68	45.0%	83	55.0%
AMIKACIN	20	87.0%	3	13.0%
CEFTRIAXONE	28	24.8%	85	75.2%
CEFUROXIME	29	27.4%	77	72.6%
AMPICILLIN	22	17.1%	107	82.9%
PENICILLIN	1	25.0%	3	75.0%
CHLORAMPENICOL	10	76.9%	3	23.1%
GENTAMYCIN	32	34.4%	61	65.6%
PIPERACILLINTAZOBACTAM	26	89.7%	3	10.3%
TIMENTIN	1	100.0%	0	0.0%
IMIPENEM	42	93.3%	3	6.7%
CEFEPIME	20	51.3%	19	48.7%
COTRIMOXAZOLE	12	54.5%	10	45.5%
CEFTAZIDIME	26	32.9%	53	67.1%
MEROPENEM	89	90.8%	9	9.2%

DOXYCYCLINE	48	64.0%	27	36.0%
LEVOFLOXACIN	88	83.8%	17	16.2%
CIPROFLOXACIN	24	85.7%	4	14.3%
TEICOPLANIN	87	93.5%	6	6.5%
ERYTHROMYCIN	3	42.9%	4	57.1%
VANCOMYCIN	33	100.0%	0	0.0%
TRIMETHOPRIMSULFAMETHOXAZOLE	0	0.0%	0	0.0%
MOXIFLOXACIN	1	100.0%	0	0.0%
CLINDAMYCIN	1	50.0%	1	50.0%
LINEZOLID	3	100.0%	0	0.0%
NORFLOXACIN	3	100.0%	0	0.0%
NETILMYCIN	3	100.0%	0	0.0%
Other Antibiotic	4	80.0%	1	20.0%

Table 3 - **General sensitivity pattern of the antibiotics**

Resistance and susceptibility of selected organisms.

Coagulase negative staphylococci showed the highest resistance to ampicillin and gentamicin(59.1%). Four out of the five organisms tested against cotrimoxazole were sensitive. There was high sensitivity to vancomycin(100%), teicoplanin(94.9%), levofloxacin(72.2%)

	Coagulase Negative Staphylococci			
	Sensitive		Resistant	
	N	%	N	%
AMOXY_CLAV	34	68.0%	16	32.0%
AMIKACIN	1	100.0%	0	0.0%
CEFTRIAXONE	15	50.0%	15	50.0%
CEFUROXIME	20	62.5%	12	37.5%
AMPICILLIN	9	40.9%	13	59.1%
CHLORAMPENICOL	1	100.0%	0	0.0%
GENTAMYCIN	9	40.9%	13	59.1%
CEFOTAXIME	7	70.0%	3	30.0%
IMIPENEM	6	85.7%	1	14.3%
CEFEPIME	3	100.0%	0	0.0%
CEFOTAXIME1	1	100.0%	0	0.0%
COTRIMOXAZOLE	1	20.0%	4	80.0%
CEFTAZIDIME	8	44.4%	10	55.6%
MEROPENEM	10	66.7%	5	33.3%
DOXYCYCLINE	20	62.5%	12	37.5%
LEVOFLOXACIN	26	72.2%	10	27.8%
CIPROFLOXACIN	3	60.0%	2	40.0%
TEICOPLANIN	56	94.9%	3	5.1%
ERYTHROMYCIN	2	66.7%	1	33.3%
VANCOMYCIN	21	100.0%	0	0.0%
NETILMYCIN	3	100.0%	0	0.0%

Table 4 – **Antimicrobial sensitivity pattern among CONS**

Klebsiella spp showed high resistance to ceftriaxone(100%),cefuroxime(100%), gentamicin(100%), cefepime(92.3%), ceftazidime(92.9%) but showed high sensitivity to amikacin(100%), piperacillin tazobactam(100%), meropenem(100%). Although the number of tested organisms were few.

	Klebsiella			
	Sensitive		Resistant	
	n	%	N	%
AMOXY_CLAV	11	47.8%	12	52.2%
AMIKACIN	11	100.0%	0	0.0%
CEFTRIAXONE	0	0.0%	14	100.0%
CEFUROXIME	0	0.0%	18	100.0%
AMPICILLIN	2	10.5%	17	89.5%
PENICILLIN	0	0.0%	1	100.0%
CHLORAMPENICOL	1	100.0%	0	0.0%
GENTAMYCIN	0	0.0%	14	100.0%
CEFOTAXIME	0	0.0%	12	100.0%
PIPERACILLINTAZOBACTAM	11	100.0%	0	0.0%
TIMENTIN	0	0.0%	0	0.0%
IMIPENEM	2	100.0%	0	0.0%
CEFEPIME	1	7.7%	12	92.3%
CEFOTAXIME1	0	0.0%	5	100.0%
COTRIMOXAZOLE	5	100.0%	0	0.0%
CEFTAZIDIME	1	7.1%	13	92.9%
MEROPENEM	22	100.0%	0	0.0%
DOXYCYCLINE	5	83.3%	1	16.7%
LEVOFLOXACIN	8	100.0%	0	0.0%
CIPROFLOXACIN	10	100.0%	0	0.0%
NORFLOXACIN	3	100.0%	0	0.0%

Table 5 – **Antimicrobial sensitivity pattern among *Klebsiella spp***

Enterobacter spp showed high sensitivity to levofloxacin(100%), meropenem((94.4%), imipenem(94.7%) but showed high resistance to ampicillin(100%), ceftriaxone(94.3%), cefuroxime(92.6%), cefotaxime(93.8%).

	Enterobacter			
	Sensitive		Resistant	
	n	%	N	%
AMOXY_CLAV	9	29.0%	22	71.0%
AMIKACIN	3	50.0%	3	50.0%
CEFTRIAXONE	2	5.7%	33	94.3%
CEFUROXIME	2	7.4%	25	92.6%
AMPICILLIN	0	0.0%	33	100.0%
CHLORAMPENICOL	2	100.0%	0	0.0%
GENTAMYCIN	4	28.6%	10	71.4%
CEFOTAXIME	1	6.2%	15	93.8%
PIPERACILLINTAZOBACTAM	3	60.0%	2	40.0%
TIMENTIN	0	0.0%	0	0.0%
IMIPENEM	18	94.7%	1	5.3%
CEFEPIME	5	55.6%	4	44.4%
CEFOTAXIME1	0	0.0%	6	100.0%
COTRIMOXAZOLE	3	75.0%	1	25.0%
CEFTAZIDIME	4	25.0%	12	75.0%
MEROPENEM	17	94.4%	1	5.6%
DOXYCYCLINE	8	72.7%	3	27.3%
LEVOFLOXACIN	21	100.0%	0	0.0%
CIPROFLOXACIN	3	100.0%	0	0.0%
TEICOPLANIN	0	0.0%	1	100.0%

Table 6 – **Antimicrobial sensitivity pattern among *Enterobacter***

Citrobacter spp showed high resistance to cefuroxime (100%), ampicillin (100%), amoxyclav(82.6%), ceftriaxone(80%)

	Citrobacter1			
	Sensitive		Resistant	
	n	%	n	%
AMOXY_CLAV	4	17.4%	19	82.6%
AMIKACIN	1	100.0%	0	0.0%
CEFTRIAXONE	3	20.0%	12	80.0%
CEFUROXIME	0	0.0%	12	100.0%
AMPICILLIN	0	0.0%	15	100.0%
CHLORAMPENICOL	0	0.0%	1	100.0%
GENTAMYCIN	3	25.0%	9	75.0%
CEFOTAXIME	0	0.0%	6	100.0%
PIPERACILLINTAZOBACTAM	8	88.9%	1	11.1%
TIMENTIN	1	100.0%	0	0.0%
IMIPENEM	9	90.0%	1	10.0%
CEFEPIME	5	62.5%	3	37.5%
COTRIMOXAZOLE	0	0.0%	0	0.0%
CEFTAZIDIME	6	33.3%	12	66.7%
MEROPENEM	22	91.7%	2	8.3%
DOXYCYCLINE	6	100.0%	0	0.0%
LEVOFLOXACIN	9	75.0%	3	25.0%
CIPROFLOXACIN	5	100.0%	0	0.0%

Table 7 – **Antimicrobial sensitivity pattern among *Citrobacter spp***

CHAPTER 6: DISCUSSION, CONCLUSION AND RECOMMENDATIONS.

6.1 DISCUSSION

Neonatal sepsis is a leading cause of morbidity and mortality. The uncertainity surrounding the clinical approach to treatment of neonatal septicaemia can be minimized by regular epidemiological surveys of aetiologic agents and their antibiotic sensitivity patterns leading to recognition of the most frequently encountered pathogens in a particular area. For effectual management of septicaemia cases study of bacteriological profile along with the antimicrobial sensitivity pattern plays a noteworthy role. (Agnihotri *et al*,2004).

Findings from this study showed that antimicrobial resistance is a problem in our setting. There were more females affected (51.3%), than males (48.7%). Other studies have shown a male predominance (Monjur *et al* 2010). This difference could be due to the fact that since the study was a retrospective study, the study population was not systematically selected. It is also possible that the males had a higher mortality rate though this was not explored in this study.

This study showed that most of the patients were from low income and low middle income regions of Nairobi. Low socioeconomic status is a risk factor for neonatal sepsis.

Other risk factors such as gestation at birth could not be assessed due to missing information in many of the patients' files.

Frequency and types of bacterial isolates.

There was a preponderance of gram negative organisms (51.3%) over gram positive organisms (42.5%). This is comparable to a study done by Muhammad *et al* in the year 2010 which showed that gram negative organisms were more predominant (54.6%) than gram positive organisms (45.4%)(Muhammad *et al* 2010.)

CoNS was the most commonly isolated organism (30.1%), followed by *Enterobacter spp* (21%), *Citrobacter* spp(14%), *Klebsiella* spp(11%), *Enterococcus* spp(9%), *Escherichia coli*(7%), *Staphylococcus aureus* (4%), *Proteus* spp(1%). This findings are comparable to those of a study done by Lee *et al* in china in the year 2004, CONS (29%), *Enterobacter cloacae*(17%)(Lee *et al* 2004). Until the 1970s CoNS was recognized as a contaminant. Since then several studies have reported increasing incidence of infections due to CoNS (Mulat *et al* 2013). However it is possible that CoNS isolates may in some cases represent contaminants from skin.

Antibiotic susceptibility patterns

The antibiotic susceptibility was studied for all isolates causing neonatal sepsis. Resistance was observed to be against commonly used antibiotics.

In this study the highest overall sensitivity was to vancomycin(100%).All 33 isolates tested against vancomycin were sensitive. High sensitivity was also seen to teicoplanin(93.5%), imipenem(93.3%), meropenem(90.8%), piperacillin tazobactam(89.7%), amikacin(87%). But this drugs should not be used indiscriminately and be kept as reserve drugs otherwise resistance to these drugs may develop thereby threatening the treatment of neonatal sepsis. High sensitivity was also seen the quinolones ciprofloxacin(85.7%) and levofloxacin(83.8%) but their use in children is restricted due to their side effects such as arthropathy.

High resistance was seen against ampicillin(82.9%), ceftriaxone(75.2%), cefuroxime(72.6%). The resistance to gentamicin was 65.6%.This is in contrast to a study done by Musoke *et al* in Kenya in the year 2000 in which the resistance to gentamicin was 20%. This could be due to emergence of resistant strains due indiscriminate use of antibiotics for both prophylaxis and

treatment of sick neonates. Other aminoglycosides like amikacin not commonly used may be recommended as alternatives or can be used in combination therapy.

Klebsiella spp showed high sensitivity to meropenem(100%), piperacillin tazobactam(100%), Amikacin(100%). The resistance to ceftriaxone and cefuroxime and gentamicin was 100% but the number of tested organisms were few.

Enterobacter spp showed high sensitivity to levofloxacin(100%), imipenem(94.7%) and meropenem(94.4%).

This study has shown that the organisms are more sensitive to the more expensive antibiotics such as meropenem, Teicoplanin. This poses a challenge since neonatal sepsis mostly affects those of low socioecomic status who may not be able to afford these medications.

6.2CONCLUSION

Gram negative organisms (*Enterobacter spp*,*Citrobacter spp*,*Klebsiella spp*) and Coagulase Negative Staphylococci are the leading cause of neonatal sepsis and most of them are resistant to multiple antibiotics. Continuous surveillance for antibiotic susceptibility should be done to look for resistance patterns.This is to inform on empirical and rational use of antibiotics so as to tackle antimicrobial antibiotic resistance and to ensure effectiveness in their use.

6.3 RECOMMENDATIONS

1. A prospective study needs to be carried out in KNH in order to properly assess the risk factors for neonatal sepsis.
2. Regular antimicrobial audits and reviews of laboratory data (surveillance) should be done so as to have proper documentation of drug resistance patterns and timely updates of antibiotic formularies.
3. Health education should be provided to the public on the dangers of indiscriminate use of antibiotics which is responsible for the emergence of resistance to the commonly used antibiotics.

BUDGET AND JUSTIFICATION

Serial Number	**Item**	**Unit Cost**	**Number of Units**	**Total Cost Kshs**
Stationary				
1	A4 papers	500	4	2000
2	Punching machine	250	1	250
3	Box Files	100	4	400
4	Stapler	250	1	250
5	Documents Binding	2500	5	12,500
6	Documents Printing	20	250	5,000
Statistician				20,000
	GRAND TOTAL			**40,400**

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APPENDICES

APPENDIX A: DATA COLLECTION FORM

TOPIC**: IDENTIFICATION AND SUSCEPTIBILITY PATTERNS OF BACTERIAL ISOLATES FOR NEONATES WITH SEPSIS AT KENYATTA NATIONAL HOSPITAL.**

DATE

DATA COLLECTION FORM NUMBER ☐

A) SOCIO- DEMOGRAPHIC CHARACTERISTICS

AGE OF PATIENT ☐ DAYS

SEX MALE ☐

FEMALE ☐

RESIDENCE…….

B) RISK FACTOR ASSESMENT

AGE AT ONSET ☐ <72hours ☐ >72hours

GESTATION AT BIRTH ☐ weeks.

BIRTH WEIGHT ☐ KGS

MODE OF DELIVERY CAESERIAN SECTION ☐ NORMAL DELIVERY ☐

PLACE OF DELIVERY; HEALTH FACILITY ☐ HOME DELIVERY ☐

C) ORGANISM ISOLATED

Klebsiella ☐

Enterobacter ☐

Escherichia coli ☐

Coagulase negative staphylococci ☐

Enterococcus ☐

Micrococcus ☐

Citrobacter ☐

Proteus ☐

Staphylococcus aureus ☐

Others…….specify……

D) ANTIBIOTIC SUSCEPTIBILITY PATTERNS

ANTIBIOTIC	SENSITIVE(S)	RESISTANT(R)
AMOXY/CLAV	☐	☐
AMIKACIN	☐	☐
CEFTRIAXONE	☐	☐
CEFUROXIME	☐	☐
AMPICILLIN	☐	☐
PENICILLIN	☐	☐
CHLORAMPENICOL	☐	☐
GENTAMYCIN	☐	☐
CEFOTAXIME	☐	☐
PIPERACILLIN	☐	☐
TIMENTIN	☐	☐
IMIPENEM	☐	☐
CEFEPIME	☐	☐
CEFOTAXIME	☐	☐
COTRIMOXAZOLE	☐	☐
CEFTAZIDIME	☐	☐
MEROPENEM	☐	☐
OTHERS…….SPECIFY……	☐	☐