CAUSES OF SEPTICEMIA, AND CHARACTERISTICS OF BABIES ADMITTED WITH PROVISIONAL DIAGNOSIS OF SEPTICEMIA, TO THE NEONATAL INTENSIVE CARE UNIT AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA,

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BY

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2000

DEDICATION

To my daughter Musawa, for all that time I was away from home working on this dissertation.

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DECLARATION

I hereby certify that this study is my own work and has not been previously submitted for a degree at any University.

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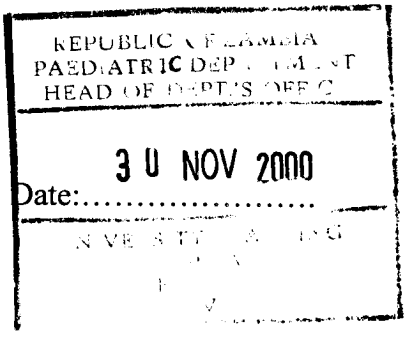
APPROVAL

This dissertation of **VERONICA MULENGA** is approved, in partial fulfillment of the requirements for the award of the Master of Medicine degree in Paediatrics by the University of Zambia.



Examiner 1.

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LIST OF ABREVIATIONS

AIDS	ACQUIRED IMMUNE DEFICIENCY SYNDROME
CSF	CEREBRAL SPINAL FLUID
CNS	COAGULASE NEGATIVE STAPHYLOCOCCUS
EOD	EARLY ONSET DISEASE
E.COLI	ESCHERISCHI COLI
GBS	GROUP B HEMOLYTIC STREPTOCOCCUS
HIV	HUMAN IMMUNO DEFICIENCY VIRUS
LOD	LATE ONSET DISEASE
NICU	NEONATAL INTENSIVE CARE UNIT
PROM	PROLONGED RUPTURE OF MEMBRANES
USA	UNITED STATES OF AMERICA
UTH	UNIVERSITY TEACHING HOSPITAL

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ABSTRACT

Neonatal septicemia is a common cause of admission to the Neonatal Intensive Care Unit (NICU) at the University Teaching hospital (UTH) in Lusaka, Zambia, accounting for twenty percent of admissions, and is the third commonest cause of mortality. Financial constraints at the UTH do not allow for blood cultures to be done routinely on all babies admitted to the NICU with diagnosis of septicemia, and therefore more often than not, these babies are treated empirically with crystalline penicillin and gentamycin as first line drugs. Use of crystalline penicillin and gentamycin as first line antibiotics in UTH is based on literature, which states that *Group B HemolyticStreptococcus* and *Escherischi Coli* are the common pathogens isolated in most neonatal nurseries.

A cross sectional descriptive study was carried out at the NICU UTH, Lusaka, Zambia, between 1st December 1997 and 31st March 1998, on babies admitted to the neonatal wing with provisional diagnosis of septicemia. This study looked at the pathogens causing septicemia and their drug sensitivity pattern, and also at the obstetric, neonatal factors and the clinical features in these babies. During the study period, 219 babies were admitted to NICU with diagnosis of septicemia. 100 babies were recruited for the study, and of these 25% were from UTH postnatal wards, 57.8% were referred from the clinics and 17.2% were straight from home. The majority of babies in this study (72.8%) were term. Average birth weight was 2.7 kilogram body weight with a male to female ratio of 1.4: 1.

Thirty (32.6%) babies had positive blood cultures. The commonest organisms isolated from blood were *Coagulase negative staphylococcus* (CNS) (36.7%), *Klebsiella pneumoniae* (23.3%), and *Staphylococcus aureus* (23.3%). *Salmonella* species were isolated from 2 babies (6.7%), and other isolates were *Pseudomonas aeruginosa* (3.3%), *Escherischi coli* (*E.coli*) (3.3%) and *Streptococcus* species (3.3%). Fourteen babies (47%) presented with early onset sepsis, while 16 (53.3%) presented with late onset sepsis. *Coagulase negative staphylococcus* and *Staphlococcus aureus* were the commonest organisms isolated in babies with early onset disease whilst *Klebsiella pneumoniae* was commonest in those with late onset disease.

In vitro sensitivity showed that all the organisms isolated were sensitive to cefotaxime. Thirteen percent of *Klebsiella* organisms were sensitivity to gentamycin, while *Staphylococcus aureus*, showed 100% sensitivity to cloxacillin. *Salmonella* species were resistant to all the antibiotics tested including chloramphenicol and were only sensitive to cefotaxime.

Significant obstetric factors for confirmed septicemia were, delivery at home, and when age of mother was below 20 years. Gestational age and birthweight were not significant neonatal factors, but male sex was significantly associated with confirmed septicemia. Clinical features like fever, poor feeding, respiratory distress and jaundice were the commonest presenting symptoms in the babies studied, however convulsions, poor feeding and umbilical sepsis presented more commonly in those babies with confirmed septicemia than unconfirmed septicemia, but there was no statistical difference.

There was no difference in mortality rates between babies with confirmed septicemia and those with unconfirmed septicemia, 16.6% and 16.1% respectively. Case fatality rate in babies with *CNS* infection was 9.1% and 14.3% in those with *Klebsiella* infection. There were no deaths among the babies with *Staphylococcus aureus.*

According to this study, *Coagulase negative staphylococcus*, *Staphylococcus aureus* and *Klebsiella pneumoniae* were the commonest organisms isolated. *Group B Streptococcus* (GBS) and *Escherischi Coli* were not common isolates in these babies, the majority of whom came from the Lusaka urban clinics. Therefore continued use of crystalline penicillin and gentamycin as first line antibiotics needs to be reviewed. Cefotaxime should be the drug of choice and should be made available at all times and cloxacillin should be added to cover for *Staphylococcus* infections.

CHAPTER ONE

1.0. INTRODUCTION

Lusaka the capital city of Zambia has a population of 1.8 million out of the country's estimated population of 10 million. Zambia like many developing countries, has a high birth rate among women of reproductive age group (43/ 1000) (1). National statistics indicate that, there are 3000 deliveries per month in Lusaka alone, of these, 1000 are conducted at the University Teaching Hospital, while the rest are in the Urban District health centres that have delivery services. Figures for home deliveries are not available.

Most newborn babies in Lusaka who need intensive care are admitted to the Neonatal Intensive Care Unit at UTH. Although UTH is the only hospital in Zambia with an established NICU, there are very few babies referred from outside Lusaka Urban. About 300 (10%) babies born in Lusaka are admitted to the unit every month (2). Statistics from the neonatal wing show that 60% of these admissions are from UTH maternity and postnatal wards, 29% from the health centres and 11% come straight from home. Criteria for admission to the neonatal wing includes, prematurity, severe jaundice, asphyxia, respiratory distress, septicemia and life threatening congenital anomalies.

Neonatal septicemia is a common cause of admission to NICU at UTH. On admission to the unit, these babies are examined and investigations are done if resources are available. Preliminary investigations include a full blood count, blood and urine for culture and sensitivity and lumbar puncture. Current first line treatment for septicemia at NICU comprises a combination of crystalline penicillin and gentamycin.

1.1. Statement of the problem.

Despite tremendous advances in technology, septicemia remains a major threat in NICUs. Neonatal septicemia is associated with fatality rates of 10-40% and substantial morbidity in surviving infants (3). Prompt diagnosis and appropriate management are paramount to reducing mortality and long-term sequelae from neonatal sepsis and meningitis. Although *Escherischi Coli* and *Group B haemolytic Streptococcus* are the predominant organisms causing early neonatal septicemia in the United States (4), studies done in different areas have shown that organisms causing neonatal septicemia differ from region to region and from nursery to nursery. Nursery epidemics are also common and occur from time to time (4).

Neonatal mortality at the UTH NICU is high, with case fatality rates of 26% (2). Neonatal septicemia is the third commonest cause of mortality, after prematurity and severe birth asphyxia. A study done by Lulembo in 1988 showed that *Enterobacter* species were the commonest organisms isolated (59%), followed by *Escherischi Coli* (13.2%) (5). Sensitivity pattern of these organisms was not done in that study. Since then no other study has been done in the unit to monitor change in the types of organisms isolated.

Currently babies with septicemia are treated empirically with crystalline penicillin and gentamycin due to nonavailability of culture media and other reagents needed for culture and sensitivity studies. Laboratory results when available are increasingly showing organisms that are sensitive only to cefotaxime (6), but cefotaxime being expensive is usually unavailable.

1.2. Study Justification.

Knowledge of the most commonly isolated bacteria in a nursery and of the antimicrobial susceptibilities is invaluable in the treatment of neonatal septicemia. Therefore it is important to carry out prevalence studies on a regular basis in order to determine the prevailing pathogens and their sensitivity pattern. This study was therefore designed to look at the pathogens isolated and determine the drug sensitivity pattern in babies admitted to the NICU at the UTH with provisional diagnosis of septicemia. The study also looked at the obstetric, neonatal factors and clinical features in these babies to determine which features were associated with laboratory proven sepsis.

CHAPTER TWO

2.0. REVIEW OF LITERATURE

Neonatal septicemia is a disease of infants who are less than one month of age, are clinically ill and have a positive blood culture (7). Sepsis may also be diagnosed on the basis of the infant's symptoms even when blood cultures are negative (7). Incidence of sepsis in different settings varies greatly. In a report by Jonathan, overall incidence of sepsis in neonates of various weights and gestations was 2.7 per 1000 live births. For those more than 2.500 kg however, incidence dropped to 1 per 1000 live births, while for those less than 1000 grams it increased to 86 per 1000 live births (8).

The prevalence rate for a specific pathogen varies from nursery to nursery and may change abruptly in any unit. The changing pattern of pathogens responsible for neonatal septicemia is reflected in a series of reports from Yale New Haven Hospital (9). In a report by Freedman et al, their 50 year experience with neonatal sepsis was analysed. During the 1930s, *Group A Streptococcus* was the predominant organism, in the 1950s, *Staphylococcus* (phage group 1) became a major cause of nursery outbreaks together with *Pseudomonas*, and from the late 1950s, *Escherischi Coli* has been an important cause of neonatal septicemia. *Group D streptococcus* and *Klebsiella* are relatively recent pathogens, with *Klebsiella* accounting for a high proportion of antibiotic resistant organisms that colonise and infect babies in neonatal intensive care units (10). In the 1970s the *Group B haemolytic streptococcus* (*GBS*) emerged and has persisted as the predominant pathogen in most U.S.A. nurseries (11). Aetiology of septicemia at three different hospitals is shown in Table 1, illustrating the varying organisms causing sepsis in these settings.

TABLE 1: AETIOLOGY OF NEONATAL SEPTICEMIA AT THREE HOSPITALS

	NEW HAVEN Connecticut (1979-1989)		PARKLAND Dallas (1968-1989)		RIGSHOSPITALET Denmark (1984-1988)	
Organism	No. Of isolates	(%)	No. Of isolates	(%)	No. Of isolates	(%)
GBS	64	(24)	277	(37)	7	(8)
E.Coli	46	(17)	127	(17)	13	(15)
*Other GNEB	47	(17)	76	(10)	20	(23)
S.Aureus	14	(5)	94	(13)	11	(13)
CNS	36	(13)	56	(7)	9	(10)
Enterococcus	18	(7)	79	(10)	5	(6)
Candida	11	(4)	Not Stated		7	(8)

*GNEB = gram negative enteric bacteria

Adapted from Rudolph's Paediatrics: Neonatal sepsis and meningitis (10).

Most neonatal infections occur during the first 5 days of life and are classified as early onset disease (EOD). Early onset infection is often caused by organisms colonising the mothers' vaginal tract and is therefore usually acquired during the intrapartum period. Organisms such as *GBS, E. Coli* and *Listeria monocytogens* may be responsible for early onset septicemia, while *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* are usually associated with late onset disease (LOD) (12).

In a study done in Malaysia, the incidence of proven or probable early onset septicemia was 56.7 per 1000 in high-risk newborns weighing over 1.5kg, and *CNS, GBS,* and *Klebsiella* species were the common organisms isolated (13). In a study by Luo in Malawi, *E.Coli* was the commonest pathogen causing early onset disease while *Streptococcal pneumoniae* was the more common pathogen in late onset disease (14). In another study by Daoud et al done over one year, there were no *GBS* or *Listeria* organisms cultured and gram negative organisms were the commonest organisms isolated, with *Klebsiella* accounting for 64% of cases (15).

LOD can occur as early as 5 days of age but is commonly recognised after the first week of life. LOD usually presents as meningitis and is mostly nosocomially acquired. Hospital acquired (nosocomial) infections have become a significant problem in many hospitals and may affect 2-5% of all hospitalised patients (16). *CNS* is a frequent isolate from neonates in many intensive care units and is most often hospitally acquired and usually diagnosed after the first week of life (17). Nosocomial outbreaks *of Klebsiella pneumoniae* with multiple drug resistance were reported at a gynaeco-obstetrical hospital in Mexico, with mortality of 50% and also at a nursery in Calcutta (18,19). In a study done in Zimbabwe, post mortem blood cultures isolated mostly *Klebsiella* and the positive blood cultures were associated with babies weighing less than 1500gm (20).

Leigh et al reported *Pseudomonas aeruginosa* as a late onset infection in very low birth weight infants, with a case fatality rate of 50% (21). *Acinetobacter* sepsis is another organism responsible for nosocomial infections and has also been associated with high case fatality rate of 42.3% (22).

Repeated prevalence surveys enable simple and cost effective assessment of hospital acquired infections, facilitating appropriate infection control interventions (23).

2.1 Microbiology and Pathogens

According to literature, the two most common bacterial pathogens isolated in neonatal period in the USA are *GBS* and *E.Coli* (4). These two organisms account for 70% of systemic disease and both organisms are usually acquired from the mother during the intrapartum period.

Group B haemolytic streptococcus

GBS is classified into four major serotypes based on the polysaccharide capsule. These are, 1a, 1b, II, III, with type III causing the majority of invasive infections (24). Epidemiologic studies have shown that 5-30% of pregnant women are vaginally and rectally colonised with *GBS* (25). In a study by Mary Pylipow et al, 16.3% of mothers were colonised with *GBS* (24). It is estimated that for every 100 infants born colonised with *GBS*, one will develop systemic disease caused by this organism (27).

Factors influencing colonisation to developing infection in the neonate are poorly understood, however in early onset disease, maternal and neonatal factors, immature host defence mechanisms especially among the low birth weight infants have been implicated.

It has also been suggested that defective opsonisation and phagocytic activity due to deficiency of maternally derived type specific antibodies, play a role (4). Early onset sepsis with *GBS* usually presents as a multi-system illness characterised by apnoea, respiratory distress and hypotension. In late onset disease, infection is related to heavy colonisation with *GBS* type III and decreased amounts of transferred maternal antibodies in these babies (4). In contrast to early onset disease, late onset sepsis presents insidiously and the commonest presentation is meningitis, but sometimes can present as bone and joint infection, skin abscesses and conjunctivitis (24).

Escherischi Coli

Approximately 40% of *E.Coli* strains causing septicemia, possess k1 capsular antigen (16). Epidemiological studies have shown that about 20-30% of newborn babies are colonised rectally with *E. Coli* (12). Vertical transmission is the major mode of neonatal gastrointestinal colonisation and has been documented in 70% of neonates with *E. Coli* meningitis and septicemia. The colonisation to disease ratio of *E. Coli* is similar to that of *GBS*, about 100-200:1. Nosocomial infections with *E.Coli* k1 have also been observed in premature nurseries (12).

Staphylococcus aureus.

During the first day or two of life the body surfaces of most babies become colonised by *Staphylococci* acquired from the mother, staff or environment. In babies born in hospital, the nose, umbilical stump and moist areas of the skin are the first to be colonised by *Staphylococcus aureus* organism, which is often virulent and a multi antibiotic resistant

strain. Thereafter, these colonised babies serve as the main source of that strain for the other babies (17).

Coagulase negative staphylococcus.

Staphylococcus epidermidis is the most frequently *staphlococcal* species associated with neonatal infection, although other species such as *Staphylococcus homini, warneri* and *hemolyticus* have been implicated (28). Clinical and laboratory diagnosis of infection with *CNS* can be difficult (29). It is likely that infected catheters are the most common source of *CNS* infection, but mechanisms by which bacteria colonise intra vascular catheters are poorly understood. The frequency of neonatal infections with *CNS* may be reduced by restricting the duration of use of intra vascular catheters, avoidance of contamination of infusion system connections and better care of the catheter insertion site (17).

Klebsiella Pneumoniae

Since early 1970's, there have been many reports of nursery infection outbreaks, and *Klebsiella pneumoniae* has been one of the commonest isolated gram-negative organisms. The majority of colonised babies are asymptomatic, and during epidemics asymptomatic colonisation may range from 0-90%. Those who develop disease usually have pneumonia, septicemia and meningitis. Infected fomites, healthy colonised babies and nursery personnel act as sources of infection (16).

2.2. Predisposing Factors.

Maternal and perinatal risk factors play an important role in neonatal infections. Maternal risk factors include black race, vaginal flora, maternal illness, age, parity, prolonged and premature rupture of membranes, and chorioamnionitis. Fetal risk factors include gestational age, sex, birth asphyxia, respiratory distress syndrome (RDS), meconium aspiration and associated congenital anomalies. Galactosemic neonates and infants receiving intramuscular iron are unusually susceptible to life threatening septicemia and meningitis caused by *E. Coli* (25). In a study by Raghavan et al, there was increased risk for neonatal infection if duration of labour was more than 24 hours, there was prolonged rupture of membranes of more than 12 hours, if the liquor was meconium stained or foul smelling, and in emergency caesarean section delivery (30).

Neonatal factors associated with neonatal infection were, premature delivery, low birth weight, birth asphyxia, assisted ventilation and intravenous alimentation (30). Identification of the high-risk pregnancies and appropriate management can minimise occurrence of neonatal sepsis.

Although the immune system of a neonate is well developed, it is functionally immature, both the specific and non-specific immunity (25). In non-specific immunity, there is defective granulocyte function, with abnormal chemotaxis, phagocytosis and bacteriocidal activity.

There is also abnormal opsonic activity due to low concentrations of complement and specific antibodies. For specific immunity, the humoral immunity is immature, and T cell mediated immunity is depressed. Although production of immunoglobulins begins in utero, only IgG levels are high enough at birth because IgG is actively transferred across the placenta, while only trace levels of IgA, IgE and IgM whose significant production only begins at birth, are found in cord blood (25).

2.3. Clinical features.

The presentation of neonatal septicemia is non-specific. There are no symptoms and signs that are 100% predictive, positive or negative. The symptoms listed below, used to define septicemia in this study, may also be due to common conditions that are noninfectious. Diagnosis therefore, requires a high index of suspicion and experience. In some of the retrospective studies done, it was been found that about 1% of term new born babies had a brief episode of fever of more than 37.8 ^{0}C in the first week of life, but this was rarely associated with infection (31). However, it was noted that, in infants with persistent fever or fever with other symptoms, bacterial disease was often found. It was also noted that jaundice occurred in about 1/3 of reported cases of neonatal sepsis and it usually resolved after appropriate antibiotic treatment (31). Meningitis is difficult to diagnose or exclude in the septic neonate if one is basing diagnosis of meningitis on clinical symptoms (31).

Routine lumbar puncture may not be required in clinically normal babies with adverse obstetric factors, but babies with clinical sepsis should have a lumbar puncture done, since there are no reliable clinical or laboratory markers to predict which babies will have meningitis (32).

2.4. Laboratory tests.

Isolation of bacteria from blood or cerebral spinal fluid in a baby with signs and symptoms is the standard and most specific method of diagnosing neonatal septicaemia (25). Factors to be considered when taking blood for culture are, thorough skin cleaning, the number and timing of blood cultures, the appropriate volume of blood for culture, culture media and additives, length, and the atmosphere of incubation, and the interpretation of positive blood culture results (28). Some laboratory tests done that provide indirect evidence of bacterial infection include C reactive protein, total white cell count and differential, absolute count of band forms, ratio of immature to mature neutrophil count, erythrocyte sedimentation count, platelet count, others are haptoglobins, nitroblue tetrazolium test. A total white cell count of less than 5000 per cubed mm, or band to mature neutrophil ratio of more than 0.2 are strong indicators of bacterial sepsis. These tests are not 100% predictive, but they are most helpful when done serially to confirm diagnosis and to monitor the course of infection as well as response to antibiotics. Gastric and tracheal aspirates may represent colonisation, while isolation of *GBS* from mucocutaneous sites indicates colonisation and not infection. Latex particle agglutination testing for antigen to Group B streptococcus has been useful in the diagnosis of *GBS* sepsis in newborns (33).

2.5. Treatment.

Different micro organisms are responsible for the early and late onset disease, and therefore the choice of antimicrobials for the two forms of disease also differ. In both early and late onset septicemia coverage for gram positive and gram-negative organisms is essential. Ampicillin is preferred over penicillin for it's better vitro activity against *Listeria monocytogens*, *enterococci*, and some gram-negative bacilli including *Hemophilus influenza*. The choice of aminoglycoside should be guided by the prevalence of resistant strains within a nursery. In late onset septicemia antibiotics should cover for *CNS* as well as other gram-negative organisms (34). In most studies the strains involved in neonatal infection by *CNS* are usually resistant to a wide range of antibiotics including penicillin, aminoglycosides, chloramphenicol, cloxacillin and erythromycin (35). Vancomycin and teichoplanin have been recommended as the drugs of choice in treatment of *CNS* septicemia (36). Rifampicin inhibits a wide range of microorganisms, including *staphylococcal* at very low concentrations and is a good alternative, but must be used with another antibiotic to avoid the emergence of resistance (36). The third generation cephalosporins are now being used in many units to treat neonatal septicemia. They are extremely effective against a wide range of Gram negative and positive organisms, and penetrate very well into the CSF. However they are not effective against *Listeria, Pseudomonas, Enterobacter* species and *Streptococcus faecalis*, although ceftazidime is effective against *Pseudomonas* (37). There also seems to be some worry about the efficacy of third generation cephalosporins in *Staphylococcus epidermidis* septicemia (36), although most studies have found these antibiotics to be effective (35).

Their activity against anaerobes is variable, and some anxiety exists about their activity against Gram positive cocci (38,39,40). Cephalosporins probably have fewer toxic effects and monotherapy with a single drug is used successfully in many units (35, 37).

2.6. Prevention.

In the last few years, strategies for prevention of infection in neonates have been developed. Intrapartum treatment with ampicillin and penicillin has proven effective in interrupting transmission of *GBS* in mothers with *GBS* and with other obstetric risk factors (41). This has been provided for in the 1992 guidelines for prevention of early onset *GBS* infections by intrapartum chemoprophylaxis of selected maternal *GBS* carriers, which have since been revised. These guidelines by the Committee on Infectious Diseases and Committee on Fetus and Newborn of the American Academy of Pediatrics, were based on proved efficacy in clinical trials, and selected only women with *GBS* colonisation who had obstetric risk factors such as premature rupture of membrane (42). In a study in Pakistan, a better outcome was noted in mothers with premature rupture of membranes (PROM), who were treated with bed rest, intravenous dextrose and antibiotics compared to those mothers who only received bed rest and analgesics (43). Administration of gamma globulin has been shown to decrease incidence of LOD in high-risk preterm infants (41). In a study by Muralt et al, prophylactic intravenous immunoglubulins showed marked therapeutic benefit (44). Neutropenia is common in septic babies, and in some centres adult white blood cells have been given to try and change the outcome (45).

Burge suggests that the role of adjunctive therapy such as granulocyte transfusions, intravenous gamma globulins, and exchange transfusions, is of limited or inconclusive value, however several studies done in the past, have shown great beneficial effects in neonates (36,44,46,47). Exchange blood transfusions have also been reported to be beneficial in the treatment of neonatal sepsis (44).

CHAPTER THREE

3.0. OBJECTIVES

3.1 GENERAL:

To determine the causes of septicemia and characteristics of babies admitted to NICU, UTH, with provisional diagnosis of septicemia.

3.2 SPECIFC

i. To determine the proportion of babies with positive blood cultures.

ii. To identify the pathogens isolated from the blood cultures.

iii. To look at the sensitivity pattern of the isolated pathogens to the commonly used antibiotics in UTH

iv. To compare the clinical features, obstetric and neonatal factors in babies with positive and negative blood cultures.

CHAPTER FOUR

4.0. METHODOLOGY.

4.1 Study Design

This was a cross sectional and descriptive study of babies admitted to NICU UTH with clinical diagnosis of septicemia, carried out between 1st December 1997 to 31st March 1998.

4.2 Study site

The study was conducted at UTH, NICU (D block), which is adjacent to the maternity wing (B and C blocks). The NICU is divided into 6 different sections. Babies born in hospital requiring resuscitation are admitted to D 11 room 1, and as they recover they graduate to D11 room 2 where observation is continued. Those born outside UTH and have severe conditions requiring intensive care are admitted to D11 room 3, while babies admitted with clinical signs of septicemia are admitted to the isolation room D 14. Stable premature babies who need to attain adequate weight before discharge are admitted to D12 room 1 for regular, supervised feeding, feeds consist of breast milk and supplemented with formula milk when necessary. Term babies who are recovering and those who need to complete treatment before discharge from the unit graduate to the last section, D 12 room 2.

4.3 Study Population

All neonates who were admitted to NICU with provisional diagnosis of septicemia during the study period were eligible to be recruited for the study, but only those who had blood cultures taken were finally recruited.

4.4 Selection of study subjects

a. Inclusion criteria

i. Babies less than one month of age, admitted to NICU with provisional diagnosis of septicemia and had blood for culture taken on admission

ii. Informed verbal consent from the mother

b. Exclusion criteria

i. Babies with septicemia who were older than 1 month

ii. Babies admitted with septicemia but did not have blood for culture taken on admission.

iii. Babies already admitted to NICU for other conditions who developed septicemia while in the ward.

iv. No consent from the mother

Definition of septicemia

In this study, provisional diagnosis of septicemia (suspected septicemia) was made in a baby who was clinically ill and had one or more of the following features (25).

- Failure or poor feeding
- Irritability
- Temperature instability
- Respiratory distress
- Convulsions
- Lethargy
- Umbilical infection
- Jaundice

Confirmed septicemia was defined as a positive blood culture with isolation of a single pathogen from the blood. Unconfirmed septicemia was when the blood culture was negative in a baby admitted with clinical signs of septicemia.

4.5 Sampling

All babies who were less than one month admitted to NICU between 1st December 1997 and 31st 1998 March with diagnosis of septicemia who had blood for culture taken, were recruited after an informed consent had been obtained. Inclusion in the study depended on availability of culture bottles and having blood for culture taken at the time of admission. Ten blood culture bottles were supplied weekly for the study. These culture bottles were used on the first 10 babies requiring blood culture. Those meeting the criteria for entry to the study were then recruited.

4.6 Sample size

The sample size was calculated based on the assumption that the incidence of laboratory proven septicemia was between 25 – 45%, according to a study by Lulembo in 1988 (11). Using this prevalence, for an estimated power of 80% and a confidence level of 95%, the sample size was calculated to be 87.

4.7 Subject Management.

Data Collection.

At recruitment to the study, information was collected using a standard questionnaire which had questions on obstetric, maternal and neonatal factors. See Appendix.

Follow up of study subjects.

Case notes of all babies admitted to the study were reviewed daily, and these babies were followed up until discharge from the hospital or until death.

Collection of Samples.

After evaluation of the baby by the admitting doctor, every baby recruited to the study, had 2 mls of blood collected from a periphery or femoral vein after cleaning the site thoroughly with spirit. The blood was put into tryptom soya broth for culture.

4.8. *Laboratory* procedures.

Blood that had been inoculated into broth was incubated for maximum of 7 days. After every 48 hours, broth was sub cultured to a solid media of Mc'conkey, blood and chocolate agar in order to cater for the majority of organisms, and them incubated at 37°c for at least 24 hours aerobically or anaerobically. Growth was indicated by presence of colonies on the solid agar and was identified using standard tests according to the organism suspected. Sensitivity tests were set up with appropriate sensitivity discs. For economical reasons, sensitivity of organisms isolated was selectively done on those antibiotics to which these organisms were most likely to be sensitive to, as opposed to sensitivity to all the drugs on the commercial strips. This was meant to save on the strips. The laboratory does not also routinely do sensitivity of *CNS* without confirmation of the sepsis with a second blood culture, so no sensitivity tests were done on *CNS* in this study.

4.9 Treatment Protocol:

Initial treatment, was started by the admitting doctor, and the choice of antibiotics was to his or her discretion. The following combinations were used, crystalline penicillin + gentamycin or ampicillin + chloramphenicol. When culture results became available, the ward doctor would change the antibiotics according to the sensitivity pattern.

Some babies had treatment changed to cefotaxime after 48 hours if they showed no response to the above drugs and laboratory results were not yet out, if cefotaxime was available.

4.10 Data Analysis

Data collected was analysed using Epi info.

a. Prevalence data on single variables was generated.
b. To determine associations between study variables, Odds Ratios with their confidence limits were calculated.

Amongst the babies admitted with clinical septicemia, two study groups were defined for analysis.

a. Confirmed septicemia - babies with positive blood cultures
b. Unconfirmed septicemia - babies with negative blood cultures

4.11 Ethical Consideration

The study was cleared by the Research and Ethics Committee of the University of Zambia, School of Medicine.

CHAPTER FIVE

5.0 RESULTS

During the study period, 1379 babies were admitted to the NICU at UTH for various conditions. Two hundred and nineteen (15.9%) of these babies were admitted with a diagnosis of neonatal septicemia, out of whom 100 were recruited for the study. Eight babies had their culture specimens discarded due to contamination and so were excluded from the final analysis. There were 57 (62%) male and 35 (38%) female babies recruited for the study. Sixty seven (72.8%) babies were term and had gestational ages above 37 weeks, 25 (27.2%) were preterm. Sixty five (70.6%) babies had birth weights of above 2.5 kg while 25 (29.4%) had low birth weights, other characteristics are shown in Table 2.

The majority of the babies in the study were referred from the Lusaka Urban Clinics (57.8%), 25% were from UTH postnatal wing and 17.2% from home.

TABLE 2: CHARACTERISTICS OF BABIES WITH SUSPECTED SEPTICEMIA

CHARACTERISTIC	CONFIRMED SEPTICEMIA N= 30	UNCONFIRMED SEPTICEMIA N=62
AVERAGE BIRTH WEIGHT – KG	2.29	3.10
AVERAGE AGE ON ADMISION IN DAYS	5.5	6.3
MALE SEX	28	29
FEMALE SEX	2.0	33

5.1 Pathogens Isolated

Thirty babies (32.6%) out of 92 babies studied had positive blood cultures.

The commonest organisms isolated, were *Coagulase negative staphylococcus* (36.6%), *Klebsiella pneumoniae* (23.3%) and *Staphylococcus aureus* (23.3%). Other organisms isolated were *Salmonella* species (6.7%), *E. Coli* (3.3%), *Streptococci* species (3.3%), and *Pseudomonas aeruginosa* (3.3%). Table 3 shows the organisms isolated.

TABLE 3: PATHOGENS ISOLATED IN CONFIRMED SEPTICEMIA

ORGANISM	NUMBER (30)	%
Coagulase Negative Staphylococcus	11	36.6
Klebsiella Pneumoniae	07	23.3
Staphylococcus Aureus	07	23.3
Salmonella species	02	6.7
Escherischi Coli	01	3.3
Streptococcus species	01	3.3
Pseudomonas aeruginosa	01	3.3
TOTAL	**30**	**100**

Causes of early onset and late onset disease

In this study *CNS* was a common cause for both early and late onset disease, while *Staphylococcus aureus* was common in early onset disease and *Klebsiella pneumoniae* was the commonly isolated organism in babies with late onset disease (Table 4).

TABLE 4: PATHOGENS IN EARLY AND LATE ONSET NEONATAL SEPTICEMIA

ORGANISM	ONSET< 5 DAYS	ONSET>5 DAYS	TOTAL
Coag. Negative Staphlococcus	6	5	11
Klebsiella Pneumoniae	2	5	7
Staphylococcus Aureus	5	2	7
Salmonella species	1	1	2
Escherischi Coli	0	1	1
Pseudomanas Aeruginosa	0	1	1
Streptococci species	0	1	1
TOTAL	**14**	**16**	**30**

5.2 Sentivity to antibiotics

As *CNS* isolation was not confirmed by a second blood culture no sensitivity tests were done for this organism. Two out of the seven *Klebsiella* isolates (13%) were sensitive to gentamycin but all the *Klebsiella pneumoniae* isolates were resistant to both ampicillin and chloramphenicol. *Staphylococcus aureus* showed 100% sensitivity to cloxacillin, and 75% sensitivity to erythromycin. *Salmonella* species were resistant to all antibiotics tested except

cefotaxime. The only isolate of *E. Coli*, was sensitive to both gentamycin and cefotaxime, and the *Streptococcus* species isolate to crystalline penicillin. All the organisms including *Staphylococcal* organisms, showed 100% sensitivity to cefotaxime (Tables 4,5,6 & 7).

TABLE 5: ANTIBIOTIC SENSITIVITY PATTERN OF KLEBSIELLA PNEUMONIA

ISOLATES N = 7	AMPICILLIN	C/PHENICOL	GENTAMYCIN	CEFOTAXIME
1	R	R	R	S
2	R	R	R	S
3	R	R	R	S
4	R	ND	R	S
5	R	ND	R	S
6	ND	ND	S	S
7	ND	ND	R	S

R = RESISTANT
S = SENSITIVE
ND = NOT DONE

TABLE 6: ANTIBIOTIC SENSITIVITY PATTERN OF STAPHYLOCOCCUS AUREUS

ISOLATES	AMPICILLIN	B/PENNICILLIN	GENTAMYCIN	CLOXACILLIN	ERYTHRO-MYCIN	CEFOTA-XIME
1	R	R	R	S	S	S
2	R	R	ND	S	ND	S
3	R	R	ND	S	ND	S
4	R	R	ND	ND	S	S
5	R	R	ND	S	S	S
6	R	R	ND	S	R	S
7	R	R	ND	S	ND	S

R = RESISTANT
S = SENSITIVE
ND = NOT DONE

TABLE 7: ANTIBIOTIC SENSITIVITY PATTERN OF SALMONELLA SPECIES

ISOLATE N =3	AMPICILLIN	C/PHENICOL	GENTAMYCIN	CEFOTAMIME
1	R	R	R	S
2	R	ND	R	S
3	R	R	R	S

R = RESISTANT
S = SENSITIVE
ND = NOT DONE

TABLE 8: ANTIBIOTIC SENSTIVITY PATTERN OF OTHER ORGANISMS

ISOLATES N = 4	AMPICILLIN	C/PHENICOL	B/PENICILLIN	GENTAMYCIN	CEFOTA-XIME
Ecsherischi Coli	R	ND	ND	S	S
Pseudo Aeruginosa	ND	ND	ND	S	S
Streptococcus species	ND	ND	S	ND	S

R = RESISTANT
S = SENSITIVE
ND – NOT DONE

5.3 Obstetric factors in babies with suspected septicemia

The majority of mothers of babies in the study were between the age of 21-29 years. Fourteen (15.2%) mothers, were teenage mothers and were below the age of 20 years, 78 (84.8%) were above 20 years. Mothers below 20 years of age in this study were more likely to have babies with positive blood cultures and had a statistically significant association with confirmed septicemia, Odds Ratio 4.89, 95% CI 1.27-20.42 (Table 9). Other obstetric factors are shown in Table 10.

TABLE 9: MATERNAL AGE IN BABIES WITH CONFIRMED AND UNCONFIRMED SEPTICAEMIA

AGE IN YEARS	CONFIRMED SEPTICEMIA N=30	%	UNCONFIRMED SEPTICEMIA n-62	(%)	OR	95% CI
< 20 YEARS	9	30	5	8.1	4.89	1.27-20-42
> 20 YEARS	21	7	57	91.9	0.20	0.05- 0.79
TOTAL	**30**	**100**	**62**	**100**		

TABLE 10: OBSTETRIC FACTORS IN BABIES WITH SUSPECTED SEPTICEMIA

FACTORS	BABIES WITH SUSPECTED SEPTICEMIA	
	NUMBER = 92	%
Premature rupture of membranes	13	14
Prolonged rupture of membranes	21	23
Spontaneous vaginal delivery	77	83.7
Caesarean section delivery	15	16.3
Delivered at the UTH	39	42.4
Delivered at the clinic	45	49
Delivered at home	08	8.6

Prolonged rupture of membranes, delivery by ceasarian section and delivery at the UTH were similar in the two groups, but delivery at home was associated with blood culture proven sepsis and was statistically significant, OR 2.23, 95% CI 0.38- 12.85 (Table 11).

TABLE 11: OBSTETRIC FACTORS IN CONFIRMED AND UNCONFIRMED SEPTICEMIA

FACTORS	CONFIRMED SEPTICEMIA N=30	%	UNCONFIRMED SEPTICEMIA N=62	%	OR	95% CI
Premature rupture of membranes	4	13.3	10	16.1	0.80	0.17-3.13
Prolonged rupture of membranes	7	23.3	14	22.6	1.04	0.33-3.27
Caesarian section delivery	5	16.6	10	16.1	1.00	0.24-0.24
Spontaneous vaginal delivery	25	83	52	83.3	0.96	0.26-3.98
UTH delivery	13	43	26	41.9	1.06	0.40-2.80
Clinic Delivery	13	43	32	51.7	0.70	0.27-1.88
Home delivery	4	13	4	6.4	2.23	0.38-12.8

5.4 Neonatal factors in babies with suspected septicemia

Birthweight, gestational age and sex of the baby were evaluated to establish any relationship with confirmed septicemia. Male sex was significantly associated with confirmed septicemia, OR 15.93, CI 3.42- 14.5 (Table 12).

TABLE 12: GESTATIONAL AGE OF BABIES WITH SUSPECTED SEPTICEMIA

FACTORS	CONFIRMED SEPTICEMIA N=30 (%)	UNCONFIRMED SEPTICEMIA N=62 (%)	OR	95% CI
MALE SEX	28 (93)	29 (46)	15.93	3.42-14.5
GES. <37 WK	07 (23)	18 (29)	0.74	0.24-2.25
B.W < 2.5KG	09 (30)	16 (25.8)	1.23	0.42-3.58

GES = GESTATION

B.W = BIRTHWEIGHT

5.5 Clinical features in babies with suspected septicemia

Most clinical features were of similar incidence in babies with confirmed and unconfirmed septicemia. Poor feeding, respiratory distress, fever and jaundice were the commonest clinical symptoms in the two groups, but convulsions, poor feeding and umbilical infection were more common in the confirmed septicemic babies. Jaundice was commonly found in the unconfirmed group (21%) compared to (12.5%) in confirmed septicemia. (Table 13)

TABLE 13: CLINICAL FEATURES IN CONFIRMED AND UNCONFIRMED SEPTICEMIA:

CLINICAL FEATURES	CONFIRMED SEPTICEMIA N=30	%	UNCONFIRMED SEPTICEMIA N=62	%	OR	95% CI
Fever	17	(53.1)	34	(56.7)	0.87	0.34-2.24
Irritability	04	(12.5)	09	(15)	0.81	0.17-3.24
Respiratory distress	04	(12.5)	08	(13.3)	0.93	0.19-3.84
Convulsions	03	(9.4)	04	(6.7)	1.50	0.20-9.50
Poor feeding	08	(25)	10	(16.7)	1.67	0.52-5.36
Lethargy	02	(6.3)	04	(6.7)	0.93	0.08-6.96
Umbilical infection	03	(9.4)	04	(6.7)	1.50	0.20-9.50
Jaundice	04	(12.5)	13	(21.7)	0.52	0.11-1.90

5.6 Outcome in babies with confirmed septicemia in relation to pathogens

The average number of days in hospitals in unconfirmed septicemia was 9.2 days, while for confirmed septicemia babies it was 9.4 days.

Out of 92 babies in the study 15 (18.4%) died. Mortality among babies with confirmed septicemia was 16.6% and 16.1% for unconfirmed septicemia. Out of the two babies with S*almonella* infection, 1 died.

Low mortality was seen in babies with *CNS* and *Klebsiella* infections, and there was no mortality in babies with *Staphylococcus aureus* infection (Table 15). Most of the babies who died, stayed a very short time in hospital, usually before culture and sensitivity results came back so that treatment could be changed to the appropriate drugs.

TABLE 15: OUTCOME IN BABIES WITH CONFIRMED AND UNCONFIRMED SEPTICEMIA

OUTCOME	CONFIRMED SEPTICAEMIA N=30 %	UNCONFIRMED SEPTICAEMIA N=62%
Died	5 (16.6)	10 (16.1)
Discharged	25 (83.1)	52 (83.6)
TOTAL	**30 (100)**	**62 (100)**

TABLE 16: OUTCOME IN RELATION TO PATHOGENS IN CONFIRMED SEPTICEMIA

PATHOGEN	TOTAL NUMBER	DIED N = 7	%
Coagulase negative Staphylococcus	11	1	9.1
Klebsiella Pneumoniae	7	1	14.3
Staphylococcus Aureus	7	0	0
Salmonella Species	2	1	50
Escherischi Coli	1	1	100
Pseudomonas Aureuginosa	1	0	0
Streptococci species	1	1	100

CHAPTER SIX

6.0. DISCUSSION

This study showed that 32.6% of babies had positive blood cultures, this is comparable to the incidence of septicemia found by Lulembo in 1988 which stood at 35% (5). In this study, *CNS* was a common cause of both early and late onset septicemia. This is surprising, as *CNS* infection is nosocomially acquired, and is usually isolated in surviving low birth weight babies who have been subjected to invasive procedures such as intravascular lines, parenteral nutrition and long term antibiotic therapy. However other studies done have had similar findings, like a study in Malaysia, found that *Staphylococcus epidermidis* and *Staphylococcus aureus* were the commonest organisms isolated in both early and late onset disease (43). In another study by Anti Obong et al, in Nigeria, *Coliforms* and *Staphylococcus aureus* were the commonest organisms isolated (48). According to Martin M A et al, *CNS* is now the commonest cause of late onset septicemia in most intensive care units, especially in low birthweight neonates who have been subjected to prolonged invasive care (28). However, he cautions that in interpreting data in a positive culture with *CNS* organisms, a positive culture may be a contaminant rather than true bacteremia. Freeman and Battist however believe that, at least half of blood cultures positive for *CNS* actually represent bacteremia, and that a positive blood culture in a baby with clinical signs in a neonatal intensive unit, represents infection rather than contamination (31).

In this study only one baby had *Streptococcus* species isolated, and this was not typed to determine the group. Other studies done in Africa have also noted the absence of *GBS* or *Listeria* organisms in babies with neonatal septicemia (48). This is unlike the USA nurseries and other western countries, which report a high incidence of *GBS*. Twenty two percent of babies in this study who had positive cultures had *Klebsiella* infection. *Klebsiella pneumoniae* is a common cause of infection outbreaks in nurseries, and is usually associated with multiple drug resistance. During the study period, there were 2 cases of *Salmonella* species isolated. This is lower than what was observed in 1997, when there was an apparent outbreak of *Salmonella* infection in NICU, UTH (2). *Salmonella* infection in neonates is associated with nosocomial nursery infections. These organisms are difficult to eradicate from tissues once a baby is infected, and even with prolonged antibiotic treatment, repeated relapses are common. In adults, *Salmonella* bacteremia is common in patients with Acquired Immune Deficiency Syndrome (AIDS) (49), this finding seems to be the same for children infected with the Human Immuno Deficiency Virus (HIV), although no HIV testing was done on the babies in this study.

Staphylococcus aureus showed 100% sensitive to cloxacillin and showed quite a high sensitivity to erythromycin (75%). *Klebsiela pneunomiae,* which was a common pathogen in late onset disease, was sensitive to cefotaxime and only few isolates (29%) were sensitive to gentamycin. Studies done before, have shown that cephalosporins should be used in treating severe sepsis, especially if *Klebsiella pnemoniae* is a common isolate in that setting (50).

In any neonatal intensive care unit, it is of great importance to have an antibiotic policy, which is logical, simple and generally acceptable, and is based on the antibiotic resistance pattern in the unit (51). The use of crystalline penicillin and gentamycin as first line antibiotics in most nurseries in based on the fact that *Group B streptococcus* and *Escherischi Coli* are the common organisms isolated in those places. This study found that, these two organisms although sensitive to crystalline penicillin and gentamycin, were not common in the babies studied, and therefore use of these antibiotics as first line drugs in such babies needs to be reviewed. The babies seen in this study were mostly from outside the UTH neonatal unit, and therefore, any antibiotic policy based on the sensitivity pattern of this study would apply only to those babies coming from outside the NICU. Other studies need to be done, to find out whether there is a difference in the organisms isolated from babies who develop sepsis while in the neonatal unit for other conditions, compared to those who are admitted to the unit specifically for septicemia.

In the western countries, the incidence of neonatal septicemia, especially early onset *GBS* infection, is highest in babies of mothers who are young and less than 20 years of age (51). In this study, 15.2% of mothers who had babies admitted to NICU with suspected septicemia were below the age of 20. It was also noted that babies of young mothers, were more likely to have a positive blood culture (30%) compared to older mothers (7%.) This is not surprising as most mothers in this age group are very young and therefore inexperienced and most likely unable to observe general hygienic measures necessary in the care of a new born baby.

Premature and prolonged rupture of membranes are well known risk factors in neonatal septicemia (30), this study however, did not find any significant difference for these factors in the two groups of babies. Delivery at home however was statistically and significantly associated with confirmed septicemia OR 2.23, 95% CI 0.38- 12.8.

Male sex was also found to be statistically and significantly associated with confirmed septicemia, O R 15.93, CI 3.42-14.5, while prematurity and low birth weight were not major factors.

The clinical features were not very different in the two groups of babies, although babies who presented with convulsions, poor feeding and umbilical infection were more likely to have positive blood cultures but this was not statistically significant. It is not surprising that these features were of similar incidence as these parameters were also used to define septicaemia. Jaundice was more prevalent in babies with unconfirmed septicemia, this implies that jaundice is a common but nonspecific feature in ill neonates.

There was no difference in case fatality rates of 16.6% in confirmed septicemia and 16.1% in unconfirmed septicemia. Despite a high incidence of *CNS* infection, mortality was low in this group with a case fatality of 9.1%. This finding is similar to that of Freeman where he observed 100% survival rate in babies with *CNS* infection (31). Mortality of babies with *Klebsiella* infection at 14% was quite low compared to other studies (18, 19). Out of the 2 patients with *Salmonella* infection, 1 died from meningitis.

Mortality in *Salmonella* meningitis has been reported to be quite high at 40- 60% despite adequate and appropriate antibiotics therapy (51). Infection with *Salmonella* infection suggests severe infection and could possibly be associated with HIV infection, but when cases suddenly increase at a particular time, this should alert medical personnel to look out for nursery infection outbreaks and take appropriate infection control measures.

CHAPTER SEVEN

7.0 CONCLUSION

Neonatal septicemia is a common cause for admission to the NICU at UTH. Blood cultures are not done on all babies admitted with septicemia, but full treatment with crystalline penicillin and gentamycin, is usually given to these babies on clinical grounds. Most admissions for septicemia are referred from the local clinics. Delivery at home was associated with higher incidence of confirmed septicemia when compared to UTH or clinic deliveries. Accuracy of confirmed septicemia by a positive blood culture was 32.6%. *CNS* and *Staphylococcus aureus* have become important pathogens in babies admitted to NICU at UTH, and this finding should be kept in mind when deciding on treatment policies for neonatal sepsis. *Klebsiella pneumoniae* is an important cause of late onset septicemia in neonates. *Group B Streptococcus* and *Escherischi Coli* are not common pathogens in babies admitted to UTH NICU with neonatal septicemia, and therefore continued use of crystalline penicillin and gentamycin should be reviewed. According to this study cefotaxime should be the drug of choice and the first line treatment in babies with severe neonatal septicemia. Cloxacillin should be added if staphylococcal infection is suspected. The case fatality rate of 18.2% in this study is well within the range quoted by Berman et al of 10- 40% (4).

7.1 RECOMMENDATIONS

1. Frequent prevalence surveys should be done to monitor changing patterns and emergency of new pathogens in babies with septicemia.
2. Cefotaxime should be the drug of choice in very sick babies and when culture results are not available.
3. Cloxacillin should be added to treatment regimes especially in those babies who are not responding to the usual antibiotics and to cefotaxime on its own.
4. A larger study should be done to determine whether there is a difference in the organisms isolated in babies who develop sepsis while on NICU for other conditions, from those admitted to the unit specifically for septicemia.

7.2 STUDY LIMITATIONS

1. Financial resources were a limiting factor in that not all babies admitted with septicemia had blood cultures taken and these were excluded from the study. Resources supplied were actually diverted and used on babies who did not qualify for entry to the study. A larger sample size would have given more accurate results.
2. Only one blood specimen per baby was taken, no repeat samples were done. Repeat specimens would have confirmed *Coagulase negative staphylococcus* infection.
3. At the beginning of the study, the doctors in the NICU were trained in how to take proper blood specimens, however the turnover of doctors in NICU was high and training was not carried out with change of doctors. This may have contributed to the low positive culture rates.

REFERENCES

1. Ministry of Health. Statistics, 1998

2. Askin D.F. Bacteria and fungal infections in the neonate. Journal of Obstetric, Gynaecologic, and Neonatal nursing, 1995; 24 (7): pp 635-43.

3. Berman RE, Kliegman RM, Arvin AM. Sepsis In: Textbook of Paediatrics. (ed. Nelson) 15th ed, pp 528. Bangalore; WB Saunders, 1996

4. University Teaching Hospital Statistics, 1996.

5. Lulembo O. The relationship between early onset septicemia and mode of delivery. Masters of Pediatrics dissertation (1988).

6. University Teaching Hospital. Laboratory statistics, 1998.

7. Beverly L.K, Frederick C.B. Bacterial sepsis In: Current Paediatric Diagnosis and treatment. (ed. Kempe C, Silver o'Brien, Fulginiti) 9th ed, pp 81. Nerwalk; Appleton +Lange, 1997.

8. Jonathan M.W, Dobyns E, Webb S. Neonatal sepsis In: Textbook of paediatric Critical Care. (ed. Peter R.H.) 2nd ed, pp 98-111. Phildephia; W.D. Saunders, 1993.

9. Freedman R.M, Ingram D.L, Gross I. A half century of noenatal sepsis at Yale. American Journal of Disease of Children, 1981; 135 (13): pp 140-144.

10. Goldman D A, Leclair J, Macone A. Bacterial colonisation of neonates admitted to an intensive care environment, 1978; Journal of Paediatrics (93): pp 288.

11. Rudolph A.M, Hoffman J.I.E, Rudolph C.D. Neonatal sepsis and meningitis In: Rudolph's Paediatrics (ed. Rudolph) 20th ed, pp536-44. Stamford; Appleton & Lange, 1996.

12. Odio C. M. Cefotaxime treatment of neonatal meningitis and sepsis. Diagnostic Microbiology & Infectious Disease, 1995; 22 (1-2): pp 111-7.

13. Malik AS, Pennie RA. Early onset septicemia in a level 2 nursery. Medical Journal of Maylasia, 1994; 49 (1): pp 17-23.

14. Luo C. Septicemia in early Infancy. Masters in Tropical Medicine thesis (1993).

15. Daoud AS, Abukkteish F, Obeidat A, EL-Nassir Z, al-Rimawi H. The changing face of neonatal septicemia. Annals of Tropical Paediatrics, 1995; 15 (1): pp 93-6.

16. Avery ED, Taeusch H.W. Septicemia In: Disease of New borns. (ed. Schaeffer) 5th ed, pp732. London; W.B. Saunders, 1984.

17. Millar MR, Todd N, Mackay P. Neonatal infections with Coagulase *Negative Staphylococci*. Archives of Disease in childhood,1990; 65 (10): pp 1015-16.

18. Nathoo KJ, Mason PR, Gwanzura L, Mubaiwa L, Kowo H. Neonatal septicemia due to *Klebsiella pneumoniae*. Revista Latino americana de Microbiologica, 1992; 34 (1): pp 11-6.

19. Banerjee M, Sahu K, Bhatachaya S, Adhya S, Bhomwick P, Chakraborty P. Outbreak of neonatal septicemia with multdrug resistant *Klebsiella pneumoniae*. Indian Journal of Paediatric, 1993; (6091): pp 25-7.

20. Anonymous. Severe *Klebsiella* infection as a cause of mortality in neonates in Harare. Paediatric Infectious Disease Journal, 1993; 12 (10): pp 840-4.

21. Leigh L, Stoll BJ, Rahman M, Mcgowan J. Jr. *Pseudomonas aeruginosa* in very low birthweight infants. Paediatric Infectious Disease Journal, 1995; 14 (5): pp 367-71.

22. Christo GG, Shenoy V, Matthai J. Shivananda PG, Venkatesh. *Acinetobacter* sepsis in neonates. India Paediatrics, 1993; 30 (12): pp 1413-6.

23. Burgner D, Hanlon M, Wong M, Kakakios A, Isaacs D. Repeated prevalence surveys of paediatric hospital acquired infection, 1996; 7 (2): pp 75-80.

24. Stalhammar C.M, Stenberg L, Lindau G. A novel *Group B Streptococci* cell surface protein. Journal of experimental medicine, 1989; 177(6): pp1593-1603.

25. Klaus M.H and Fanaroff A.A. Neonatal sepsis In: Care of the High risk neonate. (ed. Klaus + Fanafoff) 3rd ed, pp 263. Philadelphia; W.B. Saunders, 1986.

26. Pylipow M, Gaddis M. Janet S. Selective Intrapartum Prophylaxis for *Group B Streptococcus* colonisation. Paediatrics, 1994; 93 (4): pp 689.

27. Baker C.J Summary of the workshop on perinatal infections due to *Group B Streptococcus*. Journal of Infectious Diseases, 1977; (136): pp 137 – 143.

28. Martin MA, Pfaller MA, Massanari RW, Wenzel RP. Use of species identification Control, 1989; 17:pp 130-5.

29. O'Connor TA, Ringer KM. Gaddis ML. *Coagulase negative staphylococcus* sepsis in neonates. American Journal of Clinical Pathology, 1993; 99(1): pp 69-71.

30. Rhagavan M, Mondal GP, Bhat BV, Srinivasan S. Perinatal risk factors in neonatal infections. India Journal of Paediatrics, 1992; 59 (3): pp 335-40.

31. Freeman J, Epstein M, Smith EN, Platt R, Sidebottom D.G, Goldman A.D. Nosocomial *Coagulase negative staphylococcal* bacteremia in two Neonatal intensive care units.

32. American Journal of Diseases in Children, 1990; 144 (3): pp 324-329.

33. Kumar P, Saver S, Narang A. Role of routine lumbar puncture in neonatal sepsis. Journal of Paediatrics and Child Health, 1995; 31 (1): pp 8-10.

34. Greenberg DN, Ascher DP, Yoder BA, Hensley DM, Heman HS, Keith JF. Sensitivity and Specificity of rapid diagnostic tests for *Group B Streptococcus*. Journal of Clinical Microbiology, 1995; 33 (1): pp 193-8.

35. Burgh F.D, Ingerdinger J.R, Wald R.E. Meningitis In: Current Paediatric Therapy. (ed. Gellis and Kagans) 14th ed, p 54. Philadelphia; W.B. Saundaers, 1993.

36. Hall RT, Hall SL, Barnes WG. Characteristics *of Coagulase negative staphylococci* from infants with bacteremia. Paediatrics Infectious Diseases, 1987; (6): pp 377-83.

37. Scwhalbe RS, Stapleton JT, Giligan PH.) Emergance of Vancomycin resistance in *Coagulase negative staphylococcus.* New England Journal of Medicine, 1987; (316): pp 927-31.

38. De Louvois J, Harvey D R. Antibiotic therapy of the newborn. Clinics in Perinatology, 1988; 15: 365-388.

39. Low D C, Bissenden J G, Wise R. Ceftazidine in neonatal infection. Archives of Disease in Childhood, 1985; 60: 360- 363.

40. Starr S E. Antimicrobial therapy of bacterial sepsis in the newborn infant. Journal of Pediatrics, 1985; 106: 1043-1047.

41. Goldberg D M. The Cephalosporins. Medical Clinics of North America, 1987; 71:1113-1133.

42. Jessie R, Groothins W.H. Bacterial sepsis In: Current Paediatric diagnosis and treatment. (ed Kempe H.C.) 10^{TH} ed, 83, 1996.

43. Anonymous. Revised guidelines for prevention of early onset *Group B Sreptococcal* infection. Pediatrics, 1997;. 99:486-489.

44. Boo N.Y, Char C.Y. Six years of Neonatal Septicemia in a large Malaysian Maternity Hospital, 1994; 30 (1): pp 2327.

45. Muralt GV, Sidiropoulis D. Prenatal and postnatal prophylaxis of infection in preterm neonates. Pediatric Infectious Disease Journal, 1988; 7: pp72.

46. Joffe A. Granulocyte transfusion in neonates with presumed sepsis. Paediatrics, 1987; (80): pp 738.

47. Courtney SE, Hall RT, Harris DJ. Effects of blood transfusion on mortality in early on set *Group B Streptococci* septicemia. Lancet, 1979; (11): pp 462-63.

48. Van NE, Maziman JR, Swamer M. Role of exchange blood transfusion in treatment of severe septicemia. Pediatrics, 1980; (66): pp 693.

49. Antia-Obong OE, Usauto SJ, Udo JJ, Udo KT. Neonatal septicemia in Calabar, Nigeria. Central Africa Journal of Medicine, 1992; 38(4): pp 161-5.

50. Hook E W. *Salmonella* species In: Principles and practice of Infectious Diseases (ed Mandel, Douglas) 3rd ed, pp 1702. Churchill Livingstone, 1990.

51. Arrendo- Garcia KL, Diaz- Ramos R, Solorzano-Santos F, Sosa- Gonzalez I E, Beltran-Zuniga M. Neonatal septicemia due to Klebsiella Pneumoniae. Revista Latin americana de Microbilogia, 1992; 34(1): pp 11-6.

52. Fieldman G. Antibiotic use in newborns. Postgraduate doctor Africa, 1998; 20 (1): pp 24.

53. Schuchat A, Deaver-Robinson K, Plikatysis BD. Multistate case control study of maternal risk factors for neonatal *Group B Streptococcal* disease. Paediatric Infectious Disease Journal, 1998; 12: 623- 9. 1994.

54. Hurley R. Congenital and perinatal infections In: Oxford Texbook of Medicine. (ed. Weatherall, Ledingham and Warrel.) 2nd ed, pp 11.45- 11,46, 1988.

NEONATAL SEPTICAEMIA: QUESTIONNAIRE

NAME : .....

AGE : .....

MARITAL STATUS:.....

HOME ADDRESS :.....

LEVEL OF EDUATION.....

ANTENATAL HISTORY

PARITY:.....

CHILDREN ALIVE:.....

CHILDREN DIED:.....

1.....

2.....

3.....

4.....

5.....

L.M.P.....

E.D.D.....

ILLNESSES:.....

TREATMENT:.....

HIV STATUS (IF KNOWN):.....

LABOUR DATA

TIME OF RUPTURE OF MEMBRANES.....

COLOUR:.....

SMELL:.....

TIME OF DELIVERY;.....

MODE OF DELIVERY:.....

PLACE OF DELIVERY:.....

REFERRAL CLINIC:.....

BABY DATA ON ADMISSION:

GESTATION.....

BIRTH WEIGHT:.....

APGAR SCORE:.....

ONSET OF ILLNESS:.....

PRESENTING FEATURE:

FAILURE/POOR FEEDING: [ ]

TEMPERATURE: [ ]

IRRITABILITY: [ ]

RESPIRATORY DISTRESS: [ ]

CONVULSIONS: [ ]

LETHARGY: [ ]

UMBILICAL INFECTION [ ]

JAUNDICE: [ ]

TREATMENT GIVEN:.....

ADMISSION DATA

DATE OF ADMISSION TO NICU:.....

DIAGNOSIS:.....

TEMPERATURE:.....

INVESTIGATIONS.....

BLOOD CULTURE: [ ]

LUMBAR PUNCTURE [ ]

FBC [ ]

MSSU: [ ]

TREATMENT STARTED:.....

DATE O DISCHARGE:.....

DATE OF DEATH:.....