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PATTERN OF BACRERIAL INFECTION IN UNDER TWO MONTH INFANTS IN MYGOMA HOME FOR ORPHANGE KHARTOUM – SUDAN

By
Dr.Nazra Sayed Osman
M.B.B.S (University of Khartoum1996)

AThesis submitted in partial fulfillment for the requirements of the Degree of Clinical MD in Pediatrics and Child Health,

Supervisor

Prof.Salah Ahmed Ibrahim
FRCPCH, MD

Department of Pediatrics and Child Health,
Faculty of medicine, U of K

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Dedication

To

The soul of my father

My lovely mother

&

To my family.

ACKNOWLEDGMENT

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ABSTRACT

Neonatal sepsis is a life threatening emergency and any delay in diagnosis and treatment may result in death.

The objectives of this study were to a) determine the causative bacterial pathogen in under two months orphanage children, who are admitted to Mygoma Home either (i)for less than72hoursor (ii)more than 72 hours, and to study the antimicrobial sensitivity, b) to study clinical presentation and c) study the short term outcome (2 weeks) of neonatal sepsis.

The study was a prospective institution-based study, carried out in Mygoma Home for children, on daily bases from October 2004 to December 2004. Sepsis screening was done on 150 infants with signs and symptoms of neonatal sepsis, Blood, urine, Umbilical swabs and CSF culture had been taken.

The most frequent causative organisms for infants in whom sepsis assessment was done within 72 hours of admission, were *coagulase* -ve *staphylococcus* in 17 (40%) infants. *E. coli* in 6 (14.2%) infants, *Klebsiella* in 6 (14.2%) infants, and *Staph. aureus* in 6 (14.2%) infants.

On the other hand organisms isolated from infants admitted for more than 72 hrs were *coagulase* negative

staphylococcus in15 (38.4%)infants, followed by *E. coli* in 9 (23%) infants, *Klebsiella* in 5(12.8%) infants *salmonella* and *staph aureus* in 3 (7.6%)infants, for each.

The commonest five organisms had low sensitivity to ampicillin, except *Klebsiella* which had high sensitivity to it.

Coagulase negative staphylococci, salmonella, Klebsiella had a high sensitivity to gentamicin, while E. coli and Staph. aureus had low sensitivity to it.

E. coli, Klebsiella and Staph. aureus had a high sensitivity to cloxacillin, while coagulase negative staphylococcus and Salmonella had low sensitivity to it.

The mortality rate of the neonatal sepsis in this study was 8%. It is essential for every Neonatal Unit to monitor, its rate of infection and the organisms commonly encountered, as well as its sensitivity and resistance to the commonly used antibiotics, and several steps to control infections must be adopted.

ملخص الأطروحة

الخمج الدموي من الامراض المهدده لحياة الوليد؛ وأي تأخير في التشخيص والعلاج قد يؤدى إلى الوفاة.

الهدف من هذه الدراسة التعرف على البكتيريا الممرضة المسببة للتسمم الدموي في الأطفال مجهولي النسب والتي تتراوح أعمارهم أقل من شهرين؛ و كانت مدة إدخالهم وإقامتهم(في دار رعاية الطفل بالميقوما) أكثر من أو اقل من 72 ساعة؛ ومعرفة

أ مدى فعالية المضادات الحيوية.

ب.دراسة الأعراض الاكلنيكية

ج. دراسة فحوى ونتيجة العدوى في تلك الفترة القصيرة(لسبوعين).

ومن ثم تمت هذه الدراسة في دار رعاية الأطفال بالمايقوما بمنطقة الخرطوم في الفترة من أكتوبر 2004م وحتى نهاية ديسمبر 2004م وشملت150 وليدا ظهرت عليهم أعراض الخمج الدموي الوليدى؛ وتم اخذ عينات باثولوجية من البول والدم والسائل النخاعي لإجراء التحاليل اللازمة.

وكانت أكثر أنواع البكتيريا(الممرضة) في الأطفال الرضع(الذين ظهرت عليهم الإعراض) و كانت مدة إقامتهم في الدار 72 ساعة وأقل؛ هي البكتيريا العنقودية(سالبة إنزيم التجلط) 17 (40%) ثم الأشريكية القولونية 6(14.2%) ، كلبسيلا6 ((14.2% ثم العنقودية الذهبية 6 (14.2%) في الأطفال الرضع .

وفي الجانب الأخر كانت البكتيريا (الامراضية) الاكثر شيوعاً في الأطفال(الرضع) الذين كانت مدة إقامتهم أكثر من 72 ساعة كانت هي البكتيريا العنقودية(سالبة إنزيم التجلط)15

(38.4%) ثم الأشريكية القولونية19 (23%)، ثم الكلبسيلا5 (12.8%)، ثم العنقودية الذهبية 3(7.6%) والسالمونيلا3 (7.6%) في الأطفال الرضع.

وعليه كانت النتائج التالية ، حيث نجد أن عقار الامبسلين اقل فعالية تجاه الميكروبات المذكورة أعلاه، إلا أنها أظهرت فعالية عالية تجاه الكلبسيلا،

ومن جهة أخرى نجد أن عقار الجنتامسين أظهرت فعالية عالية تجاه العنقوديات سالبة إنزيم التجلط والسالمونيلا والكبسيلا، فى حين انها اظهرت فعالية قليلة تجاه الأشريكية القولونية والعنقودية الذهبية.

وأظهرت هذه الدراسة بان معدل الوفاة جراء الاخمجاج الدموي الوليدى تصل إلى (8%) .

وعلية يجب اتخاذ عدة خطوات محسوبة و مدروسة للسيطرة على الخمج الناجم في دار رعاية الأطفال بالمايقوما.

LIST OF CONTENTS

CHAPTER TWO

CHAPTER THREE

CHAPTER FOUR

LIST OF FIGURES

Page

LIST OF TABLES

List of ABBREVIATIONS

α TNF	Alpha Tumor necrosis factor
C3	Complement 3
CDC	Center of diseases control
CoNS	Coagulase negative Staphylococcus
CRP	C reactive protein
CSF	Cerebrospinal fluid
DIC	Disseminated intravascular coagulation
FFB	Fresh frozen plasma
FIG	Figure
G/L	Gram per liter
GBS	Group B Streptococcus
G-CSF	Granulocyte colony stimulating factor
GM-CSF	Granulocyte macrophage colony stimulating factor
I/T	Immature total neutrophil ratio
ICU	Intensive care unite
Ig G	Immunoglobulin G
IgM	Immunoglobulin M
IL	Interleukin
KG	Kilo gram
L3	Lumber 3
LBW	low birth weight
mRNA	Messenger RNA
N	Number
NEC	Necrotizing enterocolitis
NICU	Neonatal Intensive care unite
PGE2	Prostaglandin E2
PMN	Polymorph nuclear
RDS	Respiratory distress syndrome
SPA	Supra pubic aspiration

SPSS	**Statistic package for social science**
TNF	**Tumor necrosis factor**
VLBW	**Very low birth weight**
WBC	**White blood cells**

INTRODUCTION AND LITERATURE REVIEW

1. Introduction:

1.1. Definition:

The term neonatal sepsis or sepsis neonatorum refers to invasive bacterial infection that involve primarily the blood stream in infants during the first month of life.[1]

Commonly recognized systemic bacterial infections in newborns beside meningitis are pneumonia, otitis media, urinary tract infection, gastroenteritis, necrotizing enterocolitis, and osteomyelitis. Clinical presentation in many of these infections may be non- specific and overlapping.[2] When none of these can be clearly diagnosed in a newborn who has feature of bacterial infection, the label of neonatal sepsis is used.

Neonatal sepsis is one of the most common reasons for admission to neonatal units in developing countries.[3] It is also a major cause of mortality in both developed and developing countries.[4] The combination of a susceptible host, non-specific clinical presentation and an over changing population of pathogens makes for a great challenge.[1]

Neonatal sepsis may be categorized as early or late–onset, early-onset sepsis present within 7 days of birth, onset is most rapid in the premature neonate. Early-onset sepsis syndrome is associated with acquisition of a microorganism from the mother. Late-onset sepsis syndrome occurs at 7- 90 days of life and is acquired from the care-giving environment.

Although all infections in newborns who are born in the hospital are considered to be hospital acquired (nosocomial), infection manifesting in the first few days of life are usually caused by microorganism transmitted from mother to infant, where as infections arising late in the first week of life until discharge from the nursery are considered to be the result of nosocomial transmission.[5] The organism responsible for neonatal infection differ in different geographical areas and in different units in the same area, and it may change with time. Also the sensitivity and resistance of antibiotics vary widely in different places. So it is essential for every neonatal unit to monitor its rate of infection and the organism commonly encountered, as well as its sensitivity and resistance to the commonly used antibiotics, so that proper antibiotics are used.

1.2. Incidence:

The incidence of Neonatal sepsis is different in different geographical areas and in different units in the same area. It is affected by many factors, mainly host and socioeconomic factors. Systemic bacterial disease occurs in 1-10 per 1000 live birth in the united states, with a case fatality rate of 20 to over 75 percent.(6)

Before the wide spread implementation of the 1996 guidelines for intrapartum chemoprophylaxis for prevention of infection caused by group B Streptococcus (GBS), the incidence of neonatal sepsis in the united states varied from 1 to 10 per 1,000 live births, with average of 2 or 3 per 1,000.Although these infections are relatively uncommon, they may be associated with a case fatality rate of 15% to 30% and substantial morbidity in the surviving infants.(7)

Australia produced an incidence rate of 0.22%for early onset and o.44% for late-onset sepsis.(8)Among very low birth weight infants undergoing prolonged intensive care the rate of culture-proven sepsis may be as high as 30%.(9)

In the developing world neonatal sepsis is a greater problem. A study from Malaysia reported a rate of neonatal sepsis of 5-10 %.(10)

Late-onset invasive infection occurring in neonates older than 3 days, the incidence is in approximately 10% of all neonates, >25% of very low birth weight infant (<1500g) who are hospitalized in neonatal care units.[7]

The incidence in Sudan is not known, but one study done in Khartoum Teaching Hospital showed that the rate of umbilical colonization and infection as to be high as 100% by the third day of life.[11]

1.3. Mortality and morbidity:

It is estimated that approximately 4 million deaths occur annually in the developing countries during the neonatal period, mostly attributable to infection, birth Asphyxia, and consequences of premature birth and low birth weight.[12] Is a study done in Pakistan, mortality from neonatal sepsis was found to be 10.4 percent and from meningitis 15-50 percents. This was related to time of onset of the disease, type of disease, and the a etiological agent, the maturity of the infant and the presence and severity of associated diseases. [13]

A study of systemic bacterial and fungal infections in a neonatal unit in Austria, the mortality rate for early-onset sepsis was 15% and for late-onset sepsis 9 %.[8]

Acute mortality from sepsis has remained constant at about 15% for two decades. [14]

In Ghana the mortality rate for culture-proven neonatal sepsis is 37 %.[15]

In Sudan, in a study done in Khartoum State, death rate for all cases of neonatal sepsis was 27%. It was higher for low birth weight (LBW) infant (58%), early onset disease (32%), and for Group B Streptococcus (GBS) infected infant (40%).[16]

Neonatal infection is a common cause of prolonged stay in hospital; it prolongs the stay of LBW and delays their catch up. Long term or permanent sequalae occurs in 25-30% of survivors after neonatal sepsis. [17]

1.4 Epidemiology:

Our knowledge of the epidemiology of prenatally acquired bacterial infection is based on extensive studies of the GBS and, to lesser extend *E. coli*. [8]

The two major factors influencing the prevalence of GBS sepsis are vaginal carriage rate among pregnant women and the effectiveness of strategies to prevent infection- contamination of the baby at birth. [19]

The gastrointestinal tract is a major reservoir of *E. coli* and perhaps also of group B streptococcus and L. monoytogenes. [20] K1 strains of *E. coli* are associated with most neonatal infection with this organism, K1 *E. coli* were found in 20-40 percent of the rectal swab cultures from healthy infants and adult women. [21]

The nature of colonizing organisms is determined by the pattern of flora at the birth canal and in the environment.[22] Babies born at home are colonized by organisms derived primarily from the mother. Colonization of the upper respiratory tract occurs rapidly, and 40% of infants have positive pharyngeal culture by the third day, coagulase-negative staphylococci (CoNS) being the commonest followed by *Streptococcus viridians* and *Staphylococci aureus*. [23]

Skin colonization is very rapid, with a number of bacteria increasing 100-fold during the first week. CoNS predominate but *Staph. Aureus* may be found in 65% of infant. [24]Infant on a neonatal unit at a greatest risk of becoming colonized by pathogens, which often show resistance to antibiotics CoNS and antibiotic-resistant Gram-Negative organisms predominate.[25]

Nosocomial infection by *Staph. aureus* and Gram-Negative enteric bacilli are easily transmitted by the hands of medical staff, and equipment like sucking catheters, endotracheal and feeding tubes, intravenous cannulas, monitor leads,..etc. Thus those infants needing

resuscitation at birth or those who stay in hospital for prematurity or diseases are at a great risk of acquiring hospital infection usually with resistant organisms.

In the absence of antibiotic treatment, between 40% and 70% of infants whose mothers are colonized, at delivery, become colonized themselves with GBS by one of three mechanisms: transplacental transmission in the presence of maternal bacteraemia, ascending from the vagina and cervix through microscopic leaks in the amniotic membranes or through frankly ruptured membranes, and surface contamination during passage through the birth canal.[26] *Listeria monoytogenes* is a worldwide soil organism with a large animal reservoir. A mechanism of transfer from animal to human has not been proved. In 1993, a carriage rate of 21% was reported for a symptomatic house-hold contact of individuals with invasive listeriosis.[27]

1.5. Pathogenesis:

Various factors interact to determine whether a new-born after exposure to a potential pathogen will develop disease or become an asymptomatic carrier. Similarly, a number of factors increase the risk of infection of amniotic fluid. It is useful to consider obstetric and host factors separately.[28]

1.5.1. Obstetric factors:

Most obstetric risk factors provide opportunities for prolonged exposure of the fetus to potential pathogens carried in the maternal gastrointestinal or genitourinary tract.

Boyer and Coworkers (1983) epidemiologic study of GBS reveled significantly increased attack rate (7.6 per 1,000 liver births) with the following birth weight of less than 2.500g, rupture of membrane for more than 18 hours and maternal intrapartum fever higher than 37.5(C. A rate of 20.2 per 1.000 live births was observed in infant whose weight was 1.000g or less.[28]

A study in united kingdom-showed that prematurity, rupture of the membranes more than 18 hours before delivery, rupture of the membrane before the onset of labour, and intrapartum fever, were significant risk factors for infection.[29]

Maternal GBS bacteraemia is associated with a high GBS colonization rate, and increases the risk of neonatal GBS infection. The attack rate in infant born without intrapartum antibiotics has been reported as high as 8% in maternal GBS rectal or vaginal carriage. [30]

Neonatal sepsis may also be more frequent in other obstetric conditions settings including multiple gestation, gestational diabetes, fetal asphyxia or acidosis and meconium staining.[31]

1.5.2. Host factors:

1.5.2.1. Portal of entry:

Abrasion and cuts, mucosal injury, introduction of cannulae, catheters and endotracheal tubes, all open the way for bacterial invasion.[32]

1.5.2.2. Antibiotic exposure:

Antibiotics are used freely in neonatology and increasingly so in obstetrics. The resulting obliteration of colonizing flora predisposes to superinfection with pathogens, such as yeast and antibiotic resistance bacteria become common.[33]

1.6. Neonatal immunology:

The neonate is unable to respond effectively to infectious hazards because of deficit in the physiological response to infectious agents. The neonatal neutrophil or polymorphonuclear (PMN) cells, which is vital for effective killing of bacteria, is defective in chemotaxis and killing capacity.[34] Decreased adherence to the endothelial lining of blood vessels, reduces their ability to marginate and leave the intravascular area to migrate into the tissues. [35]

Neonatal monocyte concentration and function are at adult levels; however, macrophage chemotaxis is impaired and continues to exhibit decreased function in to early childhood. Neonatal bone

marrow stem cells, and peripheral blood cells, respond to factors such as GM-CSF and, G-CSF, 10 times more efficiently than adult cells. [36]

The infant receives immunoglobulin G (IgG) prenataly after his16th weeks of gestation. However, the infant born prematurely has less Ig_G due to the shorter period of placental transmission of immunoglobulin. Normal circulating amounts of Ig_{G3} are not achieved until the age of 10 years, and of Ig_{G2} until 12 years. Their ability to generate adequate antibody responses to polysaccharide antigens are not achieved until about 2 years.[37]

The neonate is capable of synthesizing immunoglobulin M (Ig_M) in utero at 10 weeks of gestation; however, Ig_M level are generally low at birth, unless the infant was exposed to an infectious agent during the pregnancy. The low level of Ig_M antibodies increases susceptibility to infection by Gram-negative bacterial and, coupled with low C36 production, accounts in part for the predominate of such infections in the newborn.

The fetus is capable of complement protein production as early as 6 weeks gestational age, deficiencies appear to be greater for neonates in the alternative pathway than in the classical pathway, mature complement activity is not reached until infant are aged 6-10 months.

Fibronectin, a serum protein that assists with neutrophil adherence and has opsonic properties, is found in lower concentrations in neonates therefore, neonatal sera have reduced opsonic efficiency against GBS, *E. coli*, and *S. pneumoniae*.[38]

The physical and chemical barriers to infection in the human body are present in the newborn but are functionally deficient, skin and mucous membranes are broken down easily in the pre-mature infant.[39]

The high infection rates in preterm neonates are related to immaturity of both humoral and phagocyte immunity. Infants born before 30 weeks gestation are severely hypogamma-globulinaemic.[40]

The high incidence of postnatal neutropenia in both well and septic preterm neonates is a consequence of the reduced total body neutrophil mass in infant born before 32 weeks gestation, and is an evidence of immature granulopoiesis even when peripheral blood neutrophil counts are normal. The organisms causing bacterial infections are similar to those seen in older children and adults with profound neutropenia, and this is clinical evidence of neutrophil functional immaturity.[41] These individual deficiencies of the various components of immune activity in the neonate conspire to create a hazardous situation for the neonate exposed to infectious agent.

1.7. Clinical manifestations:

The clinical signs of bacterial infections in the neonate are distinctively non-specific and may occur with viral infection or with non infectious disorders. [1]

Early recognition, diagnosis and treatment of serious infection in the neonate is essential because of the extreme rapidity with which the risk of permanent morbidity or mortality can develop. Progression from mild symptoms to death can occur in less than 24 hours.[42]

1.7.1. History:

In taking the history, it is important to consider maternal, perinatal and neonatal events that put the baby at increased risk of infections like maternal febrile illness, history of vaginal discharge history of rupture of membranes, and if the mother has overt intrapartum infection. About 15.2% of preterm babies and 4.1% of term babies usually develop infection.[43] Maternal urinary tract infection is an important risk factor for neonatal sepsis.

History of any factors predisposing to nosocomial infections, such as a history of possible contact with an infected person of the babies environment, and symptoms of sepsis such as jaundiced or bleeding tendency and abdominal distension or blood in the stool.[1]

1.7.2. Signs of neonatal sepsis:

In the early stages, signs are subtle and often noted first by the mother or the nurses. Such concerns must always be taken seriously and should not be overridden by the findings of a single clinical examination, especially when risk factors for sepsis are present.

The nonspecific clinical signs of early sepsis syndrome are also associated with other neonatal diseases, such as respiratory distress syndrome (RDS), metabolic disorders, intracranial hemorrhage and a traumatic delivery. Therefore, diagnose of neonatal sepsis should be by excluding other diseases, performing an examination, and testing for more specific indications of neonatal sepsis, by laboratory investigation .

1.7.2.1. Early Signs:

- Going off: this is difficult to define, yet is often the earliest and most important sign. The baby is just not "right". He is slightly floppy, pale or mottled (cutis marmorata), may be slightly irritable or unresponsive, loses interest in feeding or suck poorly.
- Temperature changes: After excluding the effect of an abnormal environment, temperature and pyrexia in the first 1-2 hours of age in a baby of a pyrexia mother,[44] a temperature below 36(C or above 37.5(C and sustained for more than an hour must be regarded as probably due to infection until proved otherwise. Although the presence of a fever generally indicates an infective illness, not all infective illness cause fever and 25 - 30% of infants with bacterial infection do not have a fever at the time of presentation.[45]
- Jaundice: infection should be considered as a cause of jaundice if there is no other obvious explanation. Jaundice during sepsis is due to the effect of bacterial endotoxin on the liver, plus an increase in haemolysis.[46]
- Apnoea: in the preterm baby apnoeic attacks are an early and significant sign of all types of infection.

- Tachypnoea recession: mild respiratory distress, as evidence by a raised respiratory rate (sustained above 60 breaths per minute) and slight recessions are among the first non-specific sign of sepsis.
- Cardiovascular signs: a tachycardia > 160/min is often present early in sepsis. In cases of myocarditis or endocarditis cardiovascular signs will be more marked. Poor cutaneous circulation is common and is indicted by mottling and delayed capillary filling after the skin has been blanched by gentle pressure.
- Gastrointestinal: the baby may vomit, has mild diarrhoea or may develop an ileus associated abdominal distension.
- Irritability.
- Poor weight gain: this may be a marker of chronic low-grade infection, such as a urinary tract infection or an infected central line or shunt.
- Skin: petachiae may be present or there may be peronychia, septic spots, or omphalitis.

1.7.2.2. Late signs:

The more obvious signs appear only with advanced infection, and if they occur, it usually means that the subtle signs have been present for sometime beforehand.

- Respiratory: cynosis, grunting and dispose is the classical sign of neonatal lung disease.
- Abdominal: sign of intestinal obstruction may be due to generalized sepsis as well as necrotizing enterocolitis (NEC) and structural malformation of the gastrointestinal tract.
- Central nervous system: high-pitched cry, neck retraction, bulging fontanel and convulsions are late feature of neonatal meningitis.
- Hemorrhagic diathesis: DIC with petachiae and bleeding from puncture sites, the gut or the renal tract is a late sign of sepsis. Thrombocytopenia without evidence of DIC is also common with severe infection, especially fungal.
- Sclerema: this is a non-specific feature of any serious neonatal illness.
- Pseudo paralysis: the failure to move one limb may be the only clue to septic arthritis or osteomyelitis.

1.8. Diagnosis:

No single laboratory test had been found to have acceptable specificity and sensitivity for predicting infection. Therefore, the results of laboratory studies must be assessed in conjunction with the presence of risk factors and clinical signs of sepsis. [47]

1. 8.1. Microbiological investigations:

1.8.1.1. Blood culture:

Blood culture is critical in the diagnosis and treatment of bacterial infections. When preparing for blood cultures, the site should be cleaned to remove soiling, and the remaining microorganism on the skin should be chemically killed. Skin preparation of a two-stage procedure, involving 10 to 30 second swabbing of skin, and allowing the agent to dry. Alcohol, povidone iodine, tincture of iodine, and chorhixidine have been shown to be effective.[48]

The quality of skin preparation is believed to be important in reducing contamination of blood culture with modern laboratory techniques. 0.5 ml of blood may be sufficient for a successful culture, but increasing the volume to 1- 2 ml definitely increases the chances of a positive culture.[49] Two blood cultures will increase the yield of positive results, a contaminated blood culture is often

diagnosed when only 1 of 2 culture is positive, although inconsistent growth could also represent bacteraemia with a low concentration of organisms.

The problem lies in distinguishing septicaemia from skin contamination. A pure growth appearing within 24 - 48 hours is virtually always significant, but mixed organisms, bizarre organisms or growth that does not appear until after 72 hours of incubation should raise suspicion.

The coagulase negative staphylococcus(CoNS) present the greatest difficulty because they colonize the skin of all babies and yet are the commonest pathogen among NICU in mates. However, a recent study of multiple site cultures, using plasmid typing and antibiotyping has shown an incidence of unrelated strains of CoNS from different sites of greater than 50%, suggesting a high frequency of contamination.[50]

Additional tests such as the C reactive protein and white blood count and immature to total neutrophil ratio may be helpful to distinguish a false-positive from a true-positive culture.[51]

1.8.1.2. Urine culture:

There are two practical ways to obtain urine from babies for the purpose of diagnosing infection, one is to use urine collection bag and the other is to reform on supra pubic aspiration (SPA). SPA

overcomes the problem of contamination. Urine culture may be omitted within the first 72 hours of life because bacteria recovered from urine at this period are of hematogenous origin and will be isolated from blood cultures.(44)

1.8.1.3. Lumbar puncture:

Lumbar puncture is being used as a screening procedure, although a large number of negative CSF results can be expected. In a survey 99.05% of all CSF results were normal.(52) Lumbar puncture is more likely to produce a positive result in late-onset than in early onset sepsis.(53)

1.8.1.4. CSF analysis:

Polymorphonuclear leukocyte count higher than 20/mm^3 should be regarded with suspicions, and count above 30/mm^3 are strongly indicative of meningitis. The upper normal limit of CSF protein is 1.5 - 2.0 g/L in the term and 3.7 g/L in the preterm babies.(54) The levels are usually raised in meningitis. A low CSF glucose level (< 1.0 mmol/L or a value less than 30% of the blood glucose) suggests bacterial meningitis.

1.8.1.5. Surface swab and body fluid culture

Examination and culture of fluid obtained from abscesses, septic arthritis, skin pustules or empyaema and of swabs from

suspected infected umbilicus or conjunctiva provide immediate clues to the diagnosis.

1.8.1.6.Vascular lines and thoracocentesis tubes culture:

The tips of umbilical cannulae, central lines and thoracocentesis tubes should be sent for culture when removed.

1.8.2 Radiology:

All babies with suspected sepsis should have a chest X-ray. An abdominal X-ray and ultrasound are indicated if there are abdominal signs or there is a suspicion of urinary tract infections.

1.8.3. Diagnostic markers:

Diagnostic markers of infection are useful indicators of neonatal sepsis. Serial measurements of infection markers can improve diagnostic sensitivity, and the use of multiple markers can enhance diagnostic accuracy. Current evidence suggests that promising markers may be useful for early termination of antimicrobial treatment, but none of the current diagnostic tests are sensitive and specific enough to influence the clinical decision for withholding antibiotic treatment at the onset of a suspected infection.

1.8.3.1. Haematological tests:

In the early and mid 1980s, neonatal clinicians relied mainly on haematological indices as adjunct indicators for early diagnosis of neonatal sepsis. Total leucocyte count, total neutrophil count,

immature neutrophil count, immature to total neutrophil (I/T) ratio, immature to mature neutrophil ratio, morphological or degenerative changes in neutrophil such as vacuolisation, Dhle bodies, intracellular bacteria, toxic granulation, and platelet count have been studied either singly or in combination.[55] Results of white cell counts and ratios varied widely across studies, with sensitivity and specificity ranging from (17% to 90% and 31% to 100%) respectively.[56]

In general the abnormal leucocyte ratios including the I/T ratio more than 0.2Tend to have a high sensitivity, whereas abnormal leucopenia and neutropenia, tend leucocyte counts, such as to have high specificity.[57] Low platelet counts and morphological changes in neutrophils were often severe and late signs of infection.[58]

More recently, granulocyte colony stimulating factor, a mediator produced by the bone marrow for facilitating the proliferation and differentiation of neutrophils, has been proposed to be a reliable infection marker for early diagnosis of neonatal sepsis.[58]

Circulating thrombin-antithrombin III complex, plasminogen activator inhibitor-1, plasminogen tissue activator, fibrinogen, and D-dimer concentrations are significantly raised in infected infants compared with non-infected patients.[59]

1.8.3.2 Acute phase proteins and other proteins:

Acute phase proteins are produced principally by the liver as part of an immediate inflammatory response to infection or tissue injury. This group of endogenous peptides was widely studied in the late 1980s and early 1990s, as it was recognised that haematological indices alone could not be confidently used as decision criteria for the diagnosis of infection or for guiding antimicrobial treatment. The most extensively used and investigated acute phase reactant is C reactive protein (CRP).[60] CRP is synthesised within six to eight hours of exposure to an infective process or tissue damage. It has a half life of 19 hours and may increase more than 1000-fold during an acute phase response.[61] CRP as a diagnostic marker in neonates has higher sensitivity and specificity than total neutrophil count and I/T ratio.[62] However, as the concentrations of CRP increase rather slowly in the initial phase, the sensitivity at the time of sepsis evaluation is only 60%. Serial measurements at 24 and 48 hours after the onset of illness considerably improve the sensitivity (82% and 84% respectively).[63]

1.8.3.3. Chemokines, cytokines, adhesion molecules, and components of the immune pathway:

These groups of infection markers were extensively studied in the mid and late 1990s. Although it is widely believed that preterm as well as term newborns have immature inflammatory responses, a recent study has shown that these infants display a higher percentage of interleukin IL6 and IL8 positive cells than do adults [64] The rationale for investigating this diverse group of intercellular messengers is that leucocyte indices and CRP are "late" markers and are not sensitive enough for early diagnosis of neonatal sepsis. Of the many mediators, much attention has been focused on IL6, IL8, and tumour necrosis factor (TNF).Umbilical cord blood IL6 has been consistently shown to be a sensitive marker for diagnosing neonatal infection within 72 hours of birth, the sensitivities and negative predictive values being (87–100% and 93–100%) respectively.[65]

In both early and late onset sepsis, IL8 and IL8 mRNA concentrations are substantially higher in infected than non-infected newborns.[66] IL8 is considered to be a highly accurate marker with sensitivities ranging from 80% to 91% and specificities from 76% to 100%.[67]

1.9. Treatment of neonatal sepsis:

1.9.1. Antibiotic therapy for neonatal septicemia:

Presumptive antibiotic therapy in the neonatal is directed towards the most commonly encountered pathogens for a given clinical setting. Ampicillin and an aminoglycosides, usually gentamicin is usually effective against these bacteria.

Another important consideration is the in vivo and in vitro synergy demonstrated for penicillin with aminoglycosides, especially against GBS and listeria.[12]Third generation cephalosporins are also effective against gram negative infections, but they have limited activity against listeria organisms, cephalosporins also displace bilirubin from albumin-binding sites which may place the neonate at increased risk for kernicterus in the setting of hyper bilirubinemia.[68]

Infection, although ampicillin and gentamicin provide excellent broad coverage for perinatal pathogen, this combination may not be preferred for neonate at risk for nosocomial infections. Considering the predominance of CoNS as the principal cause of nosocomial sepsis, vancomycin has become the principal agent for presumptive gram-positive bacterial coverage. Presumptive gram-negative coverage is provided with an aminoglycoside. The aminoglycoside of choice is usually gentamicin but resistant

organism may be prevalent in many nurseries. An alternative aminoglycoside is amikacin; and resistance to these antibiotics has been reported to be low, despite long-term use in the nursery. In the other hand a study done in Pakistan by Rahman *et al*[96] showed a very high degree of resistance of gram negative organisms to first line antibiotics, as about 40% of *Staph aureus* were resistant to ampicillin. Also there was a high degree of resistance to cephalosporins by both Gram positive and Gram negative organisms, and only 43.5% of *pseudomonas* were sensitive to ceftazidime. A low degree of resistance to quinolones was shown.

In a recent multicentre study, there was no difference in the mortality between units that used vancomycin as first live treatment and those that used ampicillin or another anti-staphylococcal agent, flucloxacillin together with an aminoglycoside.[70]

1.9.2. Adjunctive therapies:

- Immunotherapy for neonatal septicemia: the human neonate may be considered an immunocompromised host with incomplete development of multiple components of the immune system

- Immunoglobulin therapy: There is evidence of improved humoral immunity in babies after immunoglubulin infusion, and enhanced opsonophagocytosis of CoNS by neonatal blood after the addition of immunglobuline was proved.[71]
- Granulocyte factor and granulocyte macrophage colony stimulating factor: treatment with either (G-CSF) or (GM-CSF) could increase the neutrophil count without apparent short term toxicity.[72]

Follow up at two years of age of the small cohort treatment with G-CSF found no long term adverse effects. However, there were no data about clinical efficacy.[73]

G-CSF has been used for treatment of sepsis complicated by a lower neutrophil count, because of its powerful ability to mobilize performed neutrophils from the marrow into the circulation and its effect on neutrophil precursor proliferation. [72]

- Double volume exchange transfusions: double volume exchange transfusion using fresh blood have seen used in neonatal septicemia in attempt to remove bacterial toxins and/or decrease the bacterial burden, improve peripheral and pulmonary perfusion, and bolster the immune system of infected newborn.[68]

- Fresh frozen plasma: (FFP) is commonly used as part of the treatment of the septic infant in an attempt to enhance the humoral immunity.[72] However when, FFP was infused into infants no effect on the serum concentration of components of humoral immunity was found.

1.10. Classification of neonatal infections:

Classification is useful because it facilitates consideration of common principles of causation, presentation and treatment. The following is the most helpful to the practice of neonatal medicine:

- Early onset sepsis: Definitions range from 24 hours to 7 days, but here the term means is taken to infection presenting within the first 72 hours of life and commonly caused by microorganisms acquired from the mother before or during birth. Other terms used for this pattern of infection are "vertically transmitted" meaning from mother to infant and "perinatally acquired".
- Late the onset sepsis: this term means infection presenting after 72 hours of age and generally caused by micro-organisms acquired from environment. The other terms used for this pattern of infections are nosocomial and hospital

transmitted. Nosocomial means literally of or related, to, a hospital.

1.10.1. Early onset neonatal sepsis:

Early onset sepsis is usually a fulminating septicaemia illness, often complicated by meningitis or pneumonia. Early onset neonatal sepsis occurs at an estimated rates of 1- 2 cases per 1000 live births in the United States. Blood culture may be positive in up to 20% of infants in Neonatal Intensive Care Unit.[74] The incidence of early onset may be reducing in developed countries, especially among low birth weight infants, possibly owing to antibiotic prophylaxis for group B streptococcal infection.[75]

Most early onset sepsis is caused by *Streptococcus agalactiae*, commonly known as GBS.[76] Other important organisms are *E.coli*, *Streptococci* other than *GBS*, *H.influenza*, *L. monocytogenes*, Gram-negative anaerobes, fungi and *Chlamydia trachomatis*.

GBS and *E. coli* together account for 70 to 80%the yields of blood and cerebrospinal fluid culture. [77]

In most of the developing countries, Gram negative organisms remain the major cause of neonatal sepsis. [12]

1.10.1.1. Early onset neonatal sepsis due to group B streptococcus:

There are seven identifiable subtypes of GBS, based on capsular polysaccharide antigen: 1a, 1b, II, III, IV, V, VI, and one non-typable group. All are implicated in early onset disease, but most neonatal infection is caused by type I, II and III.

GBS is now the most important cause of bacterial sepsis in the newborn, with a reported incidence of 0.5-2 per 1000 live birth.[78] and causing significant morbidity and mortality.

In a study done in South Bedfordshire (1993 - 1998), an incidence of early onset GBS infection of 1.15 per 1000 live births had been shown, with increasing incidence over the six years period of the study.[77] Most cases of GBS sepsis developed within the first 4 - 6 hours and almost 90% of cases present within 24 hours of birth.[79]

In a multicentre study in United States, onset of GBS sepsis was in the first day of birth in 46% of cases and the mean age at onset was 1.7 days. [77] In Alwasal hospital, Dubai, Koutouby[80]Habib Alah found that out of 106 positive cultures of neonatal sepsis , group *B Streptococcus* was the commonest organism in 23%

Most of the babies present with the early signs of sepsis without prompt recognition and treatment, the baby condition rapidly worsens and he requires intubation and IPPV for apnea and severe hypoxaemia.

Hypotension, metabolic acidemia, tachycardia and poor peripheral perfusion develop in severe cases and then the prognosis becomes poor.[81]

Early onset GBS leads to hypotension, hypoxaemia and lung injury by stimulating the release of cytokines, such as tumor necrosis factor- α(TNF-α) IL1 and IL6 from antigen presenting cells, including macro-phages and monocytes. TNF-(can be detected in the serum and urine of babies with GBS sepsis (but not from healthy control).[81]

Another feature of the GBS is its ability to invade pulmonary endothelial cells,[82] especially the cells of the microvasculature and lead to the release of the prostacycline and PG_E2,[83]which leads to increase in pulmonary arterial pressure and pulmonary and systemic vascular resistance, and decreases the cardiac output and the heart rate. Host defenses against GBS include polymorphonuclear leucocytes, complement and type specific antibodies directed against the polysaccharide and protein antigens. A baby is most susceptible to GBS when his mother, despite having GBS in her vagina, has little or

no circulating anti-GBS1gG.[84] This is particularly likely if the baby is born prematurely.

Investigations of GBS sepsis:

On no account should the treatment of suspected early onset sepsis be delayed pending the results of the tests. The objective of performing test is to provide retrospective confirmation of the diagnosis, to identify the responsible organism and to look for complications.

Microbiological Investigation:

The blood cultures will almost in invariably be positive if the mother had not been treated with an antibiotic. Meningitis is unusual in infants presenting at the first hours of life, but lumbar puncture should be performed in infants, presenting with signs of early onset sepsis[85] GBS antigen can be identified by latex particle agglutination test on the urine.[86]

However, in a multicentre study evaluating the latex particle agglutination test in the urine of babies with culture proven sepsis, only 53.5% of infected babies had a positive test.[87]

Haematological Investigation

Neutropenia and the presence of the primitive cells in the peripheral blood are common,[88] and neutropenia < 1.5 x 10^9 is an ominous sign.[89] Anaemia and thrombocytopenia may develop in survivors. Acute-phase reactants such as C. reactive protein (CRP) are generally highly elevated in GBS sepsis, but there may be a delay of 12 hours or so between the onset of signs and the rise in CRP.[90]

Treatment of GBS:

Intravenous antibiotics, at the high end of the recommended dose range, must be started immediately.

When diagnosis is suspected, a combination of ampiclox and gentamicin is a good choice for blind treatment of early onset sepsis in the newborn, because of synergism between those antibiotic against GBS.[91] because it is necessary to cover other organisms responsible for the syndrome. A cephalosporin alone is an unsatisfactory initial therapy for early onset sepsis, as it will not treat *L. monocytogenes* or *Enterococci*. Once the diagnosis of GBS sepsis is confirmed, therapy can be simplified to intravenous benzyl penicillin alone given for 10 days, as GBS is very sensitive to penicillin.

Prevention of GBS sepsis:

Ever since group B streptococcus (GBS) emerged as the commonest cause of perinatal sepsis in the late 1970s, there has been controversy about prevention strategies

In 1996, the Centers for Disease Control and Prevention (CDC) in the United States published consensus guidelines for selecting women for intrapartum antibiotic prophylaxis using either of two alternative strategies. One strategy was based on maternal GBS carriage, and the other on clinical risk factors-preterm labour (< 37 weeks' gestation), prolonged rupture of membranes (>18 hours) or intrapartum fever (> 38^{o}C).[92] The rationale for the latter strategy was that, before widespread use of intrapartum antibiotics, one or more of these risk factors was found in up to 80% of mothers of infants with GBS sepsis.[93]Gradual implementation of these consensus guidelines in the US was associated with a fall in the incidence of perinatal GBS sepsis from 1.7/1000 in 1992 to 0.5/1000 in 1999.[94] In Australia, there was also a decrease in the incidence of perinatal GBS sepsis, from 1.2/1000 in 1991–1993, when three of nine neonatal units surveyed had prevention strategies in place, to 0.5/1000 in 1995–1997, when all 11 units surveyed had prevention strategies.[95] A recent review concluded that there is evidence, albeit from relatively poor-quality trials, that

intrapartum prophylaxis reduces the incidence of neonatal sepsis, but not deaths.[96]

Despite this evidence, concern continues about excessive use of intrapartum antibiotics. There have been several reports that their increasing use is associated with an increased proportion of cases of neonatal sepsis caused by penicillin-resistant bacteria.[97]Although it is sometimes difficult to prove, there is considerable empirical evidence that increased antibiotic use generally leads to increasing bacterial resistance. It is plausible that exposure to antibiotics *in utero* might delay colonisation of the infant gut with penicillin-sensitive anaerobes and allow penicillin-resistant facultative bacteria, many of which are potential pathogens- to become established.

Recently, the CDC published revised guidelines, recommending a single strategy for prevention based on universal prenatal screening for vaginal or rectal GBS colonisation.[98] The recommendation was based on a retrospective cohort study, which showed that perinatal GBS sepsis was significantly less frequent in infants of women given intrapartum antibiotics on the basis of documented GBS screening results (0.33/1000 births) than in infants of women managed on the basis of risk factors (0.59/1000 births; relative risk, 0.48; 95% CI, 0.37–0.63).[99] This result is not

surprising. A risk factor-based protocol cannot, by definition, prevent sepsis in infants whose mothers have no risk factors. On the other hand, the proportion of cases prevented by a protocol based on GBS colonisation depends on the sensitivity of the screening method, effectiveness of prophylaxis and compliance with the protocol.[100]

The GBS screening strategy results in at least a third of healthy young women (and their infants) being given intravenous antibiotics during labour, at significant cost and with some risks, but can achieve a lower rate of perinatal GBS sepsis. Whichever strategy is chosen, the most important determinant of its effectiveness will be compliance.

Neonatal prophylaxis:

Some studies have shown that giving prophylactic penicillin to all babies at risk of GBS sepsis or less than 2.00 kg will cause a significant reduction in the incidence of GBS sepsis.[101]

1.10.1.2. Other organisms causing early onset neonatal sepsis:

- ***E. coli:***

E. coli and *S. aureus* were the most common infections hazards to neonates in the 1950s in the United States. During 1990 GBS and *E. coli* continue to be associated with neonatal infection which together may account for 70% - 80% of blood and cerebrospinal

fluid culture.[77] *E. coli* is one of the common organisms causing early onset sepsis in developing countries.[12]

- ***Haemophlus influenza:***

H. influenza especially the non-capsular non serotypable strain has an affinity to the female genital tract and is responsible for almost 10% of early onset sepsis,[102] Third only important to GBS and *E. coli*. Most infant present immediately after birth with respiratory distress due to pneumonia, meningitis and conjunctivitis are relatively common. The reporting mortality is in the region of 5%.[103]

- ***Listeria monocytogenes:***

It is difficult to know the tine incidence of neonatal listeriosis, but recent active surveillance in the United States indicates a rate of 13 per 100,000 live births[104]. As in CBS infections, there is both an early onset and a late onset form of the disease.

1.10.2. Late- onset sepsis:

Most of neonatal infections, which begin more than 72 hours after birth are considerably organisms acquired from the postnatal environment, rather than transplacental or from the birth canal. In neonatal ICUs, blood stream infections were an ever-greater proportion of all infections than in Paediatric units.[105]

In a prospective epidemiological study carried out in Australia neonatal units, the incidence of late-onset systemic sepsis was 44 per 1000 live births, compared to 22 per 1000 for early onset sepsis. The mortality rate from late-onset sepsis was 9% as opposed to 15% per early onset sepsis.[106]

The commonest organism causing late-onset systemic sepsis are CoNS, gram negative bacilli (such as *Klebsiella* sp, *E. coli*, *Serratia marcescers* and *Pseudomonas* sp), *Staph. aureus* and various *Candida* sp. Late-onset sepsis occurs in approximately 10% of all neonates and in > 25% of very low birth weight infants ((1500 g) who are hospitalized in Neonatal Intensive Care Units (NICUs).[74]

1.10.2.1. Epidemiology of nosocomial spread of infection:

The important reservoirs of microorganisms involved in late-onset sepsis are people, including the subject's own skin and gastrointestinal tract, other babies, hospital staff and visitors. Rarely, the source is the physical environment. Prematurity and low birth weight are important risk factor of late onset sepsis especially that caused by CoNS.[107]

Many studies have demonstrated a strong positive correlation between rate of nosocomial infection and the use and duration of use of ventilators, lines to central vascular access, intravenous fat emulsions and implanted shunt for hydrocephalus.[108] The importance of exposure to these risk factors has bee illustrated by the finding of a positive association between the rate of nosocomial infection and the overall average duration of stay on the NICU, as well as the individual duration of stay on the NICU.[109]

1.10.2.2. Specific examples of nosocomial infection Coagulase-negative *Staphylococci*:

Before 1980, most late onset or nosocomial infections in neonatal nurseries in industrialized countries were caused by *Staphylococcus aureus* and gram negative bacilli. For the last 20 years, however, CoNS have predominated and been responsible for at least half of all late onset infection.[110]

In a multicentre study of *CoNS* infection in Australian neonatal units,[111] the over all incidence of *CoNS* sepsis was 3.4 per 1000 live birth, the single most commonly reported association was with necrotizing enterocolitis (NEC). Other important associations were skin sepsis, urinary tract infections, and infective endocarditis.Babies with CoNS infection was smaller and more premature than controls. In a recent study very low birth weight

babies with CoNS infection had a significantly higher death rate (10%) than uninfected babies (7%). The mortality associated with gram negative (40%) and fungal (28%) sepsis was much higher.[112]

There are more than 20 species of CoNS, but 60 - 80% of the isolates from babies are *Staph Epidermidis*, with *Staph haemolytic* making up most of the remainder, Staph*. warnerii* and *Staph. capitis* a long way behind.[113] Strains of CoNS isolated from preterm infants exhibit low rates of susceptibility to penicillin and aminoglycosides.[114]

Infected infants are typically long stay NICU patients on ventilators and with central venous access. Preterm infants seem particularly vulnerable to attack by CoNS, and their deficiency of complement mediated opsonic activity against *Staph. Epidermidis* may be an important factor in this. Infection is commonly with slime producing stains.[115] Slime is a viscous extracellular polysaccharide substance, which facilitates adherence to smooth surfaces, such as the plastic, or silicone used for vascular lines, shunt, and endotracheal tubes. Slime also inhibits neutrophil chemotaxis and phagocytosis and suppresses blastogenesis.[115]

***Staphylococcus aureus*:**

Staph aureus is inherently far more pathogenic than CoNS, and epidemiological evidence suggests that some strains are more virulent than others.

In developed world, *Staph. aureus* is much rarer cause of systemic neonatal infection than GBS, CoNS or the gram negative bacilli. *Staph. aureus* remains, however, the commonest cause of infection in bones, joint, skin, umbilical cord, and a common cause of eye infection.(116)

Systemic infection with *Staph. aureus* carries high morbidity and mortality rates. In the developing world *Staph. aureus* is a common cause of neonatal sepsis and in Nigeria it is the commonest pathogen causing neonatal meningitis.(117)

In a study of *Staph. aureus* colonization of the umbilicus, rate of 68% and 65% were found at 48 hours and 8/9 days respectively.(118) In that study the rate of infection with *Staph. aureus* was 12% and there was a significant positive relationship between the level of colonization and the risk of infection.

Gram negative bacilli:

Most of gram negative bacilli, which cause neonatal sepsis, belonged to *Enterobacteriaeceae* family. The most important gram negative bacilli causing neonatal sepsis in developed countries are

E. coli, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*, *Serratia marcescens*, *Citrobacter diversus*, *Proteus mirabilis* and *Enterobacter cloacae*. In the developing world these same organisms are prominent,[119] but in addition more overtly pathogenic members of the *Enterobacteriaeceae* such as the *Salmonellae* and *Shigella* are important cause of neonatal sepsis.[120]

Gram negative bacilli account for 20 - 30% of cause of late-onset sepsis in developing countries. In recent study from Northern Jordan, *Klebsiella* sp accounted for 64% of cases of culture proven neonatal sepsis,[121] similar result have been reported by Dawodu from Riyadh S audi Arabia.[122].

Enterococci:

These are mostly none haemolytic. They are normal bowel organisms, which only cause disease when they get out of their proper place. The organisms causing most disease in babies are *Enterococcus faecalis*, and *Enterococcus faecium*.[123]

In the NICU, *Enterococci* are an important cause of serious late-onset sepsis among very low birth infants. [124]

1.10.2.3. Prevention of nosocomial infection:

The principles of control of cross-infection in hospital are well established.

- Unit design: to minimize cross-infection adequate space should be allowed around the cots. In U.K, Department of Health, recommended that the minimum space allocated to each incubator in a six -cot intensive care nursery should be 3 m^2. Enough sink must be provided, so that hand washing protocols are easily to implement.
- The floor, walls and all flat surfaces could be cleaned regularly.[125]
- Equipment: Each baby in a normal nursery should have his own thermometer, and in the NICU he should have his own suction unit and stethoscope. If the equipment has to be shared, it should either be wiped clean between patients or disposable device should be used to connect the equipment to each patient.[125]
- Cleanliness of the baby: babies should be kept socially clean by the use of soap and water to reduce the level of bacterial colonization.
- Cord care: the cord stump is generally the most heavily colonized area of the baby surface. And invasive infection, particularly with *Staph. aureus* can be reduced by cord care regimens aimed at preventing heavy colonization. A common approach in the UK is to clean the cord stump with alcohol swab

and to apply chorhixidine powder [1] or to use antibiotic spray. In Mygoma Home cord stump is cleaned using gentian violet.

- Invasive procedures: All invasive procedures can introduce colonizing bacteria into the circulation. The skin should be cleaned thoroughly with either iodine or an alcohol containing solution for 30 - 50 second. Then it should be allowed to dry before the procedure is undertaken.
- Hand washing: the hands of the medical and nursing staff are the main potential route of cross-infection and of all the measurement for preventing nosocomial infection, hand washing is by far the most important and should be washed before touching any baby and again immediately afterward. Sleeves should be rolled up to the elbow and watches and jewelry removed. The highest bacterial kill rates are obtained with solution or soaps containing iodine or alcohol. Unfortunately compliance with good hand washing practice is often poor.[126]
- Gowns, masks, caps and shoes: routine use of these by staff or visitors is unnecessary on either the NICU or the post natal wards.[127]

- Stress and overwork: overcrowding and understaffing are associated with an increased incidence of nosocomial infections.[128]
- Infectious diseases in staff and parents: medical and nursing staff with significant intercurrent infection such as gastroenteritis or skin infection should stay off duty, or stay away from babies. Infected parent, if they cover infected lesion and take appropriate precautions (masks) hand washing, can usually be allowed to have access to their baby.
- Antibiotics use: these affect the pattern of nosocomial infection by influencing the colonizing flora and by predisposing to antibiotic resistance. In a study of antibiotic use in a North America NICU, 75% of all infants and 92% of VLBW babies received antibiotics within 48 hours of birth.[129]
- Human milk: human milk confers significant protection against infection, particularly in the developing world, but also in affluent population.
- Microbiological surveillance: the NICU and the microbiology departments should collaborate in a continuous microbiological surveillance programs, so that the pattern of infecting organisms and their antibiotic sensitivity is known all the time.

- **1.11. Orphanage newborn:**

Definition:

An orphanage newborn is defined as a child borne out of wedlock. Society still expects children to be provided with recognized parents and the failure of parents in this respect may be met with various degrees of social condemnation. One form of such condemnation is the legal classification of the child as illegitimate.[130]

1.11.1. Medical aspects of orphanage newborn: Orphanage newborn represents public health risk due to increased risks of young mothers.[131] Infants born out-of-wedlock suffer because of the social disadvantages of the mother's youth, poverty and lack of proper medical care, these are all characteristics disproportional occurring more in unmarried women and all contribute to increases rates of prematurity, infant morbidity and mortality.[132] One of the major factor influencing perinatal mortality are poor socioeconomic conditions. 0rphanage newborn greatly increases the chance of low birth weight. Since the mother of orphange newborn receive less or no antenatal care compared to those married.

Infant mortality is higher for orphanage than for legitimate birth. Financial difficulties and lack of antenatal care account for the differences particularly for young mothers.[133] These children are also more likely to be the victims of abuse, perhaps because their existence is seen as a cause of problems.[131]

1.11.2. Effect of institutionalization on children:

Most of the abandoned newborn are put in institutions where they lack parental care and affection, so that many of them develops psychological disorders such as anxiety and depression, particularly when they become relatively old and discover that they had no real parents.[134]

Most investigations reported substantial retardation of development and many researches were convinced that early development losses were reversible.[135]The institutionalize children are at potential risk for exposure to infectious disease, outbreaks of gastroenteritis, respiratory tract infection, hepatitis and vaccine preventable diseases. Infants require diapering or assistance in toiling; they explore the environment with their mouth and care less about their secretion. The close personnel contact and poor hygiene of young children promotes ready opportunities for the spread of enteric agent.

In study by Elshafie([136)] in Mygoma Home 1997showed that these children live in poor environmental condition, lack proper nutritional and medical care, the majority of children (65.8%) were left in the streets, she noted that these children did poorly in their life with increased vulnerability to variable infections like gastroenteritis (63.3%), acute respiratory tract infections (53.3%), septicemia(28%) and umbilical sepsis(27.6%) with high mortality rate (84.5%) of whom (77%) died during their early neonatal period, the commonest circumstances of death was due to septicemia(35.4%),severe bronchopneumonia(28.8%) and gastroenteritis(26.1%).

JUSTIFICATION

1. Orphanage infants have serious psychosocial and clinical problems leading to significant increase in the morbidity and mortality rates.
2. Infections continue to be an important cause of morbidity and mortality of under two month's infants in Mygoma Home for Orphanage.
3. The changing patterns and frequent emergence of resistant bacteria make the need of re-evaluation mandatory.

OBJECTIVES

1. To determine the causative bacterial pathogen and to study the antimicrobial sensitivity in orphanage infant under two months, who are admitted in Mygoma Home for Orphanage either (a) for less than72 hours or (b) for more than 72 hours.
2. To study the clinical pattern of infection in under two months children in Mygoma Home for Orphanage in the two groups.
3. To study the short term outcome of the study group.

PATIENT AND METHODS

2.1. Study design:

Institution-based prospective clinical case study.

2.2. Study Area:

The study was conducted at Mygoma Home for Orphanage infants, where all orphanage newborns and infants from Khartoum and other states are admitted.

Its main objectives are to receive and care for abandoned children from age zero to the age of four years. The Home provides feeding, health care and upbringing. The total number of infants in Mygoma Home range between 210 to 320.

There are 27 rooms the front rooms are used for infants less than 2 months and the back rooms for infants older than two months. Front rooms number range from 1- 8 and room number 11, 26 and 27.

Newly admitted babies are kept in room No. (1), which contain 16 beds and a phototherapy unit.

Very ill infants irrespective of their age are admitted in room No. (5) (ICU), which contains nine beds. Room No. (11),
which contains nine beds are considered as an isolation room for infants with diarrhoeal disease. Room 26 is for infants with malnutrition.

Each room is provided with a cupboard, a laundry bag and a washing basin with a separate soap for infant use and another for hand washing.

There are two kitchens, one for milk and other for solid food. There is a laundry room provided with two washing machines.

The staff consists of the director, a social worker, supervisors, surrogate mothers, three doctors, nurses, nutritionists, and a driver.

Surrogate mothers, nurses and nutritionist work on a system of three shifts per days.

All infants admitted to the Home are brought by the police with medical reports. They are either found in the streets, hospitals or handed over by the mother or the family.

2.3. Duration of the study:

The study was carried out during the period from October 2004 to December 2004.

2.4. Study population & case definition:

All infants less than two months of age admitted to Mygoma Home during the study period, with clinical signs of neonatal sepsis, i.e. two or more of the following symptoms and signs refusal or poor feeding, fever or hypothermia, unexplained respiratory distress, hypotension, tachycardia, apnea, bradycardia, pallor, vomiting, diarrhea, hepatomegaly, abdominal distension, jaundice, splenomegaly, bleeding, petachiae, convulsions, pulging of fontanelle, irritability, lethargy and extensive focal infections (umbilical sepsis, skin abscess, pyoderma).[16]

2.5. Sample Size:

According to the equation below 150, patients have been included in the study, 75 patients `who presented with symptoms and sign of sepsis within 72 hours and 75 patient who presented after 72 hours.

- $N = \frac{Z^2 \times Pq}{d^2}$

N= sample size.

Z= statistical certainly (1.96 at 95% level of confidence.)

P= probability of failure.

d= desired margin of error.

Daily examinations were done for all infants and samples were taken from any child with signs and symptoms of neonatal sepsis.

2.6. Inclusion criteria:

Infants less than two month of age of both sex, who were admitted to Mygoma Home during the period of the study and was clinically diagnosed as having sepsis, have above mentioned criteria

2.7. Exclusion Criteria:

The following were excluded:

- Patients who were receiving parenteral antibiotics at the time of evaluation.
- Patients who had been treated with parenteral antibiotics less than 1 week before onset of symptoms.

2.8. Research tools and methods:

A questionnaire for data collection were designed and pre-coded, then completed for every case. It constituted detailed history with emphasis on circumstances of admission to Mygoma Home, presenting symptoms of sepsis, physical examination, and investigation results.

Children were divided in two groups: infants presenting with clinical signs of sepsis within 72 hours of admissions, and those presenting after 72 hours.

Neonatal sepsis was considered nosocomial if symptoms and signs of sepsis was presented after 72 hours of admission.

Physical examination was done for all cases with emphasis on the general condition, state of maturity, anthropometric measurement, (weight, length, and head circumference).

Assessment of the gestational age was done using the new Ballard score (appendix).

The investigations including blood count, Hb, differential white cell count and urine analysis were done for all patients.

Blood, C.S.F, and urine samples were taken for culture and sensitivity from infants who are suspected to have infections.

A high standard of blood sample collection was considered essential, and was conducted using the following approach:

- Skin disinfection was carried at venesection site by proper swabbing with cotton moisted in tincture of iodine.
- No touch, aseptic venesection technique.
- Inoculate blood culture bottles after replacing syringe needles.

- Inoculate each bottle with an optimal volume (2 ml).
- Incubate at 37ċ immediately.

Subculture was made every two days, either until growth is found, or until one week has elapsed. Only after one week has elapsed, a report of (no growth) was given.

The antimicrobial sensitivity, in this study, was tested by disk-agar diffusion method. A filter paper disk, impregnated with various antimicrobial agent of specific concentration, was carefully placed on an agar plate that has been inoculated with a culture of the bacterium to be tested.

To collect CSF, a lumbar puncture was done as follows:

- Positioning of the infants in either the sitting position or lateral recumbent position, with hip, knees, and back flexed.
- Locate the desired intervertebral space (either L3-L4 or L4-L5) by drawing and imaginary line between the top of the iliac crests.
- Prepare the skin in a sterile fashion with alcohol (70%) and tincture of iodine.
- Puncture the skin in the midline just caudal to the palpated spinous process, angling slightly cephalad toward the umbilicus,

advance several millimeters at a time and withdraw the stylet frequently to check for CSF follow.

- Urine was collected using infant urine bags after cleaning the external genitals using chlorhexidine.

Swabs for culture were taken for those who had apparent focal infection. The applicator sticks were removed from the tube just at the time of taking the sample and returned back immediately.

Umbilical swabs were taken from the whole circumference of the stump after cleaning the area around it. Conjunctival swabs were taken from the whole length of the eyelid. For skin pustules, the area was cleaned properly and then the pustules were opened by sterile needle and the pus was swabbed.

Chest radiograph and abdominal U/S were requested when patients present with sign suggestive of chest or intra-abdominal disease, respectively.

Treatment was started immediately for any patient suspected to be infected, after taking the samples, using Ampicillin, and gentamicin.

Patients were followed for two weeks and the outcome had been determined depending on clinical improvement.

2.9. Statistics:

Data was entered in the computer and analyzed using SPSS (statistical package for social science), appropriate test of significant to 0.05 confidence level were.

2.10. Research team:

- Researcher.
- Doctors and the staff in Mygoma Home for Orphanage.
- Microbiologist and a lab technician.

2.11. Ethical consideration:

Arrangement for personal and then official consent was made with director of Mygoma Home for Orphanage. The purpose of the study was explained. Approval of the study was granted by MSF-Head of mission, the result of the data will be used to improve the services.

Chapter Three

RESULTS

A total of 150 cases between 1- 60 days of age were included in this study in the period between 19th of October 2004 to 31st December 2004 with symptoms and signs of neonatal sepsis.

Seventy-six infants were admitted in Mygoma Home within 72 hours of illness and 74 infants were admitted for more than 72 hours.

3.1. Characteristics of the cases:

3.1.1. Age:

Fig.1 shows the cases distribution according to age, 88(58.6%) cases were between 1-14 days, while 18 (12%) cases between 15-28 days, 17(11.3%) cases between 29-42 days, 24(16.0%) cases between 43 - 58 days and 3(2.0%) were between 59-60 days.

3.1.2. Gender:

Fig. 2 shows the distribution of cases according to sex, male were 69(46%) cases and females were 81(54%) cases.

Fig.1:Distribution of the study group according to the age (n=150)

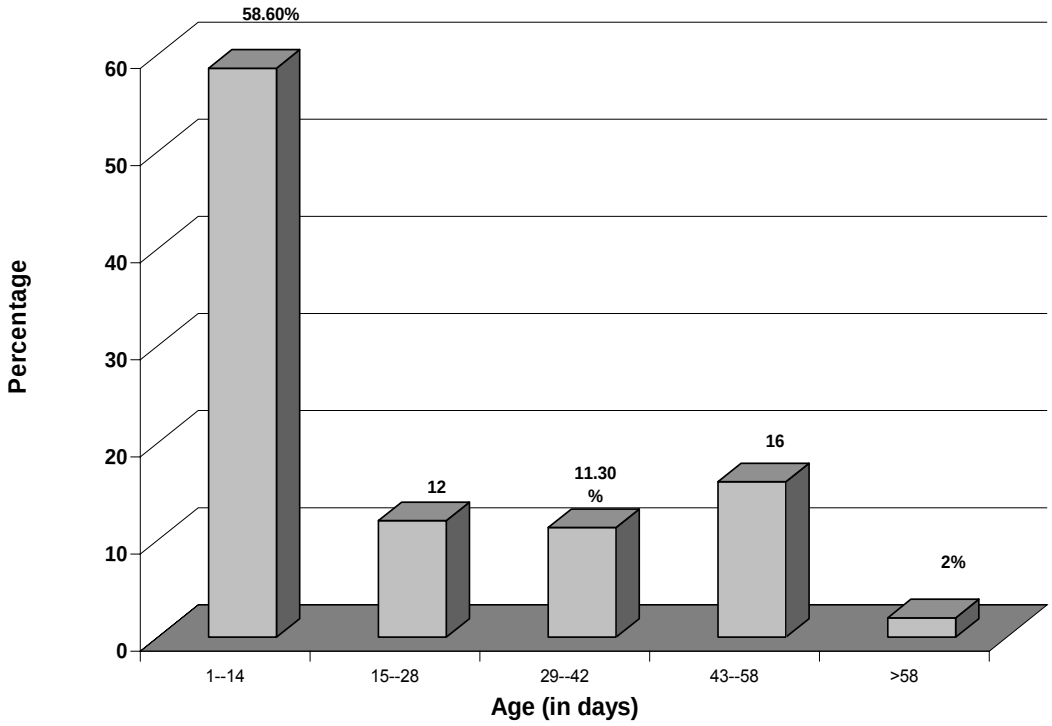
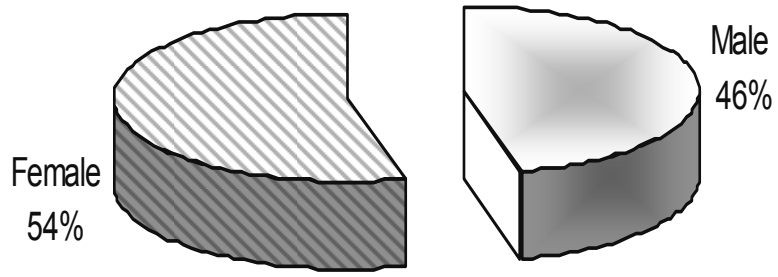


Fig. 2: Distribution of study group according to gender (n=150)



3.1.3. Duration of admission:

Table 1 shows the duration of admission to Mygoma Home 109(72.7%) were admitted for 14 days, while 14(9.3%) were admitted between 15-28 days, 14(9.3%) were admitted between 29-42 days, 12(8.0%) cases were admitted between 43-56 days, while only one (0.7%) case was admitted for 56 days.

3.1.4. Sources of admission:

Fig. 3 shows the cases distribution according to sources of admission to Mygoma Home. For the study group, all cases are admitted through the Police, of whom 104(69%) cases were picked out from streets, 22(14.7%) were leftover in hospitals after delivery, 16(10.7%) were handed over by the family and 6(4.0%) were handed-over by the mother, one infant (0.7%) was found in a latrine and one (0.7%) was found in the market.

3.1.5. Anthropometric measurements:

Weight distribution at the time of assessment was as follows, 95 (39.4%) had a weight within the range of 2.20 - 2.99 kg,

30(19.9%) of cases had a weights range between 2.00 - 2.49, 50 (37.3%) of cases their weight more than 3.0 kg, and only 5 (3.4%) cases had a weight within the range of 1.5 - 1.99 kg, none of the infant had a weight less than 1.5 kg (**Table 2**).

The mean weight for the study group was 2.930 (0.6 SD kg. The mean length was 485 (2.8 cm. The mean for the infant occiptofrontal circumference was 35.3 (2.38 cm.

3.1.6. State of maturity:

Gestational assessment of abandoned infant admitted to Mygoma Home showed that, most of the infants 127(84.6%) were term, 22(14.7%) preterm and one (0.7%) were post term (**Fig. 4**).

Table 1: Distribution of the study group according to the duration of admission to Mygoma Home (n =150)

Duration (in days)	Frequency	Percentage
1 - 14	109	72.7
15 - 28	14	9.3
29 - 42	14	9.3
43 - 58	12	8.0
59	1	0.7
Total	**150**	**100.0**

Fig.3:Distribution of the study group according to the sources of admission to Mygoma home(n=150)

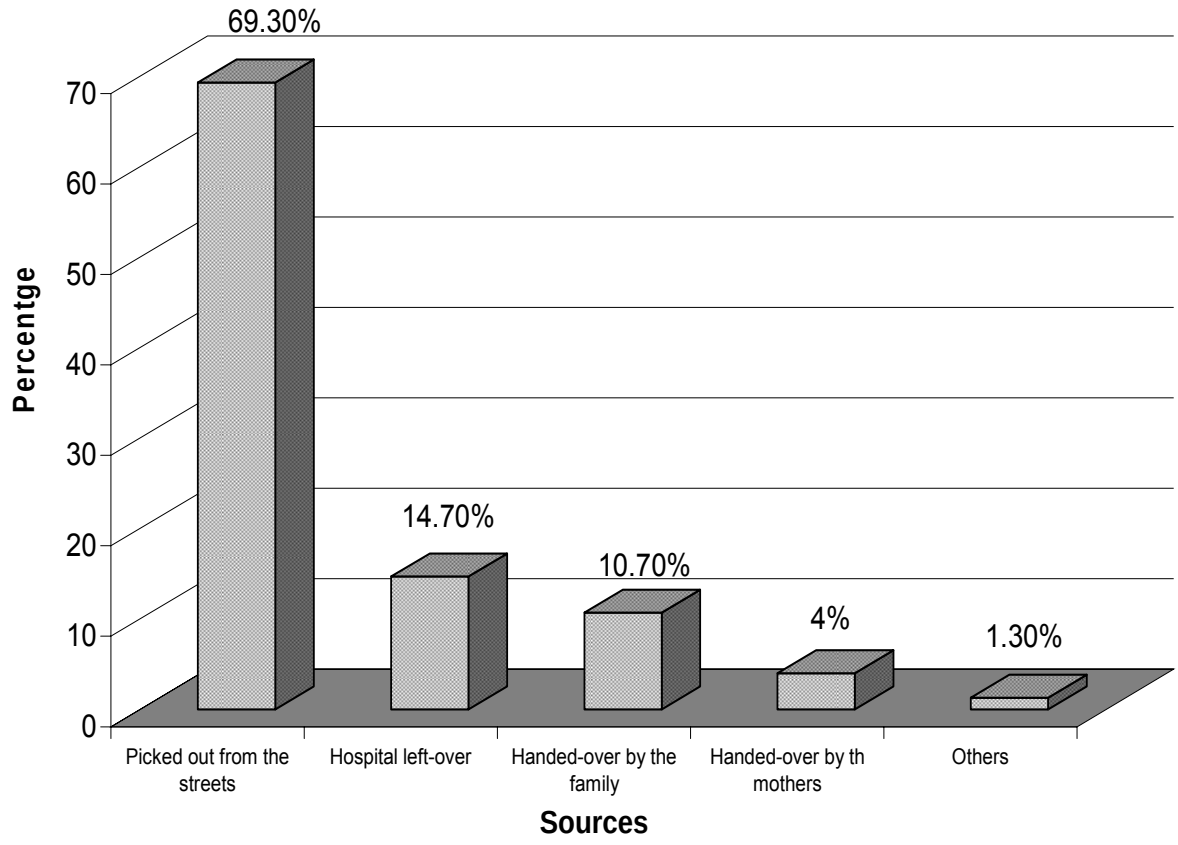
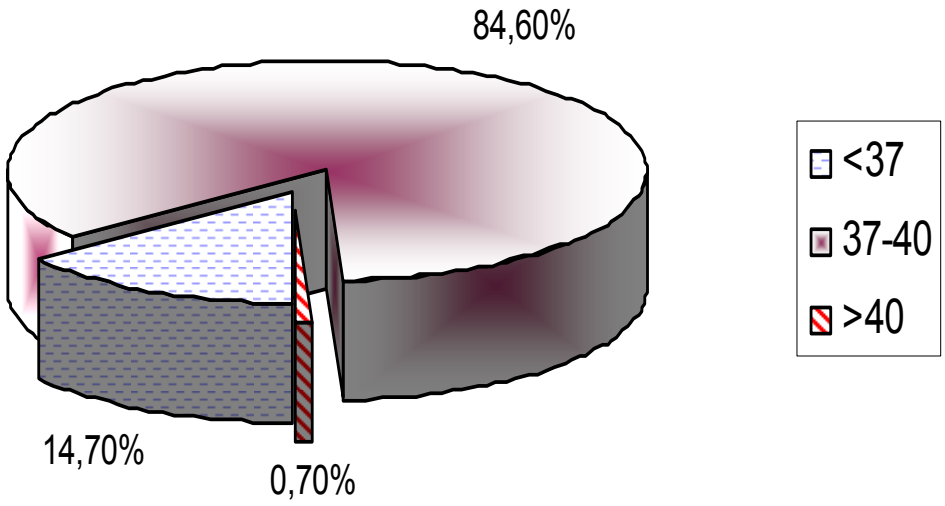


Table 2: Distribution of the study group according to the Weight

Weight (in kg)	Frequency	Percentage
1.50 - 1.99	5	3.4
2.00 - 2.49	30	19.9
2.50 - 2.99	59	39.4
3+	56	37.3
Total	**150**	**100.0**

Fig. 4: Distribution of the study group according to the gestational assessment (n=150)



3.1.7. Characteristics of the cases according to duration of admission:

- **Gender:**

In neonates admitted within 72 hours of assessment 37(48.7%) were males, 39(51.3%) were females, while in neonate admitted for more than 72 hours males were 32(43.2%), females were 42(56.8%) there was no statistical difference between the two groups **(Fig. 5).**

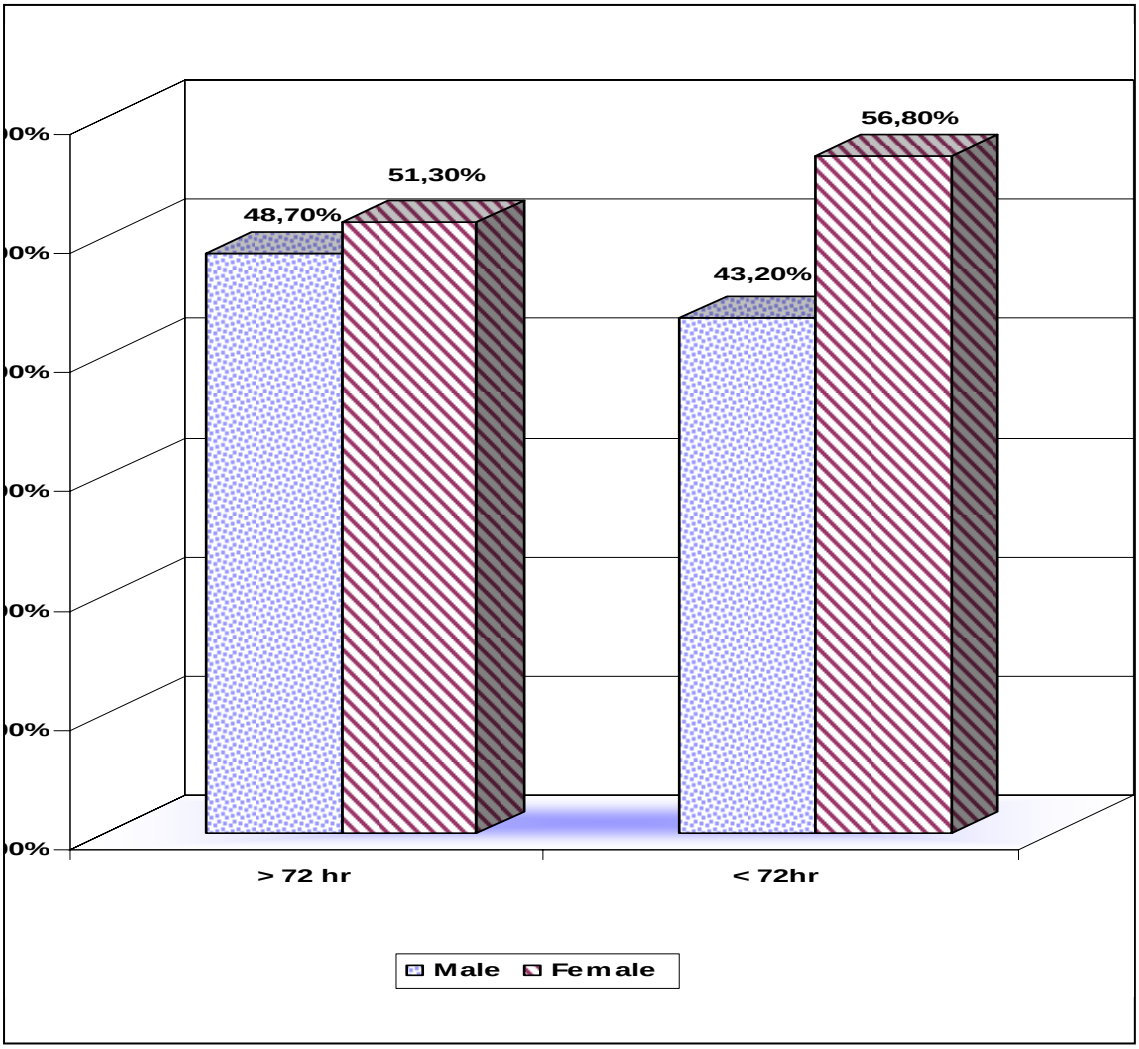
- **Age:**

Most of the neonates, who were admitted within 72 hours of assessment 65(85.5%) their age range between-14 days, 5(6.6%) neonates their age were between 15-28 days, 4(5.3%) were between 29-42 days, and only one (1.3%) were between 43-56 and more than 56 for each .In neonates admitted for more than 72 hours, 23(31.1%) their age were between 1-14 days, and 43-56 days for each, 13(17.5%)their age were between 15-28 and 29-42 days for each, and only two (2.7%) neonate their age were more than 56 days **(Table 3).**

- **Gestational assessment:**

In neonate admitted within 72 hours of assessment, 15(19.7%) were preterm, 60(78.9%) neonates their gestational age were between 37-40 weeks, and only one >40 weeks. In neonates admitted for more than 72 hours 7(9.4%) neonates their gestational age were<37 weeks, 67(90.5%) were between 37-40 weeks, none of the neonate was more than 40 weeks **(Table4).**

Fig 5. Gender distribution according to duration of admission (n = 150)



Duration of admissions

Table 3: Distribution of study group, age according to duration of admission (n = 150)

Age days	<72 hours n (%)	>72 hours n (%)
1-14	65 (85.5)	88(58.6)
15-28	5(6.6)	18(12)
29-42	4 (5.3)	17(11.3)
43-56	1 (1.3)	24(16.01)
>56	1(1.3)	3(2.0)
Total	**76(100.0)**	**74(100.0)**

Table 4: Distribution of gestational assessment according to duration of admission (n = 150).

Gestational Assessment(weeks)	>72 hours n (%)	< 72 hours n (%)
< 37	7 (4.4)	15 (19.7)
37-40	67 (90.5)	60 (78.9)
> 40	0	1(1.3)
Total	**74(100.0)**	**76(100.0)**

3.2. Clinical results:

3.2.1. Clinical presentation:

Table 5 shows the clinical presentation, 58 (71.6%) cases presented with poor feeding, 32(39.5%) presented with lethargy, 31(38.3%) had fever, 27(33.3%) had vomiting, 24(29.6%) had diarrhoea,18(22.2%) had jaundice, 12(14.8%) had abdominal distension, 22 (14.8%) had irritability, 11(13.6%) were pale, 8 (10%) breathlessness, 8 (9.3%) had skin rash, 7 (8.7%) had cyanosis and 9(11.1%) had hypothermia.

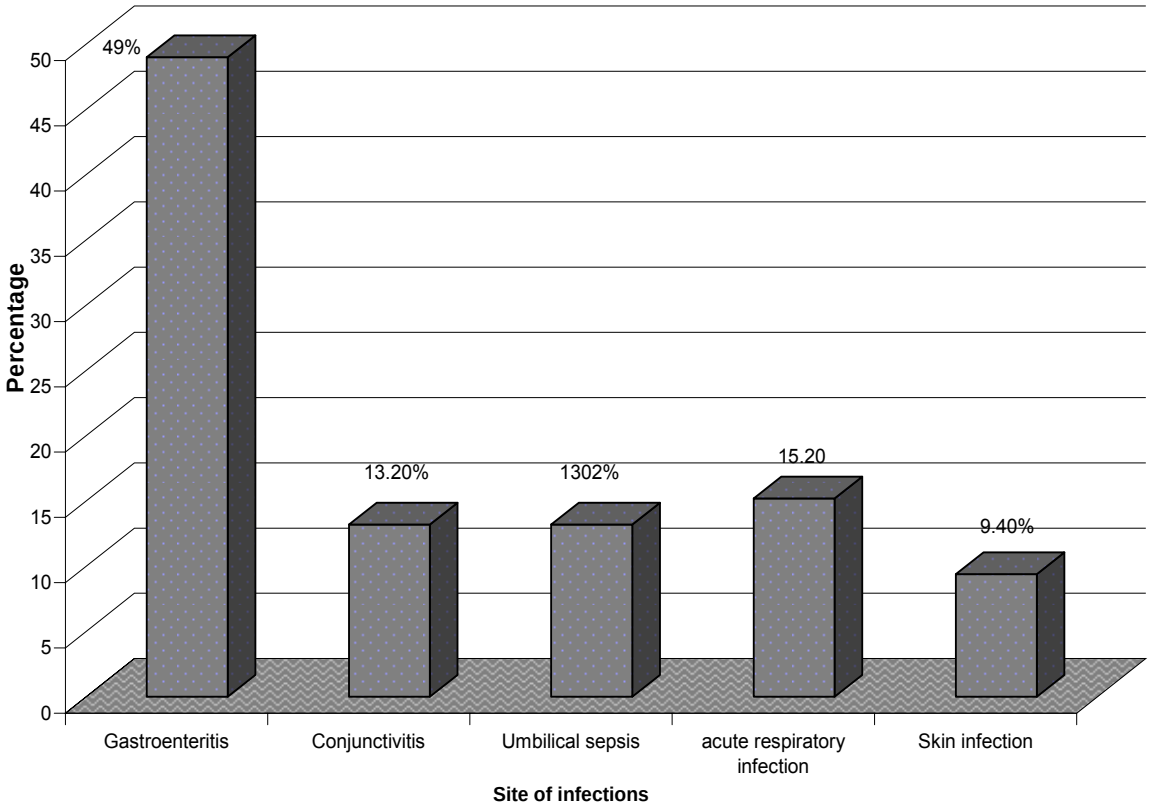
3.2.2. Focal infection:

Fig. 6 shows the focal site of infection in 98(66%) of cases no focal site of infection was identified, 26(17.3%) of cases had gastroenteritis, 7 (4.7%) had conjunctivitis, 7(4.7%) had umbilical sepsis, 7(4.7%) had ARI and5 (3.3%) of cases had skin infections.

Table 5: Distribution of the study group according to clinical presentation in Mygoma Home (n =81)

Clinical presentation	Frequency	Percentage
Poor feeding	58	71.6
Lethargy	32	39.5
Vomiting	27	33.3
Diarrhoea	24	29.6
Abdominal distension	12	14.8
Jaundice	18	22.2
Irritability	12	14.8
Fever	31	38.3
Grunting	10	12.3
Tachypnoea	7	8.7
Cyanosis	7	8.7
Skin rash	8	9.8
Pallor	11	13.6
Hypothermia	9	11.1

Fig.6:Distribution of the study group according to the focal site of infections(n=53).



3.3. Laboratory results:

3.3.1. Haematological results:

The mean hemoglobin for the study group was 15.93 ± 0.61 g/dl, while the mean TWBC was 12.64 ± 7.94, neutrophils 4.2 ± 2.77, lymphocyte 5.78(50.0, monocyte 1.64 ±1.42, bond cells 0.43 ±1.12 and the mean for platelet 332 ±167.

3.3.2. Microbiological results:

Neonatal sepsis screening was done for 150 infants with clinical diagnosis of sepsis.

Cultures were done from blood, CSF, urine, stools and swabs (taken from umbilicus, conjunctiva and skin) (**Tables 6, 7**).

3.3.2.1. Blood culture:

One hundred and fifty blood samples were tested for both aerobic and anaerobic bacteria. Out of 150 samples,positive culture obtained in 41 (27.3%) of cases. The most common organisms isolated were *Coagulase negative Staphylococcus*, in 32(78%), *Staphylococcus aureus* was isolated in 3(7.3%) cases, *Klebsiella pneumonia* was detected in two (4.8%), and only one samples (2.4%) showed *Salmonella*, *Streptococcus group D* and *Strep. viridance* for each (**Fig. 7).**

3.3.2.2. Urine culture:

Out of the150 neonates included in the study urine samples for culture were taken from 136 cases, *E. coli* was isolated in 13 (56.5%) of cases, while K. pneumonia was isolated in 7 (30.4%) of cases, and *Enterococcus, Protues* and *Providenia* were isolated in one (4.3%)for each (**Fig.8**).

3.3.2.3 CSF culture:

Out of 150 infants with sepsis CSF samples were taken from 148 for culture, only two samples showed isolated organism, one with *E. coli* and other with *Enterobacter.*

3.3.2.4. Surface swab culture:

Conjunctival swabs were taken from the seven neonates with conjunctivitis bacteria was isolated in three cases, the responsible bacteria found were *Pseudomonas* (33.3%), *Staph. aureus* and *Klebsiella* (33.3%) for each. Out of seven umbilicus swabs cultures, five organisms were isolated, three (60%) showed *Staph. aureus*. The other two cultures showed *K. pneumonia* (20%) and *Streptococcus group D* (20%). Five neonates with skin infections, had culture being done for them, three organisms were isolated, two 66.6% were *S. aureus*, while one (33.3%) was a *Pseudomonas* .

3.3.2.5. Stool culture:

In cases of gastroenteritis, 18 stool cultures were taken and only, four (2.2%) cultures were positive showing (*Salmonella).*

3.3.2.6. Association of culture results with duration of admission:

The most common organisms isolated from blood cultures in infant admitted to Mygoma Home, for more than 72 hours was CoNS in 15 (88.2%), followed by two cases (5.9%) of *K. pneumonia* and *Strep. group D* (5.9%). While in cases admitted for 72 hours or less, CoNS was isolated from 17 (70.8%), *Klebsiella* and *S. aureus* 2(8.3%) for each. In three cases *E. coli* and *Streptococcus group D* and *Strept-Viridance* were isolated 1(4.2%) for each.

Considering organisms isolated from the different sites of culture, the most common organisms isolated from infants admitted for 72 hours or less was CoNS which was found in 17 (40.4%) of cultures, *E. coli*, *Klebsiella*, and *Staph. aureus* were isolated from 6 (14.2%) cultures for each. *Salmonella*, *Streptococcus group D* were isolated from two (4.8%) cultures for each. *Pseudomonus*, *Strept viridance*, and *Enterobacter* were isolated from one (2.4%) culture for each.

On the other hand, organisms isolated in infant admitted for more than 72 hours, *Coagulase negative Staphylococcus* was isolated from 15 (38.5%) cultures, *E. coli* from 9(23%) cultures, Klebsiella from

five (12.8%) cultures, three (7.7%) cases. were infected with *S. aureus*, three (7.7%) cases were infected with *Salmonella*. *Pseudomonas*, *Providencia*, *Proteus* and *Enterococcus* were isolated from one (2.6%) culture for each organism (**Figures 9, 10**).

Table 6: Distribution of samples taken from the study group

Samples	Frequency	No. of positive		No. of negative	
		n	%	n	%
Blood	150	41	27.3	109	72.7
Urine	136	23	17	113	83
CSF	148	02	1.3	146	98.7
Stool	18	04	22.2	14	77.8
Umbilical swab	07	05	71.4	02	28.6
Conjunctival swab	07	03	42.8	04	57.1
Skin swab	05	03	60	02	40.0

Table 7: Distribution of organisms isolated in positive samples (n= 81)

Culture site / Organisms	Blood	Urine	CSF	Stool	Umbilicus	Conjunctiva	Skin	T
CONS	32	0	0	0	0	0	0	3
E. coli	1	13	1	0	0	0	0	1
K. pneumoniae	2	7	0	0	1	1	0	1
S. aureus	3	0	0	0	3	1	2	9
Salmonella	1	0	0	4	0	0	0	
Protues	0	1	0	0	0	0	0	
Strepto group D	1	0	0	0	1	0	0	
Pseudomonas	0	0	0	0	0	1	1	
Providenia	0	1	0	0	0	0	0	
Enterobacter	0	0	1	0	0	0	0	
Strepto viridence	1	0	0	0	0	0	0	
Enterococcus	0	1	0	0	0	0	0	
Total	**41**	**23**	**02**	**04**	**05**	**03**	**03**	**8**

CoNS=Coagulase negative Staphylococcus

Fig .7: Distribution of the organisms isolated from blood culture (n=41)

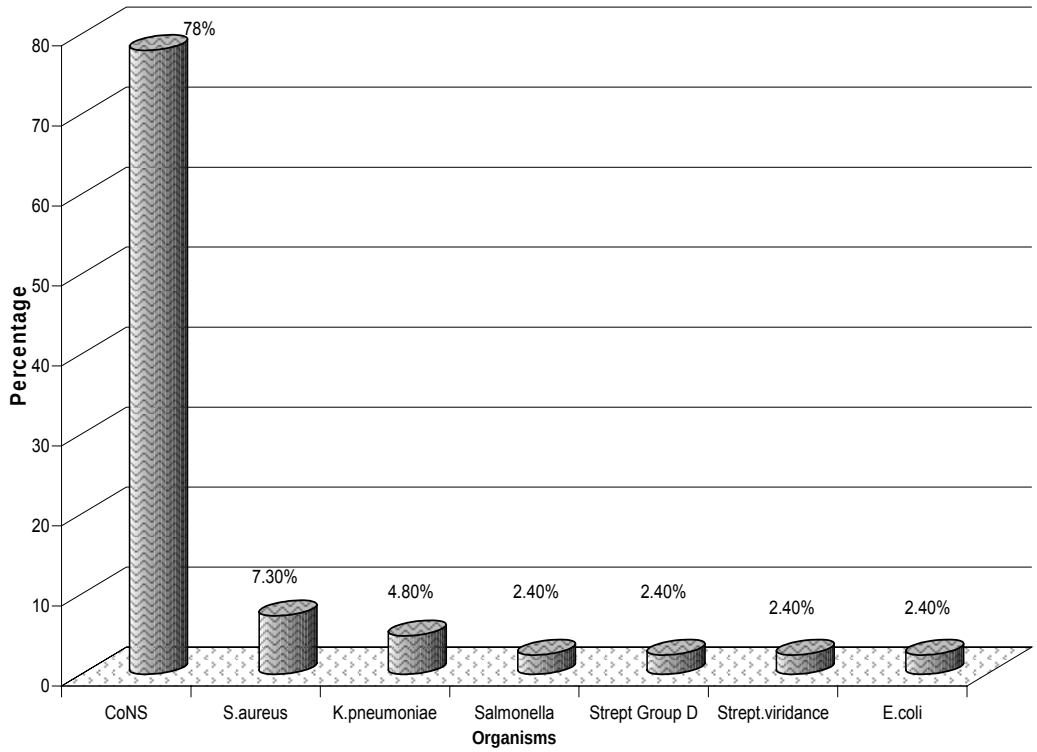


Fig.8: Distribution of organisms isolated from urine culture (n=23)

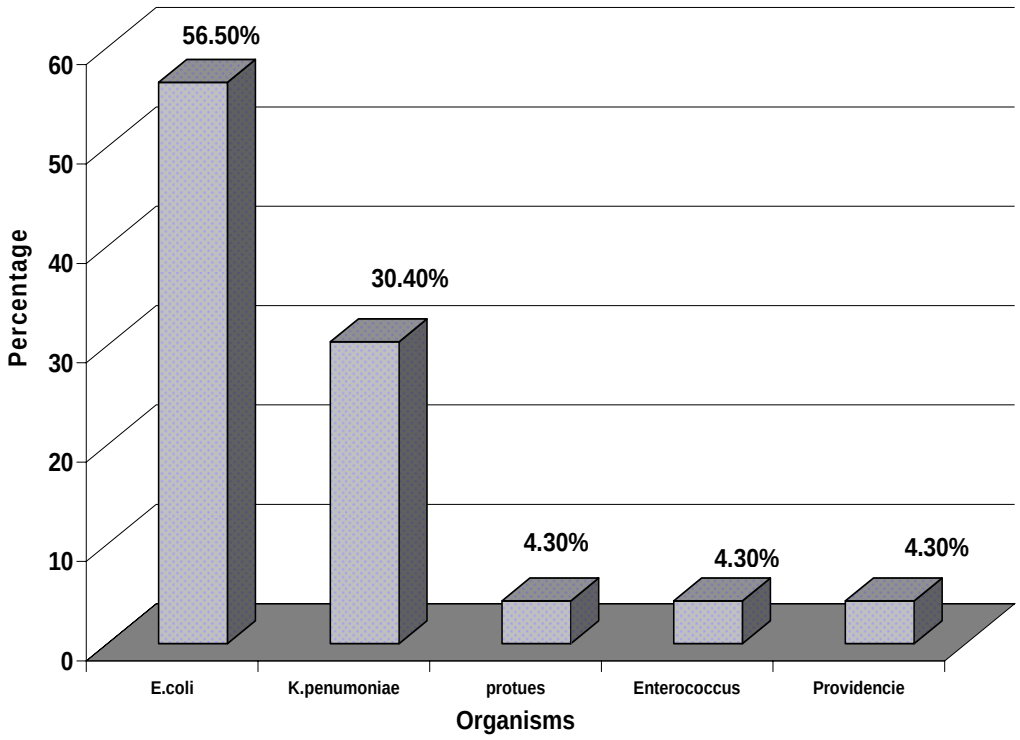


Fig.9: Distribution of organisms isolated from blood according to the duration of admission to Mygoma Home (n=41)

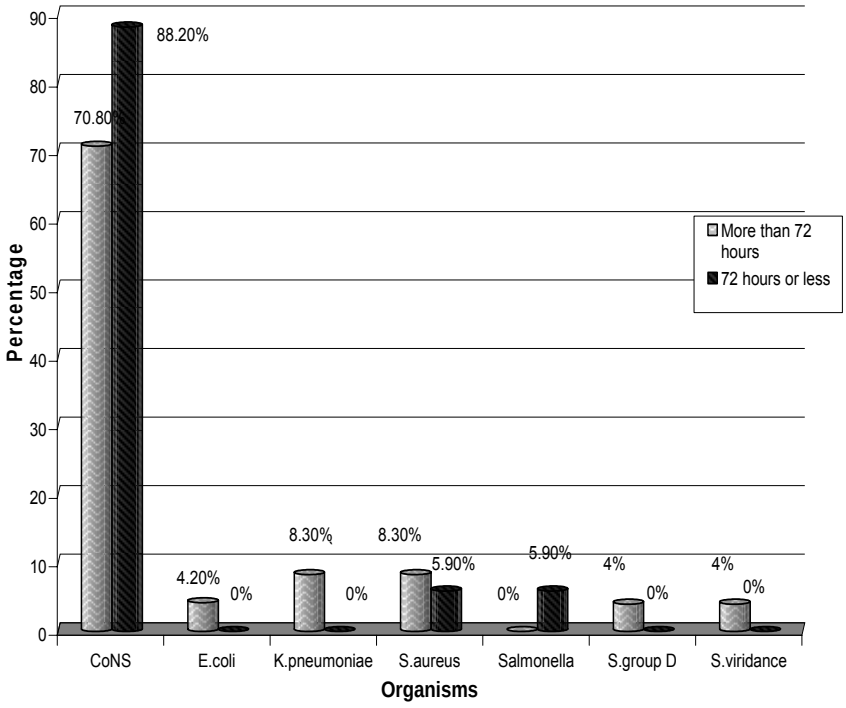
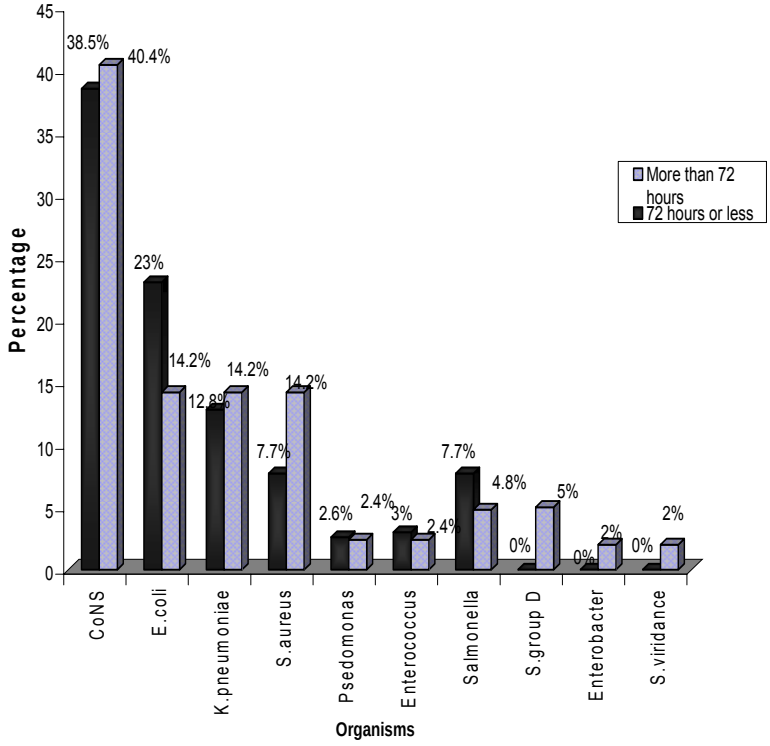


Fig.10: Organisms isolated from the study group according to the duration of admission in Mygoma Home(n=81)



3.3.5. Antibiotic sensitivity:

Table 8 shows the antibiotic sensitivity of five commonest organisms isolated, most of the five commonest organisms isolated CoNS, *E. coli, K. pneumonia,* Salmonella and *S. aureus* showed lower rate of sensitivity to ampicillin, CoNS has a low sensitivity to ampicillin (46%), but better sensitivity to gentamycin and ampicillin, while it had a very high sensitivity to nalidexic acid, cloxacillin and penicillin.

The five commonest organisms had a low sensitivity to cefotaxime. On the other hand, they had a high sensitivity to nalidexic acid. *K. pneumonia*, Salmonella and *E. coli* had a high sensitivity to clindamycin, while *S. aureus* showed a very low sensitivity to that.

Gram negative organisms had a high sensitivity to penicillin compared to gram positive organism. *Salmonella* and *K. pneumonia* had a high sensitivity to amikacin, while CoNS, *E. coli* and *S. aureus* had a low sensitivity to it.

Chloramphenicol had a high sensitivity against *E. coli*, and *K. pneumona*.

3.4. Outcome and follow up:

While following the patients for two weeks after sepsis diagnosis, 112 (47.7%) cases were recovered completely from their illness, while 16(10.7%) cases partially recovered from their illness with residual of some of their symptoms and signs, 13 (6.7%) of cases are still ill with the residual signs and symptoms of sepsis, 12(8.0%) of the study group died (**Fig. 11**).

The final cause of death was septic shock in 5 (41.6%), respiratory failure in 4(33.3%) and DIC and electrolyte disturbance and necrotizing enterocolitis in one (8.3%) case each **(Fig.12)**

During follow up, 110(73.3%) of cases gained weight, while 18 (12.0%) of cases lost weight and 22 (14.7%) had their weights static.

Table 8: level of Sensitivity of the five main organisms isolated to different antibiotics

Organisms / Antibiotic	*CoNS* %	*E. coli* %	*K. pnaeumoniae* %	*Salmonella* %	*S. aureus* %
Ampicillin	46	0	75	12.5	50
Gentamycin	80.8	16.7	75	75	40
Chloramphenicol	88.5	83.3	75	12	60
Penicillin	19	91	100	80	37.5
Erythromycin	34	41.7	100	37.5	100
Cefotaxime	53.8	16.7	25	40	62
Clindamycin	84.6	91.7	100	100	25
Cloxacillin	57.7	91.7	100	50	80
Nalidexic acid	100	100	100	80	100
Amikacin	15.4	25	80	100	16

CoNS= Coagulase negative Staphylococcus

Fig. 11: Outcome of the study group(n=150)

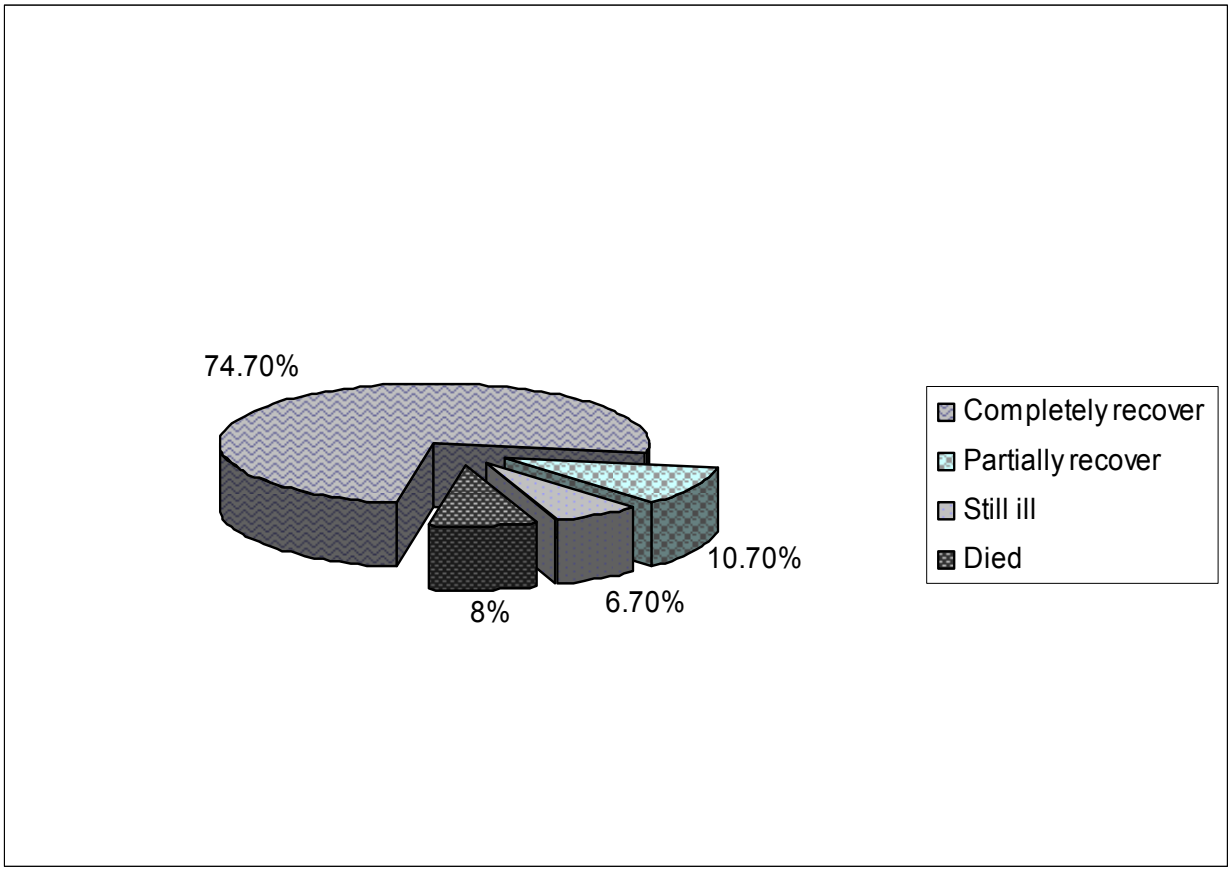
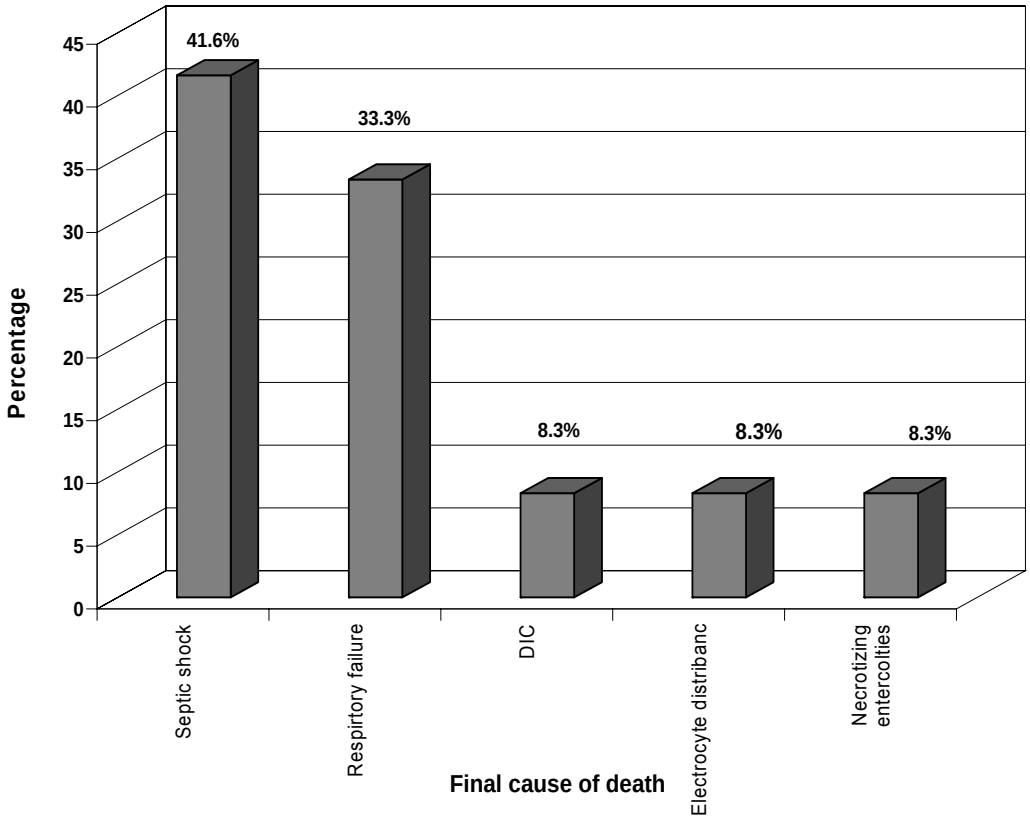


Fig.12: Distribution of the final cause of death (n=12)



DISCUSSION

Neonatal sepsis is a life threatening emergency and any delay in treatment, may result in death.

The study was conducted to determine the pattern of neonatal sepsis in Mygoma Home for children. The study group showed no significant difference in sex. Incidence in a previous study done in Sudan neonatal sepsis was more predominant in male[16]. Considering gestational assessment Twenty two cases (14.7%) were preterm, also 23.3% of the infant weight less than 2.5 kg low birth whieght(LBW). This high percentage of preterm and low birth weight reflects the importance of prematurity and low birth weight as risk factors that predispose to neonatal infections phil,Razakan, *et al* [13] in Pakistan found a very high percentage of (42%) of prematurity and LBW in patients with neonatal infections. In a Sudanese study, Ibrahim found that about one fifth of the patient with neonatal sepsis was preterm, and 30% of the patients were LBW[16].

This study also showed no significant difference in sex for the two groups classified according to duration of admission. Patients admitted for 72 hours or less, were more preterm (<37 weeks) according the gestational assessment, compared to those admitted for more than 72 hours. One hundred four (69.1%) cases were picked out from street, this pattern was comparable to a study conducted in

Sudan in 1997,the low percentage of left over in hospital reflects that most deliveries of orphanage newborns were conducted at home by untrained personale. [136]

The clinical presentation of the neonatal sepsis in this study dose not differs much from those done in different areas. The most frequent presenting features were poor feeding58 (71.6%), lethargy 32 (39.5%), temperature instability in the form of fever 31(38%) and hypothermia9 (11.1%), abdominal symptoms were common with vomiting in 27(33.3%), diarrhea in 24(29.6%), and 12(14.8%) had abdominal distension, pallor was seen in13.6, 10% were breathless, and 9.8% had a skin rash. Phil ,Razakan , *et al*[13] in Pakistan reported that fever, hypothermia, respiratory distress, cynosis, jaundice, reluctance to feed, lethargy, irritability, diarrhea, and vomiting were commonest presenting symptoms and signs of neonatal sepsis in that order of frequency. Ibrahim [16] in her study at Soba University Hospital and Khartoum Teaching Hospital in 1994, reported that, the most frequent presenting features were reluctance of feeding, lethargy, temperature instability, jaundice, and abdominal symptoms including vomiting, and diarrhoea. She also found that one third of the patients presented with respiratory symptoms including tachypnoea, breathlessness, and others chest signs. In another study done previously in Mygoma Home about the medical problems in illegitimate

children in 1997 by Elshafie [136] it was shown that poor feeding were encountered in (20.3%) children, the next common symptoms being diarrhoea detected in (15.8%) of children, vomiting in (11.5%). children, and fever in (10%).

Discussing focal infections in this study 17.3% of cases had gastroenteritis, 4.7%had conjunctivitis, 4.7% had umbilicus sepsis, 4.7%had ARI, and 3.3% of cases had skin infections. Phil , Razakan, *et al* [13] in Pakistan umbilical infection were reported in 12% of cases, gastroenteritis in 16% of cases. In the study done in Mygoma Home1997,36.2% of illegitimate children had infected umbilical stumps, this reduction in percentage of umbilical stump infections is mainly due to umbilical care protocol which is now being carried in Mygoma Home[136]. Mohammed[11] reported that rate of umbilical colonization and infection among hospital neonates was as high as100% by the third day. In this study the no of children having conjunctivitis is low compared to Ibrahim[16] who reported that conjunctivitis was found in 13% of children.

In this study the percentage of positive culture samples is relatively low as (27.3%) of blood samples, and (17.1%) of the overall samples, were found positive, when compared to results of the study by Ibrahim, who reported that 90% of overall samples and 89% of the blood samples were found positive, this difference may be due to the

fact that, in this study the evaluation of neonatal sepsis were done in the early stage of disease. philp[13] reported that percentage of positive samples was 17.9%out of 150 blood samples in this study the main organism isolated in the study were CoNS, S.aures,and *klebsiella* they accounted for 78%, 7.3% and 4.8% respectively. In the study done in Pashawer, Pakistan the most common causative organisms for neonatal sepsis were reported to be gram negative organisms in 70%, with *E.coli* being the most common, *Pseudomonas* being the second, and *Staph. aureus* being the most common gram positive organism encountered[15]. *Group B Streptococcus* was not isolated from any culture in that study. Gram negative organism were responsible for most of the cases of early onset neonatal sepsis in developing countries, similar result have been reported by Dawodu[122] from Riyadh Saudi Arabia, and in recent study from northern Jordan[121]

. In Alwasal hospital, Dubai Habib Alah [80] found that out of 106 positive cultures of neonatal sepsis , group *B Streptococcus* was the commonest organism in 23%. Ibrahim in Sudan reported that the most frequent organism isolated from all samples taken were *Staph.* aureus, followed by *E. coli* and *Group B streptococcus.*

The main causative organisms for early neonatal sepsis in this study were CoNS, *E. coli*. *Klebsiella*, and S.aures, this was partially in

agreement with a study done in Pakistan, northern Jordan and Saudi Arabia[15,121-122].On the other hand organisms isolated in cases admitted in Mygoma Home for more than 72 hours were *CoNS* followed by *E. coli* and then *Klebsiella*, *Salmonella*, and *Staph. aureus* in order of frequency, this infection was considered to be nosocomial infections. These results are comparable to a study done in United state about blood stream infection in intensive care unites where gram- positive bacteria were found responsible for most of infections, CoNS being the leading cause, followed by *Enterobacter*[109]. And also in agreement with a multicentre study of *CoNS* infection in Australian neonatal units, [111],

CoNS, being a normal skin commensal, are a common contaminant of blood and CSF cultures; this complicates the interpretation of culture results and our ability to describe the natural history of *CoNS* infections. Quantitative or semi-quantitative cultures increase the reliability of culture results, but are too expensive for routine use.

In this study we used a combination of a clinical definition together with the requirement for hematological evidence of sepsis in order to strengthen our definition of *CoNS* sepsis

In this study the four of the commonest organisms isolated were CoNS*, E coli*, *Salmonella, Staph. aureus* showed low sensitivity

to ampicillin, although it is the drug used as first line treatment for neonatal sepsis. CoNS, *Klebsiella,* and *Salmonella* have high sensitivity to gentamicin. While *E coli* and *Staph. aureus*, had a low sensitivity to it. So the first line combination treatment does not cover the most common organisms and the use of Ampicillin and gentamicin as a first line treatment probably needs farther studies. The five common organisms had a high sensitivity rate for nalidexic acid, while they had a low sensitivity to cefotaxime 3rd generation cephalosporin which are considered now to be the second line of treatment of neonatal sepsis. *CoNS*, *E coli*, *Klebsiella* had a high sensitivity to chloramphincol but chloramphicol is not recommended for the treatment of neonatal sepsis, because of its action against most gram-negative enteric pathogens is bacteriostatic rather than bactericidal, and in vitro antagonism with Ampicillin against enteric gram negative bacilli and group B streptococcus (GBS) has been demonstrated which may be associated with clinical failure. *CoNS, E coli*, had a very low sensitivity to Amikacin, while *Klebsiella,* and *Salmonella* had a high sensitivity. Clindamycin was shown to be effective against *CoNS*, *E coli*, *Klebsiella*, and *Salmonella* but very low effect on *Staph. aureus*.this was in agreement with study done in Pakistan by Rahman ,Hameed ,*et al*[69] showed a very high degree of resistance of gram

negative organisms to first line antibiotics, as about 40% of *Staph aureus* were resistant to ampicillin.

In Sudan Ibrahim[16] reported that *Staph. aureus*, *E coli,* and GBS showed a high rate of sensitivity to gentamicin. On the other hand *Staph. aureus* and *E coli* showed a very low sensitivity to ampicillin and even lower sensitivity to penicillins. The three-mentioned organism showed a relatively lower sensitivity to erythromycin, trimoxazole, chloramphenicol, and fusidic acid. According to these results, In Mygoma Home if gentamicin is used in combination with cloxacillin instead of ampicillin for treatment of neonatal sepsis, the five common organisms will be covered with effective drugs which are available and relatively not expensive. Vancomycin may be considered to act against *CoNS*, but with limitations because drugs level needs to be monitored.

The outcome of this study group after two weeks of sepsis evaluation and treatment that: 112(74.7%) of cases were recovered completely from their illness, while 16(10.7%) cases partially recovered with residual of some of their symptoms and signs, 13(6.7%) of cases were still ill, with residual symptoms and signs or deterioration of their condition. 12(8%) of them died. in Khartoum State death rate for all neonatal sepsis was 27%[16].

Isaacs in a multicentre study in Australian neonatal unitsreported that 4(0.3%) of cases to have died as a direct result of CoNS sepsis[70]. In Pakistan phil [13]reported that mortality for neonatal sepsis is (54%) and for meningitis 50%.

In a study done in Mygoma Home 1997the outcome of abandoned children admitted to the Home was very gloomy, the majority of children 257(84.5%) died,(9.9%) were adopted, and5% of children were left over.77% died during their early neonatal period and19% died during their late neonatal period[136].

CONCLUSION

- Neonatal sepsis in Mygoma home is a common serious neonatal problem that carries a high mortality rate.
- Infant pick out from street, had a high risk for neonatal sepsis.
- In significant number of infants focal infection was sources of systemic infection mainly from umbilical, skin and conjunctiva,
- Gastroenteritis is one of the comments presenting features of neonatal sepsis in Mygoma Home.
- Poor feeding, lethargy, temperature instability, jaundice, abdominal distention and respiratory distress, skin rash, pallor, and cynosis were the main presenting feature.
- The most frequent causative organisms of neonatal sepsis for infant admitted within 72 hours of sepsis evaluation to Mygoma Home were CoNS, E *coli*, *Klebsiella*, and *Staph aureus*.
- The most frequent causative organism of neonatal sepsis for infant admitted in Mygoma Home for more than 72 hours before sepsis evaluation (nosocomial infection) were CoN*S*, *E. coli, Klebsiella, Staph. Aureus* and *Salmonella*.
- The commonest five organisms except *Klebsiella* had low sensitivity to Ampicillin. *Klebsiella* was found to be highly sensitive. CoNS, *Salmonella*, and *Klebsiella* had a high sensitivity to gentamicin,

while *E. coli* and *Staph. aureus* had a low sensitivity. *E coli, Klebsiella*, and *Staph. aureus had* a high sensitivity to cloxacillin, while CoNS and *Salmonella* had low sensitivity

- The mortality rate of neonatal sepsis in Mygoma Home was 8%.

RECOMMENDATION

- Facilities to investigate neonatal sepsis should be available for early detection and management in order to decrease mortality and morbidity from the disease,
- Umbilical and eye care policies is highly recommended to be included in the routine hospitals practices
- Several steps to control infection must be adopted:
  - Isolation of the infected babies.
  - Regular and routine cleaning and sterilization of admission rooms.
- Continuous training for staff members including measures of prevention of neonatal infection, including intravenous line placement and care, nutritional practice, skin care, and hand washing.
- It may be necessary to consider the change of types of antibiotics used for treatment of neonatal sepsis specially in Mygoma Home.
- The facility of neonatal sepsis screening must be provided by whole hospitals
- The presence of nosocomial infection which are resistant to the routinely used antibiotics in Mygoma Home strongly

recommended, a policy of disinfection to the home and avoidance of unnecessary use of antibiotics.

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QUESTIONNAIRE
Pattern of Bacterial Infection in under two months Abandoned Infants in mygoma home

Personal Data:

Name: …… sex ……..☐ serial No ☐☐☐

DOB ☐☐☐☐☐☐ …… DOA …☐☐☐☐☐☐

Date of sepsis evaluation ☐☐☐☐☐☐ Date of ills ☐☐☐☐☐☐

Source of admission (all through the police):

1-street ……2-Hospital ……3-Handed over by the mother 4-Family…….5- Others ☐

History: ……

Fever. 1-Yes, 2-No ☐

Poor Feeding 1- Yes 2 No ☐

Vomiting 1- Yes 2- No ☐

Diarrhea. 1-Yes 2-No ☐

Breathlessness 1-Yes 2-No ☐

Cyanosis 1-Yes 2-No ☐

Skin rash 1-yes 2- No ☐

Convulsions 1-Yes 2-No ☐

Others Specify ……

Examinations:

Weight:(gms) ……. ☐☐☐☐

Length(cm) ……. ☐☐☐

HC: (cm) …… ☐☐☐

Age by Gestational Assessment (weeks) ☐☐

Respiratory rate …….

Pulse rate …….

Dysmorphic features 1- yes 2- No ☐

Specify …….

Major Congenital abnormality1 – yes 2- No ☐

Pallor 1- Yes 2- No ☐

Jaundice 1- Yes 2- No ☐

Cyanosis 1- Yes 2- No ☐

Dehydrated 1- mild 2- moderate 3- severe ☐

Temp:

Sucking 1- Good 2- Poor 3- Not sucking ☐

Bleeding from (0) No (1) umbilicum (3) rectal (4) mucous membrane ☐

Grunting . ☐

Subcostal Recession 1- Yes 2- No ☐

Abdominal distention. 1- Yes 2- No ☐

Liver size (cm) ☐☐

Spleen Size (cm) ☐☐

Irritability 1- yes 2- No ☐

Lethargy 1-yes 2- No ☐

Hypotonia 1- yes 2- No ☐

Hyporeflexia 1- yes 2- No ☐

Sucking reflex 1- Good 2- poor 3- not sucking ☐

Moro reflexes (0) not elicited (absent) (1) Sluggish (2) delayed (3) normal

(4) unilateral (5) asymmetrical (6) others specify …… ☐

Startle reflex 1- yes 2- No ☐

Anterior fontanel 1- normal 2- tense 3- bulging ☐

Others Signs (Specify) …….

Site of infection:

1- conjunctivitis. 2- Umbilicus sepsis ☐

3- ARI. 4- GE

5-Skin infection

7-Others (specify)

Follow up:

Weight 1- Gain 2- Loss 3- Static ☐

Feeding 1- Well 2 -Problems ☐

Out come:

1- Complete Recovery 2- partial Recovery 3- still ill 4- died ☐

5- Others (specify) . ……

direct cause of death ……

Investigations:

HB: ……..
TWBC &diff
Bands cells
Platelets count:

Blood culture. 1- growth 2-No ☐

Specify

Antibiotic sensitive:…….

Antibiotic resistance:……

CSF: 1- Sugar. …… 2- proteins …….
3- cells. …….

CSF culture. 1- growth. 2- No ☐

Antibiotics sensitive:

Antibiotics resistance:

Urine analysis:

Urine culture. 1-growth. 2- No ☐

Specify

Antibiotics sensitive ……
Antibiotics resistance:……
Umbilicus swabs culture……
Skin infection culture……
Conjunctival swab culture:……
BFFM: ……

Radiology.

1- x ray, …… 2- u/s ……. Echocardiography: …….