Review Article

Indian Journal of Maternal-Fetal and Neonatal Medicine
Volume 1 Number 1, January - June 2014

Neonatal Infections

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Abstract

Neonatal infections represent an important cause of morbidity and mortality in neonatal period. NICU patients are at increased risk of neonatal infections because of poor intra-partum and postnatal infection-control practices and also having poor immune defence mechanism. Sepsis is characterized by lethargy, poor feeding, fever or hypothermia and various nonspecific features. Sepsis screen is useful for diagnosis. Blood culture is gold standard. Simple hand washing is a good effective measure to reduce sepsis.

Keywords: Neonatal infection; Hand washing; Sepsis screen.

"An infection acquired in hospital by a patient who was admitted for a reason other than that infection. An infection occurring in a patient in a hospital or other health care facility in whom the infection was not present or incubating at the time of admission. This also includes infections acquired in the hospital but appearing after discharge."[1]

Definition

A universally accepted definition of septicemia is not yet available. According to a working definition, it is a syndrome of Bacteremia with isolation of organisms from blood, CSF, urine or some other body fluid in the first four weeks of life.[2,3,4]

Classification

According to onset of symptoms of sepsis, neonatal septicemia can be divided into 2 main classes:

Early Onset Septicemia (EOS):

Early onset sepsis presents within first 72 hours of life. Source of infection is generally the maternal genital tract. Clinical manifestations include:

- Generalized sepsis
- Pneumonia
- Meningitis

90 % neonates are symptomatic by the first 24 hours of life. Western studies indicate that Group B streptococcus is the most common organism involved in EOS.[2]

Risk factors associated with EOS are as under:

1. Prematurity (< 37 weeks)
2. Low Birth Weight(LBW)(<2500gram)
3. Intrapartum fever in the mother (> 37.5° C)
4. Chorio-amnionitis (foul smelling liquor)
5. Prolonged Rupture Of Membrane(PROM) (> 24 hours)
6. Prolonged and difficult instrumental delivery
7. Perinatal asphyxia[2,3,5,6,7,8]

Late Onset Septicemia (LOS)

Late onset septicemia presents after 72 hours of age. It can be further divided into two distinct entities:

- Disease occurring in the otherwise healthy newborns in the community known as community acquired septicemia.
- Disease affecting premature or sick neonates in the neonatal intensive care unit (NICU) or Nursery who require to stay for other morbidities. This is often known as nosocomial sepsis or Hospital Acquired Infection (HAI) in newborn.

Risk Factors Associated with LOS in NICU

1. Prematurity
2. Low birth weight
3. Intravenous Cannulation, esp. central lines
4. Ryle's Tube insertion
5. Overcrowding in NICU & Nursery
6. Mechanical ventilation.[6,7,8,9,10]

Epidemiology

Incidence of neonatal septicemia in various studies is 1-4/1000; there is almost equal distribution of early and late onset cases. [11, 12]

- Sanghvi *et al*, found the incidence to be 5.6/1000 live birth and 3.87% of NICU admissions.[13]
- According to recent data from National Neonatal Perinatal Database (NNPD) 2002-03, incidence of neonatal sepsis has been reported to be 3.0% in intramural live births in tertiary care centers.[14]

Pathogenesis

Infection in the neonate may be acquired by one of the following routes:

1. In Utero (Congenital)

Intrauterine infections Mechanisms are as under:

a) Trans placental blood stream infection: Apparent or in apparent maternal bacteremia through maternal circulation is carried into intervillous space of placenta and into the fetal blood stream.

b) Ascending infection: PROM, prolonged labour causes infection of amniotic fluid and fetal infection.

The sequence of events in ascending infection is as under:

a. Colonization of birth canal,
b. Upward spread of organism leading to chorio-deciduitis,
c. Development of Chorio-amnionitis,
d. Inhalation and ingestion of contaminated amniotic fluid.

Babies infected in this way exhibit the highest mortality rate.

2. At the Time of Birth (Natal)

During birth, fetus comes into contact of bacteria from maternal vagina, perineum and skin and gets colonized. This may lead to EOS. Microorganisms acquired at the time of delivery colonize mucous membranes and proliferate locally before causing blood stream infection.

3. After Birth during the Neonatal Period (Postnatal)

This is the most important mode of transmission of infection for late onset sepsis(LOS). Infection may be acquired in the NICU/Nursery or in the community.[2,3,15]

In a hospitalized neonate, major portals of entry are:

1) *Umbilicus:* Devitalized umbilical cord tissue allows proliferation of microorganism. Use of umbilical vein catheters, umbilical cord blood sampling in the NICU promotes entry of microorganisms.[2,3]
2) *Trachea and Respiratory Tract:* Endotracheal intubation(ET) done during resuscitation as well as ET tube kept in situ for invasive mode of ventilation is an important portal for the entry of pathogens. Contamination of respiratory equipment especially with

Gram Negative (Gram -ve) organisms that thrive in moist environment such as Acinetobacter, pseudomonas and fusobacterium frequently lead to colonization of the respiratory tract. Aspiration of colonized gastric and oro-pharyngeal secretion around the endotracheal tube may also occur.[2,3]

3) *Site of Intravascular Catheter:* Intravascular devices commonly used in the NICU are peripheral intravenous catheters, peripherally inserted central catheters, surgically placed Central venous catheters and percutaneous arterial catheters.

The rate of catheters related blood stream infections is directly related to the number of days catheters are in place and inversely related to the gestational age and birth weight of the patients.

Immunology

The newborn has a well-developedand functional immune system with certain limitations. During first 8-12 weeks of intrauterine life, fetus is immunologically incompetent. There are maturational deficiencies in complement activity, immunoglobulin content and defective phagocytic response causing defective inflammatory response in the newborn.[15,16]

Humoral Immune Response

Immunoglobulins: Immunoglobulins are a heterogeneous group of proteins detectable in plasma and body fluids and on the surface of B lymphocytes. The five known classes of immunoglobulins are IgG, Igram, IgA, IgE and IgD. [16,17]

Passive Transfer: Immunoglobulins of the IgA class are passively transferred to the fetus from the mother beginning at approximately 20 weeks of gestation. The full term infant has a complete repertoire of maternal IgG antibodies. Transplacentally acquired IgG protects the neonate against bacterial and viral infections.

Active Antibody Production: At 12 weeks, G-lymphocytes are seen in the fetal liver. They produce immunoglobulins. Sequence of appearance of immunoglobulins is Igram followed by IgGand IgA. Presence of elevated concentrations of Igram is suggestive of intrauterine infection.Igram is the most important immunoglobulin type in neonatal host defenses. Adult concentrations of IgA are not achieved until approximately 10 year of age. IgA is almost undetectable in cord blood. Colostrum derived secretory IgA may provide a source of IgA found in both the gastrointestinal tract and other secretions of the newborn infant.

The role of IgD and IgE in immunogenicity is not very well defined.

Passive Transfer

Immunoglobulins of the IgG class are passively transferred to the fetus from the mother beginning at third month of gestation.

The Igram, IgA, IgD and IgE do not cross placental barrier and are absent at birth. IgG offers protection against gram positive bacteria.

Active Antibody Production

At 12 weeks, B-lymphocytes are seen in the fetal liver. They produce immunoglobulins. Sequence of appearance of immunoglobulins is Igram followed by IgG and IgA. At birth newborns have only a small amount of actively produced immunoglobulin.

Humoral Mediators

There is no passive transplacental transfer of complement. The levels of complement proteins increase rapidly after birth reaching adult values by 3 to 6 months of age.

Due to deficiency of complement at birth, opsonic activity is markedly deficient especially towards gram negative organisms.

Cellular Immune Response

The various phagocytes, macrophages (neutrophils, eosinophil) and macrophages, (histiocytes, monocytes, RE cells) are functionally active by the end of first trimester.

Functional Differences between Fetal and Adult Lymphocytes

Fetal T-cells produce less IFN-r than adult T-cells, B-lymphocytes have weaker ability to induce immunoglobulin synthesis. Other limitation of fetal lymphocytes included less mitogen induced proliferation, presence of different proportions of helper and regulatory cell surface marker.

Polymorphonuclear Neutrophils

Neonatal Polymorphonuclear neutrophils (PMNs) are present at early stages of gestation but their functional capacities are different from those of adult PMNS. There is lack of neutrophils precursors in bone marrow aspirates of infected neonates.

Systemic bacterial infections in newborns are commonly associated with profound neutropenia.

Polymorphonuclear leucocytes in the new born have deficient chemotaxis and deficient phagocytic activity thus producing ineffective inflammatory response.

Preterm babies have lower levels of IgG and various components of complement system. Neonates with IUGR suffer from poor cell mediated immune response. Hence these two groups of neonates are susceptible to infection.

Clinical Feature

The spectrum of symptoms in LOS ranges from a mild increase in apnea to fulminant sepsis.

The earliest signs of sepsis may be subtle or may be a part of variability in the course of the infant.

Lethargy, poor feeding, fever or hypothermia are the most commonly reserved features in various studies.[2,3,4,5, 15,16,17,18,19,20,21]

Non Specific Features

1) Lethargy
2) Poor feeding / Feed intolerance
3) Tachycardia
4) Respiratory Distress
5) Poor perfusion, prolonged Capillary Refilling Time(CRT)
6) Hypothermia
7) Fever
8) Jaundice
9) Pallor
10) Sclerema
11) Hypoglycemia

Specific Features Related to Various Systems

Respiratory (R/S)

- Tachypnea
- Distress
- Apnea
- Grunting

Cardio Vascular System (CVS)

- Tachycardia
- Poor perfusion
- Shock
- Hypotension

Central Nervous System (CNS)

- Lethargy
- Irritability
- Neck Retraction
- Abnormal Moro's reflex
- Bulging fontanelle

- Convulsions
- Abnormal / shrill cry

Gastro Intenstinal System (GI)

- Vomiting
- Diarrhea
- GI bleed
- Abdominal distension
- Hepato-splenomegaly
- Necrotizing enterocolitis

Hepatic System

- Hepato-splenomegaly
- Hyperbilirubinemia

Hematology

- Bleeding
- Petechiae

Different etiological agents cause similar clinical picture, hence differentiation based on clinical features is not possible.

Associated Illnesses

According to report of NNPD 2003 and other studies meningitis and pneumonia are commonly associated with sepsis. Pneumonia is seen in around 50% of cases of septicemia[15,19] especially along with EOS. Meningitis is seen in one third of cases of LOS.

Superficial infections like conjunctivitis, pyoderma, and abscesses are seen in association with Gram Positive(Gram +ve) organisms.

Superficial Infection

1) Pyoderma: In various studies incidence is found to be 1-2% in extramural babies and 0.3% in intramural babies.[14]

It is generally associated with sepsis by Coagulase Negative Staphylococcus, Staphylococcus aureus and Streptococcus pyogenes.[2,3]

2) Conjunctivitis: The incidence of conjunctivitis too is more in extramural (3-4.5%) as compared to intramural babies (0.9%). Organisms associated with conjunctivitis include Chlamydia trachomatis, Gram Positive (Gram +ve) cocci. Purulent conjunctivitis should be suspected to be caused by gonococci. [2,3,14]

Conjunctivitis usually responds to topical application of Tetracycline, 1.0% or Erythromycin, Ciplox or Tobramycin eye drops. For gonococcal conjunctivitis, crystalline penicillin is the drug of choice.[3]

3) Umbilical Sepsis: Incidence is between 0.2-2.1percent, greater in extramural babies. Predisposing factors are unclean delivery and cord tie, application of unhygienic substance to cord in the community.[15]

In hospital deliveries, umbilical catheterization is a common predisposing factor.

4) Thrush: Incidence is 0.3-1.3%. In the community use of feeding bottles, contaminated nipples, passage through infected birth canal are predisposing factors.

Prolonged antibiotic usage in NICU contributes to fungal colonization. Thrush is characterized by discrete white patches or spots over the buccal mucosa and gums, sometimes extending to the posterior pharyngeal wall. Perineal moniliasis and monilial diarrhea may be associated.

The baby presents with difficulty in sucking and swallowing. Oral applications of 0.5% gentian violet or Nystatin or Ketoconazole mouth washes are effective.[2,14]

Systemic Infection

1. Pneumonia

In a neonate with respiratory distress, pneumonia is diagnosed in the presence of a positive blood culture if any two of the following are present: (According to NNPD definition).[15]

a. Predisposing factors
b. Maternal fever, PROM, foul smelling liquor.
c. Clinical picture suggestive of pneumonia
d. X-Ray picture suggestive of pneumonia
e. Positive septic screen.

Organisms commonly associated with pneumonia are Group B streptococcus especially in western studies. Other organisms are Staphylococcusaureus, Streptococci and Gram -ve organisms like Klebsiella pneumonia. [14,19]

2. *Meningitis*

About one - third of neonates with LOS have coexistent meningitis. [15] Evidence of meningeal irritation is generally absent in neonates. Common signs observed are:

- Irritability/lethargy
- Convulsions
- Bulging fontanelle
- Neck retraction

Mortality of neonatal meningitis in developing countries is around 33-48%.[6]

A multicenter WHO study in developing countries found that organisms in meningitis are mainly Gram –ve such as Klebsiella, E coli, Pseudomonas and Salmonella.[2,6] After 1 week to 90 days, streptococcus pneumonia becomes very common. Among Gram +ve organisms, Staph aureus and CONS are common causative organisms.

In developed countries GBS (36%) Serratia (31%) and Listeria (5-10%) account for majority of cases[2,6]. Ideally meningitis should be suspected in all cases of LOS and a lumbar puncture should be done.[20]

The above CSF values suggest meningitis,

Cerebrospinal Fluid (CSF) Chemistry[2]

	TERM NEWBORN	PRETERM NEWBORN
TC	0-32	0-29
DC	61% PMNC	57% PMNC
PROTIEN	20-170 mg%	65-150 mg%
GLUCOSE	34-119 mg%	24-63 mg%

Culture and sensitivity is confirmatory.

Other deep infections found in conjunction with LOS with lesser incidence are as follow.

3. *Arthritis/Osteomyelitis*

It occurs through hematogenous seeding or direct extension from overlying skin following venipuncture or skin abscess. Staphylococcusaureus & Neisseria gonorrhea. Hip, Knee, and wrist are commonly involved in septic arthritis while Osteomyelitis may affect any bone.[3]

4. *Urinary Tract Infections*

It incidence is reported to range between 0.1-1% and more common in preterm and male babies.[3]

5. *Necrotizing Enterocolitis (NEC)*

There is marked abdominal distention, bilious vomiting and passage of blood and mucous per rectum. The bowel sound is absent or diminished with evidence of peritonitis and free air under diaphragram with obliteration of hepatic dullness in terminal stages.[3]

Microbiology of LOS

According to studies done in developed countries nearly half of the cases of LOS are caused by Coagulase negative staphylococci (CONS). In the NICHD study, 22% of cases occurred by other Gram +ve organisms (GBS, Staph. aureus, Enterococcus), 18% by Gram – ve organisms (E coli, Klebsiella, Pseudomonas, Enterobacter, Serratia) and 12% by fungal species (Candida albicans and Candida parapsilosis).[20]

However, in studies from developing countries like India, the Klebsiella species was the most common organism isolated and followed by Staph. Aureus, E. coli and Pseudomonas.[20]

According to NNPD, data in 2002-2003 extramural as were as intramural neonates,

Klebsiella and Staphylococcus were the most prominent isolates.[14]

Laboratory Investigations

Definitive diagnosis of septicemia is by isolation of etiologic agent from the blood,CSF, urine or other body fluids. However, result of these investigations is available only after a few days.

When there is suspicion of sepsis, it is reasonable to draw a CBC, rapid diagnostic tests and blood culture. If results of CBC are abnormal or the neonate worsens clinically, empirical antibiotic therapy should be started.[2,3,15,19,20]

Investigations Helpful in the Diagnosis and Management of LOS ...

Sepsis Screen

All newborn suspected sepsis should have septic screen to corroborate the diagnosis of sepsis. The components of septic screen are following.[15,18,20]

1. Total leukocyte count: <5000/cumm
2. Absolute neutrophil count: as per Monroe chart
3. Immature/total neutrophil count: >0.2
4. Micro ESR: >15 mm in 1st hour
5. C-reactive protein: >1 mg/dl

Leucocytes Counts

a) *Total Leucocytes Counts (TLC):* At birth it is 18,000/mm^3. At 1st week of life it falls to around 12,000. In septicemia, TC may be deceased, increased or remains normal. Leucopoenia (TC< 5.000) is considered a sensitive indicator of sepsis.[15,18,21]

b) *Differential Leucocytes Count (DLC):* There is a neutrophilic predominance at birth which decreases rapidly in the 1st few days of life. After the 1st week lymphocytes were predominate. The relative predominance of neutrophils or lymphocytes has not been reported to suggest septicemia.[15,18,21]

c) *Absolute Neutrophil Count (ANC):* The lower limit of ANC is 1800 / mm^3, rise to 7200/ mm^3 at 12 hours of age and declines and persists at 1800/mm^3 after 72 hours of age. The stable value between 1800-5400 remains throughout the neonatal period. In sepsis, either neutropenia or neutrophilia may be found.[15,18,21]

d) *Band Cells:* Band cell is animmature neutrophil in which the width of the narrowest part of the nucleus is less than half of the widest part. Presence of increased number of band cells is considered the most sensitive indicator of sepsis. Band cell to total neutrophils ratio of >20% or absolute band cell count (ABC)> 500 suggest inflammation.[19]

Platelet Count

Normal platelet count in a new born is 150,000 - 400,000/mm^3. Thrombocytopenia commonly accompanies systemic infections in neonate. Late onset thrombocytopenia (48hours) is almost always associated with sepsis or necrotizing enterocolitis.[19]

Serum C - Reactive Protein (S.CRP)

It is an acute phase reactant. It is raised in various conditions like infections, trauma or infraction, malignancy, collagen vascular disease. In neonates, rise in Sepsis. CRP is usually associated with septicemia CRP > 1 mg/dl is considered a positive screen for probable sepsis. Quantitative essay, rising value and fall after therapy is an important parameter for detection of sepsis.[19,21]

Micro ESR

Positive value for sepsis screen > 15 mm/1st hour. [21]

These parameters were also found to be useful in the differentiation between viral and bacterial infection in infants.[3]

Other tests indicative of morbidities present along with sepsis are:

1) *Packed Cell Volume (PCV):* To maintain normal range of PCV is impotent dueto ensure adequate tissue oxygenation during intensive care periods and also after intensive careto treat clinically significant symptomatic anaemia.[20,22]
2) *Blood Sugar Estimation:* Babies born prematurely or smaller than average, or to mothers with diabetes, are tested for hypoglycemia at birth.Hypoglycemia means that you have glucose< 45mg%. Glucose is a vital source of fuel for the brain, and a lack of it will negatively affect brain growth and function.

Hyperglycemia seen in low birth weight and premature infants is usually a transient phenomenon. The various risk factors are low birth weight, stress factors, sepsis, asphyxia, respiratory distress syndrome and high glucose infusion rate (>6 mg/kg/min).[23]

Isolation of Organisms from Body

1. *Blood Culture:* It is the definitive diagnostic test for neonatal septicemia to isolate the organism causing the illness. It also helps in determining the use of specific antibiotics and the duration of treatment.

However results of blood culture are available only after 48-72 hours and antibiotic use cannot be deferred until then. In about 40% of highly suspected cases blood culture might be sterile.

It is now possible to detect bacterial growth within 12-24 hours by using improved bacteriological techniques such as BACTEC and BACT/ALERT blood culture system.

These advanced techniques can detect bacteria at a concentration of 1-2 colony forming unit/ ml. [2,3,21]

2) *CSF Culture:* The incidence of meningitis in neonatal sepsis has varied from 0.3-3% invarious studies[15,21].

The clinical features of septicemia and meningitis often overlap; it is quite possible to have meningitis along with septicemia without any specific symptomatology.

This justifies the extra precaution of performing Lumbar puncture (LP) in neonates suspected to have sepsis.

In EOS, lumbarpuncture is indicated in the presence of a positive blood culture or if the clinical picture is consistent with septicemia. It is not indicated if antibiotics have been started solely due to the presence of risk factors.

In situations of late onset sepsis,Lumbar puncture (LP) should be done in all infants prior to starting antibiotics. Lumbar puncture could be postponed in a critically sick neonate.

It should be performed once the patient condition is stabilized.[2,3,19]

3) *Urine Culture:* In early onset sepsis, urine cultures have a low yield and are not indicated. Urinecultures obtained by suprapubic puncture or bladder catheterization have been recommended in allcases of LOS.

Since the procedures are painful and the yield is often poor, we do not recommend aroutineurine culture in neonates with sepsis.

However, neonates at risk for fungal sepsis and very low birth weight infants with poor weight gain should have a urine examination done to excludeurinary tract infection (UTI).[3,19]

UTI may be diagnosed in the presence of one of the following:

- Supra-pubic aspiration specimen, greater than 1,000 colony-forming units per mL;
- catheter specimen, greater than 10,000 colony-forming units per mL;
- clean-catch, midstream specimen, 100,000 colony-forming units per mL Or greater.[24]

4) *Pus Swab Culture:* From umbilical, conjunctiva or ear discharge from pustule or abscess.

5) *Buffy Coat Smear Examination:* It is a useful test for early diagnosis of neonatal bacteremia. Blood collected from peripheral vein in EDTA bulb is centrifuged at 2500 RPM

for 15 minutes, supernatant plasma is aspirated with a pipette and two smears are prepared from the buffy layer below.

It is stained with methylene blue which helps in easy detection of organism and other stained with gram stain which helps in knowing the type of organism.

6) Procalcitonin: The adjunctive tests, including measurements of Procalcitonin (PCT) levels have been studied for their ability to predict sepsis in neonates with clinical symptoms of infection.. The positive predictive values of IL-6,IL-8 and PCT were higher than of CRP.[25]

Radiological Investigations

X ray chest and abdomen: A chest x-ray should be considered in the presence of respiratory distress Orapnea.

An abdominal x-ray is indicated in the presence of abdominal signs and/or Suspicion of necrotizing enterocolitis (NEC). [19]

Treatment

Antimicrobial Therapy

There cannot be single recommendations for the antibiotic regimen for neonatal sepsis in all settings. The choice of antibiotics depends on the prevailing flora responsible for sepsis in the given unit and their antimicrobial sensitivity.[21]

Adjunctive Therapy

Intravenous Immunoglobulin

Multiple studies have been conducted to study role of IVIG. Immunoglobulins administered intravenously in high doses contains intact antibody molecules and maintain normal biologic activities at the Fc fragment such as compliment activation, opsonic activity, binding to cell surface receptors. Several studies have been carried out to evaluate the efficacy to IgG for the prophylaxis of infection in high risk infants with variable results.

The common finding of their studies was: no significant immediate or late side effects have been reported. IVIG dosage most commonly used in these studies was 0.5-0.8 g/kg/d to a maximum of 2-2.5g/kg/d total dosage.

Therefore meta-analyses suggested that treatment with IVIG was of unequivocal benefit in preventing death in neonates with sepsis; the survival rate could be improved two to six fold when IVIG was added to standard therapies in septicemic infants.

A meta-analysis of 19 trials revealed that use of IVIG decreases LOS by 3-4%. However, IVIG was not associated with a decrease in mortality or other serious outcomes.[26,27]

Granulocyte Colony Stimulating Factor

G-CSF has been shown to resolve preeclampsia associated neutropenia, and may decrease the rate of LOS in this population of neonates.

CSFs comprise a family of glycoproteins whose physiological role involves proliferative

Guidelines for initial combination thearapy[21]

	1st line	2nd line
Community-acquired (resistant strain unlikely)	Penicillin or Ampicillin and Gentamicin	Cefotax and other aminoglycoside (as per C/S report)
Hospital-acquired (Some strains are likely to be resistant)	Ampicillin or Cloxacillin, Gentamicin or Amikacin	Add Cefotaxime (as per C/S report)
Hospital-acquired sepsis. (Most strains are likely to be resistant)	Cefotaxime or Piperacillin-Tazobactam or Ciprofloxacin or Amikacin	Same (Avoid Cipro)

changes on early stem cell precursors and late progenitor cell and functional activation of mature peripheral blood cells.

Treatment with CSFs is associated with an increase in absolute neutrophil, eosinophil, monocyte, lymphocyte, and platelet counts and decreased mortality in critically ill septic neutropenic neonates and results suggest that CSF may be effective in the treatment of neonatal sepsis with neutropenia.[28]

Exchange Transfusion

Mechanisms of exchange transfusion are:

1) Improved oxygen carrying capacity of blood.
2) Increased opsonic and granulocyte activity.
3) Removal of bacteria, endotoxins and inflammatory mediators.

Problems with Exchange Transfusion

1) Technical difficulties especially after falling of umbilical cord
2) Increased risk of infection transmission
3) Increased risk of graft versus host disease
4) Production of leucocyte and platelet antibodies.
5) Increased RBC deformability and its consequent increased destruction. Current status of exchange transfusion in neonatal sepsis can be only considered experimental. Its use can be considered are in septic neonates with Sclerema or unresponsive DIC, as an adjunct to antibiotic and other supportive care.[2,3]

Prevention of Hospital Acquired Infection in NICU

Reducing Person-to-Person Transmission

- *Hand Decontamination:* Specific hand disinfectants: alcoholic rubs with antiseptic and emollient gels which can be applied to physically clean hands.
- There must be written policies and

Figure 1

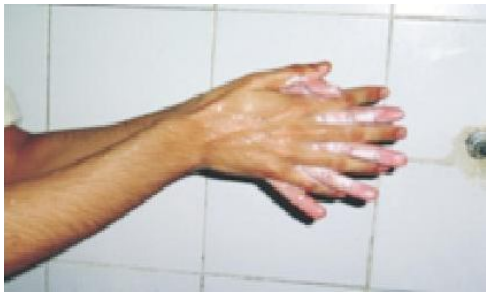
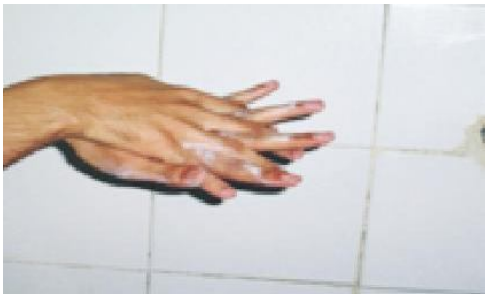


Figure 2



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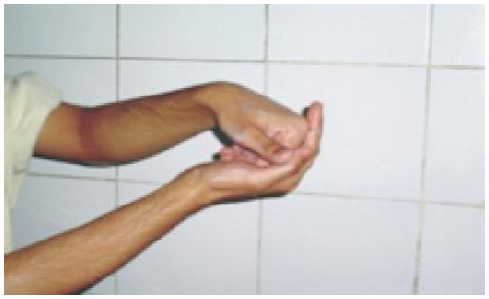

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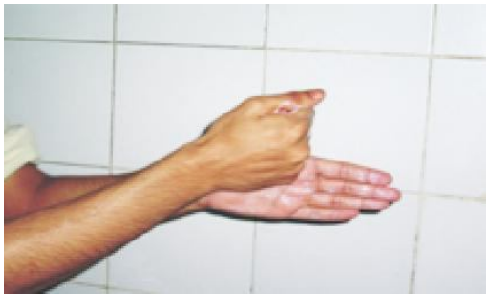

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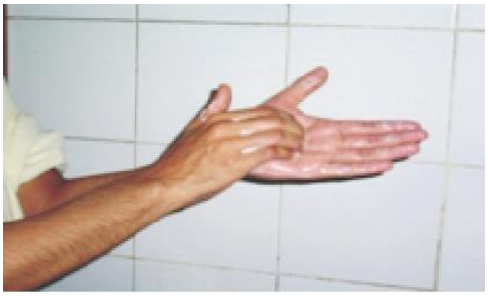

Figure 6

procedures for hand washing.[29,30]

Hand Washing-Simple and Effective for Prevention of Nosocomial Sepsis:[21]

Six Steps are:-

1. Palm and fingers
2. Finger & knuckles
3. Finger tips
4. Back of hands
5. Thumbs
6. Wrists and forearms

Wash hands for 2 complete minutes before entering NICU& before any procedure wash hands for atleast 20 seconds before and after touching the baby.

Personal Hygiene

- All staff must maintain good personal hygiene.
- Nails must be clean and kept short.
- Hair must be worn short or pinned up.
- Beard and moustaches must be kept trimmed short and clean.

Cleaning of the Hospital Environment

- Routine cleaning is necessary to ensure a hospital environment which is visibly clean, and free from dust and soil.
- Ninety per cent of microorganisms are present within "visible dirt", and the purpose of routine cleaning is to eliminate this dirt.
- Neither soap nor detergents have antimicrobial activity, and the cleaning process depends essentially on mechanical action.
- There must be policies specifying the frequency of cleaning and cleaning agents used for walls, floors, windows, beds, curtains, screens, fixtures, furniture, baths and toilets, and all reused medical devices.

Disinfection of Patient Equipment

MEA

Measures to Prevent Sepsis

- Disinfection removes microorganisms without complete sterilization to prevent transmission of organisms between patients.
- It must be high level of sporicidal, virucidal, fungicidal and bactericidal activity.

Sterilization

- Sterilization is the destruction of all microorganisms. Operationally this is defined as a decrease in the microbial load by 10^{-6} Sterilization can be achieved by either physical or chemical means.

Ethylene Oxide and Formaldehyde, Acetic Acid.

- Well Designed NICU[3]
- Prevention of overcrowding
- Space 120-180 square feet per bed.
- Sinks within 20ft. of each bed.
- Commonly used equipment close to bed side.
- Isolation of infected new born.

Recommendation is that anyone who enters in the nursery must take off bangles, wrist-watches, rings etc. Soap and water should be applied from tips of fingers to the elbow.

Practices to Prevent Entry of Microbes into the Nursery Environment:[2,3,30]

1) *Restricted Entry*
   a. Family member should be allowed after procedure of hand washing and gowning.
   b. Segregating infected babies into separate facility.
   c. Staff having fever, rhinorrhea, respiratory infection, pyoderma, intestinal infections and conjunctivitis should not be allowed in nursery.
2) *Use of Gowns/Mask/Slippers:* of doubtful value
3) *Air Changes:* Air conditioners should provide 12 air changes in the nursery per hour.
4) *Decontamination of equipment like*
   a. Incubators
   b. Ventilators
   c. Resuscitation bags
   d. laryngoscopes.
5) Good housekeeping practices.
6) Use of disposable items in plenty
7) Laminar flow systems should be used to prepare fluid reconstitute drugs and to make TPN solutions
8) Prohibiting use of stock solutions
9) Prevention of spread of infection through fomites:
   a. Files
   b. Stethoscopes
   c. Thermometers
   d. Measuring tapes
10) Use of separate equipment for each baby
11) Safe injection practices

Prevention of IV Line Related Infection [34,35]

- Intravenous (IV) fluids to be used judiciously and when absolutely necessary. Discourage over use of antibiotics.
- IV line insertion under strict aseptic precautions.
- Reducing the time IV line is in place.
- A recent study suggests that removal of central venous line promptly after identification of positive culture results in fewer complications.

Establishment of Early Enteral Feeds[2]

Concept of Minimal Enteral Nutrition (MEN)

MEN or trophic feeds are feedings that are delivered in very small volumes (< 10 ml/kg Id) for induction of gut maturity.

Benefits of MEN include:

1) Improved levels of gut hormones
2) Less feed intolerance.
3) Earlier progression to full enteral feeds
4) Improved weight gain
5) Improved calcium and phosphorus retention
6) Fewer days on parenteral nutrition early colostrum could be used as MEN. Early enteral feeds in VLBW infants may have the greatest effect on reducing LOS by reducing exposure to hyper alimentations and decreases use of central catheters. A retrospect cohort study of 212 VLBW infants from a single center revealed lower rates of LOS in infants receiving breast milk (20%) versus infants receiving formula (47%).

Antibiotic Restriction

The following points should be considered before starting antibiotics:

1) Need to start antibiotics: A precise clinical diagnosis of sepsis should be established before starting antibiotics. It should be based upon sign, symptoms, and laboratory tests.
2) Choice of antibiotics and right combination: It depends on the following:
   a. Most probable etiologic agent: It can be decided on the basis of prevailing organism at that time in the nursery and community.
   b. Bacterial isolates from culture
   c. Sensitivity pattern of organism isolated. (2,3,18,19, 32, 33, 34, 35)

Reserve Drugs

- Ceftriaxone
- Aztreonam and Imipenem
- Vancomycin (for Methicillin Resistant Staph Aureus)
- Linezolid, Polymyxin-B, etc.

Complication of over use of broad spectrum antibiotics in neonatal ICU has been emergence of resistant strains of organisms and fungal growth. [2,18,19]

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