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Original Article

Early Onset Septicemia in Term Neonates: Corelation Between Sepsis, Maternal and Neonatal Risk Factors and Clinical Profile

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ABSTRACT

Neonatal sepsis is a clinical syndrome of bacteremia characterized by systemic signs and symptoms of infection in the first month of life. Neonatal sepsis encompasses systemic infection of the new born including septicemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infection of newborn [AIIMS] [1]. A prospective nonrandomised study was conducted in neonatal intensive care unit. At risk babies were further evaluated and investigations like complete blood count, C reactive protein, chest xray, body fluid examination(cerebrospinal fluid and urine) and blood culture was sent. Then according to the clinical presentation and the investigations reports, antibiotic pattern was decided. Majority of the neonates had hypothermia as the presenting clinical feature followed by respiratory distress and poor perfussion. Hypothermia was the most common clinical feature steps can be taken to minimise hypothermia by proper maintenance of warm chain and early initiation of breast feeding .Higher incidence of septicemia is seen in male patients as compared to female patients. Early identification of the presenting feature and early initiation of antibiotics can play a major contributing role in reducing mortality and complications of early onset septicemia. Practicing and maintain aspetic precautions from the place of delivery and in the neonatal intensive care unit can also reduce the incidence of early onset septicemia.[Nelson][2]

Key Words: *Early onset septecemia , hypothermia , term neonates , CRP*

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INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Bacterial sepsis and meningitis continue to be major causes of morbidity and mortality in newborns. Neonatal survivors of sepsis can have severe neurologic sequelae due to central nervous system infection as well as from secondary hypoxemia resulting due to septic shock, persistent pulmonary hypertension of newborn and severe parenchymal lung disease. Neonatal sepsis is the commonest cause of neonatal mortality and it responsible for 30-50% of total neonatal deaths in developing countries[1].

MATERIALS AND METHODOLOGY

Aims and Objectives

1. To study the incidence of early onset septicaemia in term neonates
2. To correlate early onset septicaemia with presence of neonatal risk factors
3. Correlate the incidence of early onset septicaemia with maternal risk factors

A prospective nonrandomised study was conducted in neonatal intensive care unit of Civil Hospital Ahmedabad. Informed consent was taken from patients relative after explaining the purpose of study and involved procedures. Mother baby pairs were approached for participation in the study.

Mothers history was taken to determine the presence of risk factors for early onset sepsis. The information was documented in a structured questionnaire. The questionnaire contains biographic details of participants, antenatal history, perinatal history and postnatal history.

The newborns had their baseline characteristic and examination findings recorded in the newborn assessment form. At risk babies were further evaluated and investigations like complete blood count, C reactive protein, chest xray, body

fluid examination(cerebrospinal fluid and urine) and blood culture was sent. Then according to the clinical presentation and the investigations reports, antibiotic pattern was decided.

Blood culture is considered to be one of the gold standard method and should be performed in all cases of suspected sepsis. Blood culture samples for the study were collected using strict aseptic precautions. About 1- 2 ml of venous blood was withdrawn and collected in blood culture bottles. The sample containing bottles were kept in bact alert machine in microbiology laboratory, after 7 days the bottle of blood culture were assessed for growth of organism. If no growth was seen the report was labelled as no organism isolated, and if growth was seen further on the organism was isolated and antibiotic sensitivity testing was performed. Antibiotics were changed depending on the clinical parameter and blood culture reports. supportive care was given. C reactive protein assessement was done in the microbiology laboratory using rapid latex agglutination test[1,3,4].

INCLUSION CRITERIA:

[Nelson][2], [P. Jyothi][5], [Chacko, B., Sohi, I][3], [AIIMS][1]

Term new borns having

- Clinical features of early onset septicaemia in form of:
  1. Lethargic/refusal to suck
  2. Refusal of feeding
  3. Vomiting
  4. Abdominal distention
  5. Hypothermia(axillary temperature < 35.5 degree celcius)
  6. Hyperthermia(axillary temperature > 37.5 degree Celsius)
  7. Convulsion
  8. Tachypnea
  9. Severe chest indrawing
  10. Poor perfusion, prolonged capillary refill time
  11. Hypotonia, absent neonatal reflexes
  12. Metabolic acidosis

- New borns who have risk factors for early onset septicaemia like:
  [AIIMS][1], [Cloherty][6], [Chacko, B., Sohi, I][3]
  Risk factors in mother:
  1. Multiple vaginal examinations (>3 sterile vaginal examinations) or single unclean examination during labour
  2. Febrile illness in mother within 2 weeks prior to delivery
  3. Foul smelling liquor
  4. Prolonged rupture of membrane(>18 hours)
  5. Instrumental delivery(forceps, vacuum delivery)

- Risk factors in newborns:
  1. Perinatal asphyxia (apgar score of <4 at 1 minute)and difficult resusitation
  2. meconium staines liquor
  3. low birth weight

EXCLUSION CRITERIA

1. Premature infants (gestational age < 37 weeks)
2. Lethal Congenital anomaly

OSERVATION AND DISCUSSION

Prospective study was conducted in neonatal ICU of civil hospital and following results were obtained

1. Neonates at Risk of Septicemia

	INTRAMURAL	EXTRAMURAL	TOTAL
MALE NEONATES	854	858	1712
FEMALE NEONATES	678	734	1412
TOTAL	1256	1883	3124

Out of the total full term neonates at risk of septicaemia 54.8%neonates were male and 45.2% were female neonates.

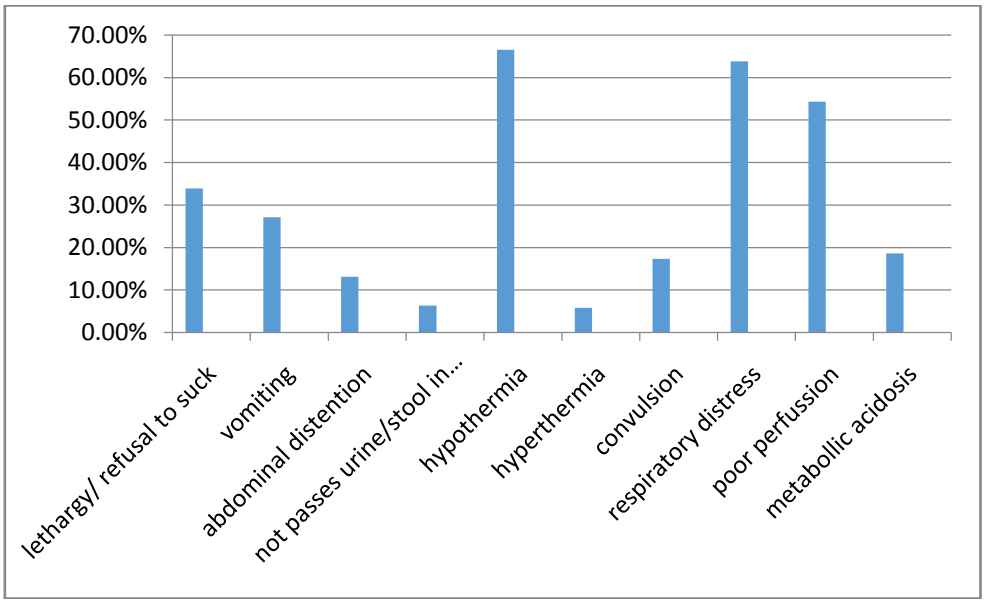
40.20% of the admitted patients were males and 60.27% were females.

It was observed that higher incidence of probable sepsis was noticed amongst extramural admissions.

2. Clinical features of at risk neonates

CLINICAL FEATURE	NEONATES(n=3124)
LETHARGY/REFUSAL TO SUCK	781(33.9%)
VOMITING	624(27.14%)
ABDOMINAL DISTENTION	302(13.13%)
NOT PASSED URINE IN 24 HOURS/ STOOL IN 48 HOURS	147(6.3%)
HYPOTHERMIA	1530(66.5%)
HYPERTHERMIA	134(5.8%)
CONVULSION	398(17.31%)
RESPIRATORY DISTRESS	1468(63.85%)
POOR PERFUSSION	1249(54.32%)
METABOLLIC ACIDOSIS	428(18.6%)

Majority of the neonates had hypothermia as the presenting clinical feature followed by respiratory distress and poor perfussion. Hypothermia was the most common clinical feature steps can be taken to minimise hypothermia by proper maintenance of warm chain and early initiation of breast feeding.



3. Maternal risk factors in at risk neonates

MATERNAL RISK FACTOR	AT RISK NEONATES
MULTIPLE VAGINAL EXAMINATIONS	980(42.62%)
PREMATURE RUPTURE OF MEMBRANES	789(34.31%)
FOUL SMELLING LIQUOR	345(15%)
FEVER TWO WEEKS PRIOR TO DELIVERY	105(4.5%)
INSTRUMENTAL DELIEVERY	478(20.7%)

42.62% patients mother had history of multiple p/v examinations followed by premature rupture of membranes .

4. Risk Factor in Neonates Suspected to Have Sepsis

RISK FACTOR	NEONATES
MECONIUM STAINING OF CORD	1765(76.66%)
PERINATAL ASPHYXIA	1245(54.54%)
SMALL FOR GESTATIONAL AGE	320(13.91%)

Major risk factor in neonates to have sepsis was meconium staining of cord followed by perinatal asphyxia

5. Number of Neonates Diagnosed to Have Early Onset Sepsis

PATIENTS HAVING EOS	MALE NEONATES	FEMALE NEONATES	TOTAL
INTRAMURAL	596(69.5%)	309(45.5%)	905
EXTRAMURAL	750(87.41%)	646(87%)	1394
TOTAL	1244	1055	2299

EOS= early onset septicemia

- Out of total 3124 admission suspected to have sepsis, 2299 were diagnosed to have septicemia. The incidence 73.5%.
- out of a total of 5613 total full term intramural deliveries septicemia was found in 905 patients. The incidence is 16.12%.
- Higher incidence of early onset septicemia was seen amongst the extramural admissions as compared to intramural admissions. it can also be concluded that the incidence is higher in male neonates as compared to the female neonates.

6. Associated Comorbid Conditions in Neonates Diagnosed to Have Early Onset Septicemia

COMORBID CONDITION	TOTAL
BIRTH ASPHYXIA	842(36.62%)
MECONIUM ASPIRATION	516(22.44%)
PPHN	286(12.44%)
PNEUMOTHORAX	80(3.48%)
ICH	48(2.08%)
HYPERBILIRUBINEMIA	1595(69.37%)

Most Common Associated Comorbid Condition Was Found To Be Hyperbilirubinemia Followed By Birth Asphyxia And Meconium Aspiration.

7. Clinical spectrum of patients with early onset septicemia

Clinical spectrum	Number of patients(n=2299)
Pneumonia	36.87%
Meningitis	10.42%
Urinary tract infection	6.61%
Myocarditis	5.63%

Majority of the patients diagnosed to have early onset septicaemia had pneumonia as the comorbid condition.

8.Laboratory investigations inpatients of early onset septicemia

LABORATORY FINDING	TOTAL NEONATES(n=2299)
Abnormal total counts	854(37.14%)
Thrombocytopenia	542(23.57%)
Low absolute neutrophil counts	450(19.57%)
C Reactive protien positive	798(34.71%)
Blood culture positive	690(30.01%)
Abnormal urine examination	152(6.61%)
High micro ESR	657(28.57%)
Cerebrospinal fluid examination positive	239(10.39%)

Elevated c reactive protien levels were found in 34.71% of patients and abnormal total leucocyte counts in 37.14%

8. Detection of Early Onset Septicemia Based on Radiological Parameters

RADIOLOGICALFINDING	TOTAL NEONATES
Abnormal chest xray	1154
Abnormal Ultrasonography cranium	95
IVH	48
Ventriculitis	36
Abnormal echogenicity	11

Most of the patients diagnosed to have early onset sepsis had abnormal chest Xray

DISCUSSION

Early onset sepsis:

Early onset sepsis usually presents within the first 72 hours of life. In severe case, the neonate may be symptomatic in utero (fetal tachycardia,poor beat to beat variability) or within a few hours after birth. The source of infection is generally the maternal genital tract. Clinically, neonates usually present with respiratory distress and pneumonia. Presence of some perinatal risk factors has been associated with an increased risk of early onset sepsis

Presence of the following high-risk factors has been associated with an increased risk of early onset sepsis[2] [6] [1].

1. Prolonged rupture of membranes >24 hours
2. Prolonged labour (including lst and 2nd stage of labour >24 hours)
3. Low birth weight (<2500grams) or Prematurity
4. Foul smelling or meconium stained liquor
5. Intrapartum fever in mother

6. Single unclean or 3 sterile vaginal examinations during labour
7. Perinatal asphyxia (Apgar score 4 at 1 minute)

Neonates with presence of three of the above mentioned risk factors or foul smelling liquor should be considered to have early onset sepsis and treated with antibiotics. Presence of 2 risk factors should be investigated with a septic screen and treated accordingly.

The earliest signs of sepsis are often subtle and nonspecific; indeed, a high index of suspicion is needed for early diagnosis.
Neonates with sepsis may present with one or more of the following signs and symptoms:

a) Hypothermia or fever (former is more common in preterm low birth weight infants)
b) Lethargy, poor cry, refusal to suck
c) Poor perfusion, prolonged capillary refill time
d) Hypotonia, absent neonatal reflexes
e) Brady/tachycardia
f) Respiratory distress, apnea and gasping respiration
g) Hypo/hyperglycemia
h) Metabolic acidosis.

Specific clinical features
Features related to various systems: [AIIMS][1] , [Neloson][2]

Centralnervous system (CNS): Bulging anterior fontanelle, staring look, high-pitched cry, excess irritability, stupor/coma, convulsion, neck retraction. Presence of these features should raise a clinical suspicion of meningitis.
Cardiac: Hypotension, poor perfusion, shock.
Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic , necrotizing enterocolitis (NEC).
Hepatic: Hepatomegaly, direct hyperbilirubinemia (especially with urinary tract infections).
Renal: Acute renal failure**.**
Hematological: Bleeding, petechiae, purpura.
Skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge.

DIAGNOSIS:
[cloherty][6], **[**Sagori Mukhopadhyay][7], [AIIMS][1], [Chacko, B., Sohi, I.][3]

Early diagnosis and treatment of the newborn infant with suspected sepsis are essential to prevent severe and life threatening complications. Antenatal diagnosis: Amniotic fluid tumour necrosis factor α (TNFα) is a marker for the prediction of early onset neonatal sepsis.

IL1β was the best predictor of vascular extension of chorioamnionitis, and TNFα was the best predictor of the development of severe early onset neonatal infection

Post natal diagnosis

Septic screen

Components	Abnormal value
Total leukocyte count	<5000/mm3
Absolute neutrophil count	Low counts as per Manroe chart for
Immature / total neutrophil	>0.2
C reactive protein (CRP)	>1mg/d1
Micro-ESR	>15mm in 1st hour

• BLOOD CULTURE

It is the gold standard for the diagnosis of septicemia and should be done in all suspected cases of sepsis prior to starting antibiotics. A positive blood culture with sensitivity of the isolated organism is the best guide to antimicrobial therapy

Lumbar puncture (LP):

The incidence of meningitis in neonatal sepsis has varied from 0.3-3% in various studies. It is quite possible to have meningitis along with septicemia without any specific symptomatology

Radiology:

Chest x-ray should be considered in the presence of respiratory distress or apnea. Radiologic abnormality caused by retained lung fluid or atelactasis usually resolve in 48 hours

Urine culture
UTI may be diagnosed in the presence of one of the following

a) >10 WBC/cumm in 10ml centrifuged sample
b) >100000 organisms / ml in urine obtained by catheterisation
c) any organism in urine obtained by suprapubic aspiration
d) **Random Blood sugar**
random blood sugar should be done to rule out hyper/hypoglycemia
e) **Arterial blood gas analysis**
Metabollic acidosis is common with septicemia. Arterial blood gas analysis should be done and appropriate treatment should be given to correct the detected abnormality if any.
f) **C reactive protein**
CRP is a non specifc marker of inflammation and tissue necrosis

COMPLICATIONS OF NEONATAL SEPSIS

- Septic Shock
- Disseminated Intravascular Coagulation
- Respiratory Failure
- Hypoglycemia
- Neurological Sequale

CONCLUSION

- It was observed that higher incidence of probable sepsis was noticed amongst extramural admissions.
- Majority of the neonates had hypothermia as the presenting clinical feature followed by respiratory distress and poor perfussion.
- 42.62% patients mother had history of multiple p/v examinations followed by premature rupture of membranes
- Out of total 3124 admission suspected to have sepsis, 2299 were diagnosed to have septicemia. The incidence 73.5%.
- Incidence of early onset sepsis in intramural admissions suspected to have sepsis is less and that in extramural admissions is more.
- Higher incidence of early onset septicemia was seen amongst the extramural admissions as compared to intramural admissions. It can also be concluded that the incidence is higher in male neonates as compared to the female neonates.
- Most common associated comorbid condition was found to be hyperbilirubinemia followed by birth asphyxia and meconium aspiration.

Majority of the neonates had hypothermia as the presenting clinical feature followed by respiratory distress and poor perfussion. Hypothermia was the most common clinical feature steps can be taken to minimise hypothermia by proper maintenance of warm chain and early initiation of breast feeding Higher incidence of septicemia is seen in male patients as compared to female patients. Early identification of the presenting feature and early initiation of antibiotics can play a major contributing role in reducing mortality and complications of early onset septicemia. Practicing and maintain aspetic precautions from the place of delivery and in the neonatal intensive care unit can also reduce the incidence of early onset septicemia.

Conflict of Interest: The authors declare that there is not conflict of interest regarding publication of this paper.
Author's Contribution:
Dr. Aditi Parekh : data collection and analysis
Dr. Gargi Pathak : Data analysis
Dr. Alpa Parekh : Data analysis

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