

## Neonatal Sepsis - A Study of Predisposing Factors and Causative Organisms

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### Abstract

### Original Research Article

Neonatal sepsis is the most common cause of neonatal mortality and morbidity. Studies have recorded an incidence of neonatal sepsis, varying between 11 and 24.5 per 1000 live births. It is responsible for about 30-50% of the neonatal deaths. Depending on the onset of symptoms, it can be classified into early onset sepsis within 72 h of life and late onset sepsis usually after 72 h of life. It has been one of the major diagnostic problems for physicians due to non-specific symptoms and the absence of a reliable Para clinical marker. The common risk factors for neonatal sepsis include an Apgar score 6 at 5 minutes, prolonged rupture of membranes, placental inflammation, and clinical amnionitis (maternal fever, fetal tachycardia, and amniotic or gastric fluid leukocytes or bacteria), prematurity and very low birth weight, central vascular catheterization, parenteral nutrition, use of broad spectrum antibiotics, H2 blockers and corticosteroids, endotracheal intubation, and prolonged hospital stay. Early signs of sepsis are non-specific and may present with episodes of fever, respiratory distress, diarrhea, low blood sugar level, decreased movements, decreased suckling, seizures, bradycardia, swollen belly area, vomiting, jaundice or rash. A heart rate above 160 can also be an indicator of sepsis, this tachycardia can present up to 24 hours before the onset of other signs. Culturing for microorganisms from a sample of CSF, blood or urine, is the gold standard test for definitive diagnosis of neonatal sepsis. Widespread infection despite negative culture is common. In addition to fluid resuscitation and supportive care, a common antibiotic regimen in infants with suspected sepsis is beta-lactam antibiotic in combination with an aminoglycoside or a third generation cephalosporin and organism specific antibiotics. Granulocyte-macrophage colony stimulating factor is sometimes used in neonatal sepsis to correct neutropenia if present but it has no effect on reducing sepsis.

**Keywords:** Neonatal sepsis, Amnionitis, Low birth weight, APGAR score.

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## INTRODUCTION

Neonatal sepsis is defined as a disseminated disease with positive blood culture during the first month of life and encompasses various systemic infections of the newborn. It is more common in developing countries compared to developed countries. Neonatal sepsis is the most common cause of neonatal mortality and morbidity. Studies have recorded an incidence of neonatal sepsis, varying between 11 and 24.5 per 1000 live births. It is responsible for about 30-50% of the neonatal deaths [1]. Depending on the onset of symptoms, it can be classified into early onset sepsis within 72 h of life and late onset sepsis usually after 72 h of life. Knowledge about potential risk factors would help in the early diagnosis of sepsis. Early signs of sepsis are non-specific and subtle. It has been one of the

major diagnostic problems for physicians due to the non-specificity of its symptoms and the absence of a reliable Para clinical marker [2]. Advances in neonatal management have led to considerable improvement in newborn survival. However, early (<72 hours) and late (>72 hours) onset systemic infections, both bacterial and fungal remain a devastating complication and an important cause of morbidity in these babies [3]. The objective of this study is to identify risk factors and different infections causing sepsis in neonates depending on their birth weight and gestational age.

## OBJECTIVE

To study causative organisms and predisposing risk factors for sepsis in neonates.

## METHODS

This study is a hospital based prospective observational study, conducted during October 2017 to December 2018 in Department of Paediatric Medicine, SMS Medical College and attached group of hospitals, Jaipur. Neonates from birth to 28 days of life who were suspected neonatal septicemia were enrolled in the study. A sample size of 110 cases was covered. Detailed history and physical examination was done for all the patients. Blood samples from cases of neonatal septicemia were taken. The samples were processed in the Department of Microbiology to identify causative organism of suspected infection. For blood culture,

Brain Heart Infusion (BHI) broth in 1:10 dilution were inoculated and incubated at 37°C for 48 hrs. Any growth observed was subcultured on Blood Agar, Mckonkey's Agar and Sabroud's Dextrose Agar (SDA) with Chloramphenicol (0.05%). Species of fungal infection were identified by Colony Morphology on SDA, Color on Chromogenic Media, Growth at 45°C, Germ Tube test, Chlamyospore formation and Carbohydrate Fermentation. Neonates other than blood stream infection, seropositive mothers and refusal to give consent were not included in the study.

## RESULT

**Table-1: Neonatal and Maternal risk factors associated with Neonatal Sepsis**

VARIABLES		NO OF CASES		
		BACTERIAL	FUNGAL	TOTAL
NEONATAL RISK FACTORS	>2 Broad Spectrum Antibiotics	24	5	29
	Prolonged Hospital Stay	20	5	25
	Nil Orally >5 days	21	5	26
	Central Line Insert	22	5	27
	Mechanical Ventilation	4	1	5
	Use of H <sub>2</sub> Antagonist	5	3	8
PRENATAL RISK FACTORS	Pregnancy induced hypertension	3	1	4
	Bleeding	2	1	3
	Antenatal Steroids	12	3	15
	History of Fever	18	4	22
	Foul Smell Discharge	12	3	15
	Leaking Per Vaginal	17	5	22

Interpretation: Use of broad spectrum antibiotics and mechanical ventilation is most common neonatal risk factors leading to overall cases of neonatal

sepsis. Use of antenatal steroids and fever with PV leaking is most common prenatal risk factors (Table-1).

**Table-2: Factors affecting Neonatal Septicemia**

VARIABLES		NO OF CASES			TOTAL NO OF CASES	PERCENTAGE
		BACTERIAL	FUNGAL	STERILE		
NEONATAL SEX	MALE				65	59
	FEMALE				45	41
BIRTH WEIGHT (Kg)	< 1.0 Kg	2	0	0	2	1.8
	1.0- 1.5 Kg	8	0	27	35	31.8
	1.6-2.5 Kg	19	3	29	51	46.3
	> 2.5Kg	4	1	17	22	20
GESTATIONAL AGE (Weeks)	≤ 32 weeks	15	2	25	42	38.1
	33-36 weeks	8	2	19	29	26.3
	> 37 weeks	9	1	29	39	35.4
PARITY	Primi	10	5	50	75	68.1
	Multi	21	1	23	35	31.8

Interpretation: Premature birth, low birth weight and male newborns are most prone for neonatal

septicemia so precautions and extra care must be done to prevent from septicemia (Table-2).

**Table-3: Clinical signs and symptoms presented by septicemic neonates.**

CLINICAL SIGN and SYMPTOMS of SEPTICEMIC NEONATES	NO OF CASES	PERCENTAGE
Cyanosis	4	3.6
Edema	11	10
Perinatal Asphyxia	23	20.9
Respiratory Distress	60	54.5
Refusal to Feed	97	88.1
Apnoea	65	59.1
Neonatal convulsion	17	15.4
Oliguria	17	15.4
Hypothermia (< 35.4 °C)	47	42.7
Hyperthermia (> 37.5 °C)	53	48.1
Hypoglycemia (< 45 mg %)	2	1.81
Shock (CRT > 3 sec)	17	15.4
Bleeding	24	21.8
Jaundice	18	16.3
Bulging Anterior Fontanelle	54	49.1

Interpretation: Most common clinical presentation in fungal septicemic neonates is feed

refusal, apnoea, respiratory distress etc. Sign of meningeal involvement is bulging fontanelle (Table-3).

**Table-4: Isolated causative organism causing Neonatal Septicemia**

	ISOLATED ORGANISM ON CULTURE	NO OF CASES	PERCENTAGE
FUNGUS	CANDIDA	5	4.54
BACTERIA	ACINETOBACTER	7	6.36
	CITROBACTER	1	0.90
	CONS	5	4.54
	E.COLI	3	2.72
	KLEBSIELLA	9	8.18
	PSEUDOMONAS	7	6.36
STERILE		73	66.36
TOTAL		110	--

## DISCUSSION

Neonatal sepsis is the most common cause of neonatal mortality. Depending on the onset of symptoms, it can be classified into early onset sepsis, within 72 h of life and late onset sepsis, after 72 h of life. Mortality ranges from 30% to 70 % among those infants who have early onset septicemia and is inversely related to the birth weight [4-7]. Risk factors for neonatal sepsis include an Apgar score 6 at 5 minutes, prolonged rupture of membranes, placental inflammation, and clinical amnionitis (maternal fever, fetal tachycardia, and amniotic or gastric fluid leukocytes or bacteria), prematurity and very low birth weight (VLBW), central vascular catheterization, parenteral nutrition, use of broad spectrum antibiotics, H<sub>2</sub> blockers and corticosteroids, endotracheal intubation, and prolonged hospital stay [7]. Decreased gestational age and male sex have also been associated with an increased incidence of early neonatal sepsis [4, 5, 8]. Early signs of sepsis are frequently non-specific and subtle. It is difficult to clinically exclude sepsis in newborns less than 90 days old that have fever (defined as a temperature > 38 °C (100.4 °F)). The overall incidence of neonatal sepsis has changed very little, as there has been a marked decrease in documented early onset sepsis, possibly due to the increased use of prenatal antibiotics [4]. The clinical features of early onset sepsis in babies of 34 weeks gestation are often

indistinguishable from those of birth asphyxia or respiratory distress syndrome. More mature infants may present within 24 hours of birth with episodes of fever, respiratory distress, diarrhea, low blood sugar level, decreased movements, decreased suckling, seizures, bradycardia, swollen belly area, vomiting, jaundice or rash. A heart rate above 160 can also be an indicator of sepsis, this tachycardia can present up to 24 hours before the onset of other signs. The diagnosis can be made by Complete workup including complete blood count with differential, blood culture, urinalysis, urine culture, and cerebrospinal fluid (CSF) studies and CSF culture, admit the newborn to the hospital, and treat empirically for serious bacterial infection for at least 48 hours until cultures are demonstrated to show no growth. Culturing for microorganisms from a sample of CSF, blood or urine, is the gold standard test for definitive diagnosis of neonatal sepsis. This can give false negatives due to the low sensitivity of culture methods and because of concomitant antibiotic therapy. This is particularly challenging in cases in which intrapartum maternal antibiotic therapy has been administered, which may affect the ability to detect organisms in the neonatal blood cultures. Lumbar punctures should be done when possible as 10-15% presenting with sepsis also have meningitis, which warrants an antibiotic with a high CSF penetration. CRP is not very accurate in picking up cases of neonatal sepsis [9]. In neonates, sepsis is difficult to diagnose

clinically. Neonates remain relatively asymptomatic until hemodynamic and respiratory collapse is imminent, so, if there is suspicion of sepsis, they are frequently treated with antibiotics empirically until cultures are sufficiently proven to be negative. In addition to fluid resuscitation and supportive care, a common antibiotic regimen in infants with suspected sepsis is a beta-lactam antibiotic (usually ampicillin) in combination with an aminoglycoside (usually gentamicin) or a third generation cephalosporin (usually cefotaxime - ceftriaxone is generally avoided in neonates due to the theoretical risk of kernicterus). The organisms which are targeted are species that predominate in the female genitourinary tract and to which neonates are especially vulnerable to, specifically Group B Streptococcus, Escherichia coli and Listeria monocytogenes (This is the main rationale for using ampicillin versus other beta-lactams.) Of course, neonates are also vulnerable to other common pathogens that can cause meningitis and bacteremia such as Streptococcus pneumoniae and Neisseria meningitidis. Although uncommon, if anaerobic species are suspected (such as in cases where necrotizing enterocolitis or intestinal perforation is a concern, clindamycin is often added. Granulocyte-macrophage colony stimulating factor (GM-CSF) is sometimes used in neonatal sepsis. However, a 2009 study found that GM-CSF corrects neutropenia if present but it has no effect on reducing sepsis or improving survival [10].

## SUMMARY AND CONCLUSION

Neonatal sepsis is associated with significant morbidity and mortality. Blood culture, although not a sensitive test, remains the only reliable method for diagnosis. This study indicated that the prevalence of neonatal sepsis was high. Although, this study also tells that several factors like maternal age, multiple per vaginal examination, exclusive and immediate breastfeeding within an hour of delivery, put on Kangaroo Mother care (KMC) within 1 hour, and age of the neonate are the factors affecting or predisposing neonates for sepsis. Mechanical ventilation > 5 Days, central line > 7 Days, 20 % intra lipid infusion > 7 Days, use of > 2 broad spectrum antibiotics, prolonged stay in hospital > 7days and thrombocytopenia were the most common risk factors. Based on this study we recommend strengthening of provision of health information on exclusive and immediate breastfeeding and KMC for mothers during postnatal and antenatal care services. Using Information Education Communication / Behavior Change Communication materials (posters, flip charts, wall paintings, manuals, brushers, and pamphlets) focused on breastfeeding and KMC to mobilize and sensitize the community. In

addition, it should be recommended that the healthcare providers decrease multiple per digital vaginal examination as it is not indicated but better to be promoted. Prevention of risk factors in susceptible neonates with early removal of central line, timely blood culture, causative species identification and susceptibility testing are necessary for appropriate institution of treatment and better outcome. Frequent antibiotic use should be avoided as it may lead to a shift in species distribution and higher pathogenic resistance.

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