Original research article

Neonatal Sepsis Present on as Acute Febrile Illness in A Tertiary Care Centre

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Abstract

Background: Neonatal sepsis is one of the commonest cause of neonatal mortality in the developing world accounting for 30 -50 percent of 5 million neonatal deaths per year. The incidence of neonatal sepsis varies from 1 to 4 per 1000 live births in developed countries.

Objectives: Antibiotic sensitivity pattern of neonatal sepsis and to assess risk factors in neonatal sepsis.

Methodology: Cross sectional study, All neonates born in IGIMS, and admitted in NICU, IGIMS, Patna. Study duration of Eighteen Months. with clinically suspected neonatal septicemia were includedin the study irrespective of the gestational age.

Conclusion: Neonatal sepsis was common in males, term and low birth weight babies. Most common organisms isolated were gram negative and were sensitive to carbapenems. Prevention of risk factors like PROM and prolonged labour in decreasing sepsis playsa major role.

Keywords: neonatal sepsis, PROM, respiratory distress.

Introduction

Neonatal septicaemia refers to a clinical syndrome characterized by systemic signs and symptoms due to generalized bacterial infection with a positive blood culture in the first four weeks of life.[1, 2] Bacterial infections are the commonest cause of morbidity and mortality during the neonatal period. Fulminant and fatal course of infection may result from complications such as shock, disseminated intravascular coagulation and multi-system organ failures. Thus, the early diagnosis of this life- threatening condition is mandatory for a timely treatment and a favourable outcome.[1,3,4] According to the National Neonatal Perinatal Database (NNPD) report 2002- 2003, the incidence of neonatal septicaemia in tertiary care institutions has been reported to be 14.5 per 1000 live births (2.3%) and contributes to 16% of all mortalities among the hospital born neonates. [5] The

case fatality rate of neonatal septicaemia is high without treatment, but with the presently available antimicrobial agents, theoretically, all cases of neonatal septicemia may be treated successfully. Thus, there is an urgent need for early diagnosis and treatment.[1]The gold standard for the diagnosis of neonatal septicemiais a positive Blood culture.[1] Bacterial isolates and their antibiotic susceptibility has constantly been changing [6], which depends on several factors like gestational age, birth weight, maternal risk factors, place of delivery, mode of delivery; to mention a few. The antibiotic abuse has resulted in further confusion in diagnosis and the emergence of drug resistant bacterial strains in the nurseries with grave sequelae. Thus the successful treatment with a favourable outcome of the neonate depends on an ongoingreview of the causative organisms and their antibiotic susceptibility pattern.[3,6]

Neonatal sepsis has some unique features

Infection can be transmitted from mother to fetus or new born by diverse modes. Coexisting condition often complicates the diagnosis & management ofneonatal infection. Clinical manifestation of new born infections vary & include sub clinical infection, mild to severe manifestation of focal or systemic infection & rarelycongenital malformation resulting from infection in first trimester. Maternal infection is often undiagnosed during pregnancy as she was either asymptomatic or had non-specific signs & symptoms at the time of acute infection. The present study has been undertaken to study the clinico-bacteriological profile isolate and to identify the organisms responsible for Neonatal septicaemia from blood with their antibiotic susceptibility pattern. The study also through light towards the risk factors associated with neonatal septicaemia.

Objectives

Neonatal sepsis present on as acute febrile illness a tertiary care centre. To assess risk factors in neonatal sepsis.

Review of Literature

The incidence has been reported to vary between 1-10 /1000 live births in thedeveloping countries and 1-4 / 1000 live births in the developed countries.[7] According to the National Neonatal Perinatal Database report 2002-2003, theincidence of neonatal septicaemia in India varies from 0.1 to 4.5 % and has been reported to be 14.5 / 1000 live births (2.3%) in tertiary care institutions during this period.[5] In the developed countries like USA, UK the incidence varies from 1-8 per 1000 live births.[2] In India, various studies have shown the incidence to vary between 10 – 20 / 1000 live births.[8] In a survey conducted by Freedman et al., (1981) at the Yale – New Haven Hospital over a period of 13 years from 1966 to 1978, reported an increased incidenceof early onset septicaemia from 1 /1000 live births for the year 1966 - 67 to 3.9 /1000live births for the year 1974 - 75 and 2.2 /1000 live births in 1977.[9] They found a 3 to 10 fold increase in the incidence of infection and septicaemia in premature and low birth weight infants. Bhakoo ON (1980) found a higher incidence of primary neonatal septicaemiaof 4.7/1000 live births among low birth weight (<2500 grams) hospital inborn babiesas compared to 1.2/1000 live births in neonates with birth weight ≥2500 grams.[10] Tallur et al.,(2000) reported an higher incidence of 37.6 /1000 live births in their study among hospital born babies and found that the incidence was higher among premature and low-birth weight babies.[11] Observations over a period of 30 years have shown that males had approximately two to six fold higher incidence of septicaemia compared to females accounting for 59 to 82 % of cases.[12] This may be related to the X-linked immunoregulatory genes that regulate the synthesis of Y- globulins. As

males have only 1 X chromosome, they are immunologically more susceptible to infections than the females.[13] Infections in males were found to be significantly culture positive with a predominance of gram negative bacterial septicaemia. Stoll BJ (1997) reported a predominance of gram-negative septicaemia (21%to 85 %) over gram positive septicaemia (5 %).[14] According to a report from the National Neonatal Perinatal Database (NNPD) 2002-2003, neonatal septicaemia ranked the second most common cause of neonatal mortality contributing to 16% of neonatal deaths among the hospital born babies.[5] In the pre-antibiotic era, prior to 1937 the mortality from neonatal septicaemiawas as high as 90%. Since the advent of antibiotics and early recognition of the nonspecific signs of septicaemia the morality rate has fallen significantly to 13%-45% in the 1980s and 1990s. WHO estimates 5 million deaths a year of which 98% occur in the developing countries.[15] Neonatal mortality is affected by factors like early and late onset of septicemia, etiological agent and the availability of supportive care. Mortality with early onset septicaemia is as high as 5% - 50% when compared to 2%- 6% in late onset septicemia.[5] Kuruvilla et al (1998)[16] reported a mortality rate of 16.7% and 13.6% in the early and late onset septicaemia respectively. According to the Yale data, the microorganisms responsible for early onset septicaemia was Group B Streptococcus while Escherichia coli and Coagulase negative Staphylococci were the major pathogens of late onset septicaemia.

Material and methods

This prospective study was conducted in the Department of Pediatrics, at Indira Gandhi institute of medical sciences patna, Bihar. Study duration of two years. Blood samples were collected from 63 clinically suspected cases of neonatal septicaemia admitted to the Neonatal Intensive Care Unit, constituted the material of the study.

Inclusion Criteria

All term, pre-term and post-term neonates admitted in Neonatal Intensive Care Unit, IGIMS, Patna with neonatal septicaemia irrespective of mode of delivery, delivered.
The study includes
All clinically suspected septicaemic neonates on the basis of Maternal fever, Foul smelling lochia, Prolonged rupture of membrane, Meconium stained liquor Suspected neonates with signs and symptoms of sepsis (Temperature instability, Feeding difficulties, Respiratory distress, Jaundice, Convulsions, hypotension, poor perfusion with pallor, tachycardia or bradycardia ,apnea, grunting, cyanosis, irritability, lethargy, abdominal distension, petechiae, purpura/bleeding).

Exclusion criteria

Out-born neonates. Babies who had received antibiotics prior to admission. Gross surgical, chromosomal or congenital anomalies or dysmorphism were excluded.
Detailed history and complete physical examination is carried out on each patient. Detailed and relevant maternal history was collected. Blood sample for culture is taken from a peripheral vein or an artery ensuring standard antiseptic measures. Relevant information including age, gender, weight, mode and place of delivery, presenting complaints and signs suggestive of sepsis were collected

Sample collection:

An area of approximately 5 cm over the veni-puncture site was disinfected with 70% alcohol rubbing vigorously and allowed to dry. This was followed by application of Povidine Iodine in concentric circles over the site and allowed to dry for 1 minute. About

3-4 ml of blood was drawn using a sterile syringe, out of which 1ml of the blood sample was inoculated aseptically into a blood culture bottle, 1 ml ofthe blood, was allowed to clot in a sterile bottle to collect serum for the estimation ofC-reactive protein, and the remaining 2 ml of blood was collected in a sterile bottle containing the anticoagulant EDTA (2-2.5 mg/ml) for estimation of the Total WBC count, Absolute neutrophil count, I/T ratio, platelet count and Micro ESR.

Results

This prospective study was carried out in the Department of paediatrics, IGIMS Patna. Blood samples were collected from sixty three cases of clinically suspected neonatal septicaemia.

Of the 63 cases studied, 27 cases yielded a positive blood culture giving a success rateof 42.8%.

Table 1: DISTRIBUTION OF CASES ACCORDING TO SEX

Sex	Clinically suspectedcases	Culture positivecases
Males	34 (53.96%)	15 (55.6%)
Females	29 (46.04%)	12 (44.4%)
Total	**63 (100%)**	**27 (100%)**

Of the 63 cases studied, 34 (53.96%) were males and 29 (46.06%) were femalebabies. Males were more affected compared to females with a ratio of 1.17:1. Males were 55.6% among the culture positive babies.

Table 2: Age distribution of Babies studied

Age in days	No. of babies	%
<3	55	87.30
>3	8	12.69
Total	**63**	**100.0**

Table 3: Mode of delivery distribution of babies studied

Mode of delivery	Gender		Total
	Female	Male	
Vaginal Delivery	24(82.8%)	19(55.9%)	**43(68.3%)**
LSCS	5(17.2%)	15(44.1%)	**20(31.7%)**
Total	**29(100%)**	**34(100%)**	**63(100%)**

P=0.022*, Significant, Chi-Square test

Out of the 63 babies 43 (68.3%) of the neonates had spontaneous vaginal deliveryand 20 (31.7%) were delivered by caesarean section.

Table 4: FEEDING INTOLERANCE IN CULTURE POSITIVE ANDCULTURE NEGATIVE SEPSIS

Feeding Intolerance	Culture positive sepsis	Culture Negative sepsis	Total

Present	18	22	**40**
Absent	9	14	**23**
TOTAL	**27**	**36**	**63**

Table 5: CRP IN CULTURE POSITIVE AND CULTURE NEGATIVE SEPSIS

CRP	Culture positive sepsis	Culture negative sepsis	Total
Present	14	15	**29**
Absent	13	21	**34**
TOTAL	**27**	**36**	**63**

Positive predictive value and negative predictive value of CRP in culture positivesepsis was 48% and 61.7% respectively.

Discussion

Neonatal septicaemia is a serious disease with subtle manifestation. The disease continues to pose a challenge to the pediatricians in making a definitive clinical diagnosis due to the subtle and non-specific signs and symptoms; hence laboratory diagnosis plays a major role. Definitive diagnosis rests on a positive blood culture, toidentify the pathogen and determine its antibiotic susceptibility pattern, but for bettersurvival and outcome, simple and rapid diagnostics tests are required as adjuncts to the blood culture for early and effective initiation of treatment to the septicemic neonates.

Table 6: COMPARITIVE STUDIES SHOWING SEX DISTRIBUTION

NO.	AUTHORS	YEAR	CULTURE POSITIVE CASES (NO.)	MALES (%)	FEMALES (%)
1.	Tallur et al [11]	2000	157	63.60%	36.40%
2.	Uddin Ahmed et al [20]	2002	30	63.00%	37.00%
3.	Varsha et al [17]	2003	150	59.00%	41.00%
4.	Betty Chacko et al [4]	2005	42	50.00%	50.00%
5.	**Present study**	**2014**	**27**	**55..60%**	**44.40%**

The ratio of culture positive neonatal septicemia cases were higher among males than the females in the present study, showing a ratio of 1.17 : 1.

Similar observations were seen in the studies done by Tallur et al.,[11] Roy et al.,[3] andVarsha et al.,[17] who also reported a higher proportion of early onset septicaemia cases. This could be due to ascending infection following rupture of membranes orduring the passage of the baby through the infected birth canal or at the time of resuscitation in the labour room. Our results differs from the study by G. Karthikeyan et al.,[19] who reported an equalproportion of EOS and LOS cases in their study, while the study by R.S. Jaswal etal.,[18] shows a higher proportion of LOS cases than EOS cases. These findings could be because of the

geographical variation in the occurrence of infection among the neonates, also suggests a nosocomial source of infection. In the present study, Leucopenia i.e Total WBC counts <5000 cells/ cu.mm wastaken as the diagnostic criteria for detecting neonatal septicaemia. Sensitivity, specificity, positive predictive value and the negative predictive values of leucopenia in our study were 29%, 83.3%, 57.1% and 61.2% respectively.
Thrombocytopenia i.e Platelet counts < 1.5 lakhs / cu,mm was taken as thediagnostic criteria in the present study. Micro- Erythrocyte sedimentation rate of >15 mm after 1 hr was taken as the diagnostic in the present study. It is clear from the above table that micro-ESR had very low specificity and positivepredictive value, while a higher sensitivity in detecting septicaemia. Micro-ESR was a poor predictor of neonatal septicaemia in our study compared tothe studies conducted by other authors. These variations are due to the fact that atleast four hours are required for haematological response to develop after the onset of infection and blood samples collected and analysed before this will have normal reports. In the present study, sensitivity, specificity, positive predictive value and negative predictive value of CRP test were 51%, 58%, 48% and 61.7% respectively. For a positive CRP test, a cut off value of > 6 µg/dl was taken as the diagnostic criteria for detecting neonatal septicaemia. This test had 61.7% negative predictive value in diagnosing septicaemia. The differences in the results of this parameter shown by the different studies is dueto variations in the diagnostic criteria, the time of onset of infection (early or late) and different methods of CRP estimation.

Conclusion

Neonatal septicaemia is still a leading cause of mortality and morbidity in developing countries like India. It is more common among males, low birth weight and term neonates. It was also found to be more common among the neonates with spontaneous vaginal delivery. Majority of the cases were early onset septicaemia 55 (87.3%) compared to late onset septicaemia 8 (12.7%). Staphylococcus aureus is the commonest Gram positive organism causing neonatal septicaemia. Multidrug resistant S.aureus is emerging as a significant problem in our NICU.

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