A STUDY OF LABORATORY PROFILE OF NEONATAL SEPSIS AT NICU (SNCU), WARANGAL

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ABSTRACT

BACKGROUND

Of the 130 million babies born worldwide each year, 26 million are born in India alone. Four million babies die with in first 30 days of birth and another four million are stillborn. Newborn mortality represents 40% of all deaths of children less than five years of age. Of the four million deaths each year, nearly 98% occur in developing countries. Globally major causes of neonatal deaths are due to preterm births (28%), sepsis or pneumonia (26%) and birth asphyxia (23%). Neonatal sepsis is one of the commonest causes of neonatal deaths in the developing world accounting to 30-50% of all neonatal deaths per year. The present study is intended to help the practising paediatrician to accurately diagnose the sepsis early using the specific laboratory tests and avert the progression of the disease.

METHODS

It is an observational cross-sectional study in NICU, Mahatma Gandhi Memorial Hospital. The study was conducted in the period November 2013 to October 2014.
After admission, detailed history and thorough clinical examination was done. Required data was entered in a pre-set proforma and statistical analysis was done. Blood culture was sent. Bacterial culture and sensitivity was checked.

RESULTS

In proven sepsis, 50.25% were Gram-positive, 43.65% were Gram-negative and 6.09% were fungal sepsis Candida). Klebsiella (32.48%) was the most common organism followed by Coagulase positive Staphylococcus (25.38%) and CONS (20.81%). In this study, Gram-negative sepsis was more common in preterm and Gram-positive sepsis was more common in term neonates. Early onset sepsis was the common presentation of proven sepsis, Klebsiella was common organism causing EOS. Whereas CONS was commonest causing late onset sepsis. Among Gram-negative organisms, 58.1% and 27.9% were resistant to cefotaxime and ampicillin+sulbactam respectively. Among Gram-positive isolates, 35% and 22% were resistant to cefotaxime and ampicillin+sulbactam respectively. Klebsiella, most common organism was found to be resistant to cefotaxime (60.9%), ampicillin+sulbactam (32.8%), gentamycin (17%). Resistance of Gram-negative and Gram-positive isolates to first line antibiotics and even with cefotaxime is emerging and is a major concern in neonatal intensive care unit.

CONCLUSION

The study is of great help to the practising paediatrician and the future scope of the study is very good. The demographic pattern has to be understood and any geographical variation has to be understood.

KEYWORDS

Neonatal Sepsis, Laboratory Profile, Newborn.

HOW TO CITE THIS ARTICLE: Ambati V, Ajmera S, Akula A. A study of laboratory profile of neonatal sepsis at NICU (SNCU), Warangal. J. Evid. Based Med. Healthc. 2016; 3(40), 1976-1980. DOI: 10.18410/jebmh/2016/440

INTRODUCTION: Of the 130 million babies born worldwide each year 26 million are born in India alone. Four million babies die with in first 30 days of birth and another four million are still born.[1] Newborn mortality represents 40% of all deaths of children less than five years of age. Of the four million deaths each year nearly 98% occur in developing countries.[2] Globally major causes of neonatal deaths are due to preterm births (28%), sepsis or pneumonia (26%) and birth asphyxia (23%).[3] Neonatal sepsis is one of the commonest causes of neonatal deaths in the developing world accounting to 30-50% of all neonatal deaths per year.[3,4] The incidence of neonatal septicaemia is 1-4 per 1000 live births in developed countries with considerable fluctuation over time and geographical location.[5] The reported incidence of neonatal sepsis varies from 7.1 to 38 per 1000 live births in Asia[6] and from 6.5 to 23 per 1000 live births in Africa.[7] Studies from India, Pakistan, Thailand and Malaysia reported incidence of neonatal sepsis ranging from 27-69%. Incidence of neonatal sepsis among hospitalised is approximately 5-6 per 1000 live births and incidence of meningitis approximately 0.7 – 1.0 per 1000 live births.[8] The incidence of neonatal sepsis

Financial or Other, Competing Interest: None.
Submission 22-04-2016, Peer Review 06-05-2016,
Acceptance 16-05-2016, Published 18-05-2016.
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DOI: 10.18410/jebmh/2016/440

according to data of National Neonatal Perinatal Database (NNPD) is 30 per 1000 live births.[9] Several hospital based studies reported sepsis as the commonest cause of neonatal deaths.[10] In India, sepsis has been reported as cause of neonatal deaths is 20-50% cases in community based studies.[11]

Early onset type: In most cases, foetus or neonate is not exposed to potentially pathogenic bacteria until the membranes rupture and the infant passes through the birth canal and/or enters the extra uterine environment. The human birth canal is colonized with aerobic and anaerobic organisms that may result in ascending amniotic infection and, or colonisation of neonate at birth.[5] Chorioamnionitis results from microbial invasion of amniotic fluid, often as result of prolonged rupture of chorioamniotic membrane. Amniotic infection may also occur with apparently intact membranes or with a relatively brief duration of rupture. The term chorioamnionitis refers to the clinical syndrome of intra uterine infection which includes maternal fever with or without local or systemic signs of chorioamnionitis (uterine tenderness, foul smelling vaginal discharge/amniotic fluid, maternal leucocytosis, maternal and or foetal tachycardia). Chorioamnionitis may also be asymptomatic only diagnosed by amniotic fluid analysis. Histologically chorioamnionitis is inversely related to gestational age at birth and directly related to duration of membrane rupture[12]. Infant born to a mother with infected amniotic fluid has a 1-5% chances of becoming infected, risk is greater if gestation is <34 weeks or if the membranes have ruptured for more than 18 hours. Term infants may be protected by antibacterial activity of amniotic fluid that first appears at 20 weeks of gestation and steadily increases thereafter.

Late onset type: Postnatal infections are transmitted by direct contact with hospital personnel, the mothers and other family members. The most common source of infection in hospitalised new born is hand contamination of health care personnel. Most cases of meningitis result from haematogenous dissemination. Less often, meningitis results from contiguous spread as result of contamination of open neural tube defects, congenital sinus tracts or penetrating wounds from foetal scalp sampling.[5]

Laboratory diagnosis in neonatal sepsis would include:

- Screening tests for rapid diagnosis of suspected sepsis.
- Tests to localise the infection such as chest radiograph, lumbar puncture, etc.
- Cultures from body fluids to confirm infection.

The present study is dedicated to study the laboratory profile of the neonatal sepsis in NICU. The present study is intended to help the practising paediatrician to accurately diagnose the sepsis early using the specific laboratory tests and avert the progression of the disease.

AIMS AND OBJECTIVES:

1. To study the laboratory profile of the sepsis in NICU.
2. To know the sensitivity, specificity, positive predictive value and negative predictive value
3. To identify various micro-organism and their antibiotic susceptibility pattern.

MATERIALS AND METHODS:

Design: It is an observational cross sectional study.
Source: NICU, Mahatma Gandhi Memorial Hospital.
Period of Study: November 2013 to October 2014.

INCLUSION CRITERIA: Neonates were included when at least three of the following risk factors were present[1]:

1. Febrile illness in the mother during or within two weeks of delivery (more than 38^0 C, oral temperature).
2. More than 3 vaginal examinations during labour.
3. Prolonged rupture of membranes (more than 12 hours).
4. Foul smelling or meconium stained liquor.
5. Preterm baby or LBW baby.
6. Birth asphyxia and difficult resuscitation.
7. Pathological evidences of funisitis.

In addition, neonates who presented with symptoms of septicaemia like refusal of feeds, decreased activity, lethargy, respiratory distress, fever, hypothermia, sclerema, abdominal distension, seizures and shock were all included.

EXCLUSION CRITERIA:

1. Neonates with lethal congenital anomalies.
2. Neonates whose parents didn't give consent.

All cases of suspected septicaemia considering inclusion and exclusion criteria admitted in the NICU, Mahatma Gandhi Memorial Hospital, from November 2013 to October 2014 was taken up for study.

After admission detailed history and thorough clinical examination was done. Required data was entered in a pre-set proforma and statistical analysis was done. Blood culture was sent.

Sepsis screen:

i. Total leukocyte count was done. Leukopenia with count <5000 /mm^3 was considered positive for septicaemia.
ii. Peripheral smear: The neutrophil and Toxic granules, coarse darkly stained granules were identified and its percentage was calculated.
iii. Micro-ESR
During neonatal period a value of more than 15 mm at the end of 1^{st} hour was considered suggestive of infection
iv. CRP: CRP was detected by latex agglutination test. Span CRP kit was used for detection of CRP

Blood culture: A 1 mL of blood was drawn and inoculated into blood culture bottle containing 10 mL of brain heart infusion broth aseptically and this constituted 1 in 10 dilution of blood which nullifies the natural bacteriostatic or bactericidal activity of the blood. Then, it was sent to the lab for blood culture and antibiotic sensitivity:

RESULTS: Mean Haemoglobin in Blood culture positive sepsis was 12.96±0.22 g%.

Mean TLC in blood culture positive sepsis was 12,493±673/cu.mm.

Leucopenia (<5000/cu. mm) was noted in 46(23.35%) cases of proven sepsis.

Platelet count mean in blood culture positive sepsis was 1,23,253±5609.

Thrombocytopenia (<150,000) was seen in 149 (75.63%) of blood culture positive sepsis.

CRP	Blood Culture Positive Sepsis	Blood Culture Sterile	Clinical Sepsis
Positive	112	132	244
Negative	85	90	175
	197	222	419

Table 1: C-Reactive Protein Positivity between Blood Culture positive And Clinical Sepsis

In the present study, sensitivity, specificity, positive predictive value and negative predictive value of CRP between blood culture positive sepsis and clinical sepsis with blood culture sterile were 56.85, 40.54, 45.9 and 51.43 respectively.

Hypoglycaemia seen in 51 neonates.

Chest X-ray: Chest x-ray abnormalities seen in 42 (10%) of cases of clinical sepsis.

CSF Analysis: Meningitis seen in 17 (4.05%) cases of sepsis.

Organism	No. of Patients
Gram-negative	86 (43.65%)
Klebsiella	64 (32.48%)
E. coli	11 (5.58%)
Pseudomonas	6 (3.04%)
Proteus	4 (2.03%)
Serratio	1 (0.5%)
Gram-positive	99 (50.25%)
Coagulase positive Staphylococcus	50 (25.38%)
CONS	41 (20.81%)
Streptococcus pneumonia	8 (4.06%)
Candida	12 (6.09%)
Total	197

Table 2: Bacterial Profile in Proven Sepsis

	Gram-positive blood culture sepsis	Gram-negative blood culture sepsis	Bacterial sepsis(total)
No. of organisms	86(46.48%)	99(53.5%)	185
			p-value 0.17

Table 3: Bacterial Profile in Gram-Positive and Gram-Negative Blood Culture Sepsis

	Early Onset Sepsis (EOS)	Late Onset sepsis	Total no. blood culture positive sepsis
No. of organisms	155(78.68%)	42(21.31%)	197
			p-value 0.000001

Table 4: Bacterial Profile in Relation to Onset of Symptoms

Organism	EARLY ONSET SEPSIS (EOS)	LATE ONSET SEPSIS (LOS)	p-value
E. coli	8(5.16%)	3(7.14%)	0.61
Klebsiella	58(37.4%)	6(14.28%)	0.008
Proteus	4(2.58%)		
Pseudomonas	6(3.87%)		
Serration	1(0.64%)		
Streptococcus. pneumonia	6(3.87%)	2(4.76%)	
Coagulase positive staphylococcus	38(19.28%)	12(28.57%)	0.1
CONS	26(16.77%)	15(35.71%)	0.007
Candida	8(5.16%)	4(9.52%)	0.31
	155	42	

Table 5: Bacterial Profile in Relation to EOS and LOS

The yield of various microorganisms in EOS was 155(78.7%) when compared to LOS 42(21.3%) which is statistically significant (p-value 0.00001), Klebsiella (37.4%) was common organism causing EOS (p-value 0.008), whereas CONS (35.7%) was commonest in LOS (p-value 0.007).

ANTIBIOTIC SENSITIVITY AND RESISTANCE TO CAUSATIVE: In this study, Coagulase positive staphylococcus was observed to be resistant to cefotaxime (32%) and sensitive to ciprofloxacin (58%) and ampicillin+sulbactam (16%).

In this study, CONS seem to be resistant to cefotaxime (34.14%) and ampicillin+sulbactam (17.07%) and sensitive to ciprofloxacin (46.34%) followed by cefotaxime (34.14%), imipenem (26.8%) and amikacin (19.51%).

In this study, E. coli was observed to be resistant to cefotaxime (27%) and ampicillin+sulbactam. (27.27%) and sensitive to ciprofloxacin (36.36%) and amikacin (9%).

Among Gram-negative organisms 27.9% and 6.9% were resistant to ampicillin+sulbactam and amikacin respectively. Among Gram-positive isolates 22% and 5% were resistant to ampicillin+sulbactam and amikacin respectively.

Resistance to Cefotaxime to Gram-negative and Gram-positive isolates were 58.1% and 35% respectively.

Among Gram-negative organism sensitivity and resistance to ciprofloxacin were 30.2% and 53.48% respectively. Among Gram-positive organism sensitivity and resistance to ciprofloxacin were 54% and 34% respectively.

DISCUSSION: In the study done by Shitaye D et al (2010)[13] abnormal WBC counts (high and low) were strongly associated with culture proven sepsis.

Thrombocytopenia was more in preterm neonates (63.63%) than term (57.97%) neonates. In the study done by Manzoni P et al (2009) platelet count <80,000 was seen in 17.2% of proven sepsis.[14] Mannan MA et al(2010) observed thrombocytopenia in 50% cases of culture proven sepsis.[15] Mannan MA et al (2010) studied utility of CRP in the detection of neonatal sepsis by comparing 100 cases of suspected sepsis and 50 controls. In their study, sensitivity and specificity of CRP were 78.6% and 62.5% respectively. In the following study, out of 419 clinical sepsis, 197 (47.01%) were blood culture positive. Out of 197 organisms isolated in blood culture, 99(50.25%) were Gram-positive, 86(43.65%) were Gram-negative and 12(6.09%) were fungal sepsis (candida). Gram positive and Gram-negative sepsis occurred in equal proportions in the present study. In the study done by Viswanathan R et al (2012)[16] among 216 cases of clinical sepsis, 100(46.3%) cases had blood culture positive, which was similar to our study. In their study Gram-negative infection were predominant (58/100 cases). Most common organism was Klebsiella followed by E. coli, Enterobacter sp.

In the study done by Shrestha S et al (2013),[17] blood culture yield by conventional method was 44.13%,[7] which is similar to our study. Gram-positive organisms were 39.36% in which Staphylococcus aureus most common followed by CONS. Gram-negative organisms were 60.64%, amongst Klebsiella most common followed by Pseudomonas.

In the present study 78.6% cases were EOS and 21.3% were LOS. EOS was common presentation of proven sepsis, Klebsiella (37.4%) was common organism causing EOS. Whereas CONS (35.7%) was commonest in LOS. Similar observations were made by Shrestha S et al (2013)[17] in which 84.08% were culture proven early onset sepsis and 15.95% were late onset sepsis.

ANTIBIOTIC SENSITIVITY AND RESISTANCE TO CAUSATIVE ORGANISM: In the present study, among Gram-negative organisms 58.1% and 27.9% were resistant to Cefotaxime and ampicillin +sulbactam respectively. Among Gram-positive isolates 35% and 22% were resistant to Cefotaxime and ampicillin +sulbactam respectively. Klebsiella most common organism in our NICU found to be resistant to cefotaxime (60.9%), gentamycin (17%), Ampicillin+sulbactam (32.8%). Similar observations were made by Shrestha S et al (2013),[17] in which the most common organism Klebsiella was 87.5% and 78.3% resistance to ampicillin and gentamycin respectively.[7] Among Gram-negative isolates 87.5% and 77.2% were resistance to ampicillin and gentamycin respectively. Among Gram-positive isolates 58.5% and 31.5% resistance were noted to ampicillin and gentamycin respectively. Resistance to cefotaxime to Gram-negative and Gram-positive isolates were 87.34% and 59.35% respectively. Resistance to both Gram-negative and Gram-positive isolates among first line antibiotics and even with cefotaxime is emerging and is a major concern in neonatal intensive care unit.

In study conducted by Viswanathan Ret al (2012)[16] 100% resistance was noted for ampicillin, cefotaxime and gentamycin. Amikacin showed 95% resistance and ciprofloxacin showed 83.3% resistance among Gram-negative bacteria.

In the study done by Kapoor Let al (2005)[18] resistance to commonly used antibiotics was seen in more than 35% of isolates.[18] An alarming observation was the very high incidence of resistance to amoxicillin +clavulanic acid and ceftriaxone.

CONCLUSION: In proven sepsis, 50.25% were Gram-positive, 43.65% were Gram-negative and 6.09% were fungal sepsis (Candida). Klebsiella (32.48%) was the most common organism followed by Coagulase positive Staphylococcus (25.38%) and CONS (20.81%). In this study, Gram-negative sepsis was more common in preterm and Gram-positive sepsis was more common in term neonates. Early onset sepsis was the common presentation of proven sepsis, Klebsiella was common organism causing EOS. Whereas CONS was commonest causing late onset sepsis. Among Gram-negative organisms, 58.1% and 27.9% were resistant to cefotaxime and ampicillin+sulbactam respectively. Among Gram-positive isolates, 35% and 22% were resistant to cefotaxime and ampicillin+sulbactam respectively. Klebsiella, most common organism was found to be resistant to cefotaxime (60.9%), ampicillin+sulbactam (32.8%), gentamycin (17%). Resistance of Gram-negative and Gram-positive isolates to first line antibiotics and even with cefotaxime is emerging and is a major concern in neonatal intensive care unit.

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