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Original Research Article

Clinicobacteriological profile, antibiotic sensitivity patterns and mortality of neonatal sepsis in a tertiary care hospital in Kashmir, Jammu and Kashmir, India

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ABSTRACT

Background: Neonatal sepsis refers to generalized bacterial blood stream infection in first 28 days of life documented by positive blood cultures. It is one of leading causes of neonatal mortality. Objectives was to study clinicobacteriological, antibiotic sensitivity patterns and mortality of neonatal sepsis.
Methods: This prospective study was conducted in the Department of Pediatrics of Government Medical College Srinagar in collaboration with Department of Microbiology of same medical college after ethical clearance from ethical committee of Government Medical College Srinagar. One hundred (100) neonates out of 731 neonates admitted between octomber2007 and September 2008 with signs and symptoms of neonatal sepsis were included in our study by random sampling method. After history, examination and laboratory investigation blood culture results were analyzed by standard statistical methods.
Results: The blood culture was positive in 40% of neonates. Fifty one (51) neonates were males while as 49 were females. Sixty three (63) neonates had late onset of sepsis while as 37 had early onset sepsis. The positive blood culture was more common in males, late onset sepsis, babies born in rural areas, home born, vaginal births, preterm and other low birth weight neonates .The gram negative isolates were most common followed by positive ones .The best sensitivity of gram negative isolates was to ciprofloxacin followed by amikacin and cephalosporins while as gram positive isolates were sensitive to imipenum followed by vancomycin. Pseudomonas was most responsive to pipercillin +tazobactum combination. The neonatal mortality was 35% being higher in early onset sepsis and low birth weights.
Conclusions: This study depicts a high rate of neonatal sepsis, mainly caused by gram negative organisms followed by gram positive organisms with rising drug resistance that could bear far reaching implications to the times to come, mandating the implementation of sepsis preventive measures and administration of specific antibiotics.

Keywords: Clinicobacteriological profile, Antibiotic sensitivity patterns, Mortality of neonatal sepsis

INTRODUCTION

Neonatal sepsis is defined as the presence of positive bacterial cultures in blood, cerebrospinal fluid and or urine associated with systemic clinical signs of infection such as fever, temperature instability, irritability, poor feeding and respiratory distress.[1] Neonatal sepsis is the most common cause of neonatal mortality. It is responsible for 30-40% of neonatal deaths in developing countries.[2] The incidence of sepsis is 3 per thousand live

births according to national neonatal perinatal database.[3] According to World health organization (WHO) estimates, there are about 5 million neonatal deaths a year, with 98% occurring in developing countries.[4] The epidemiology of neonatal sepsis in developing and developed countries shows some important differences in pattern of etiological agents and their antibiotic susceptibilities. More ever epidemiology within a geographical area may also be different, highlightening the need for surveillance of neonatal sepsis in various regions for optimal therapy.[5]

Neonatal sepsis can be divided into early onset sepsis (EOS) or late onset sepsis (LOS) depending on onset is during the first 72hours or later. EOS occurs due to ascending infection following rupture of membranes or during passage of baby through the infected birth canal. LOS occurs mainly as nosocomial infection from the nursery or ward.[2] The EOS infections are caused by organisms prevalent in maternal genital tract or in the delivary area. The predisposing factors include low birth weight (LBW), prolonged rupture of membranes, foul smelling liquor, multiple per vaginum examinations, maternal fever, difficult or prolonged labour and aspiration of meconium. The LOS infections are caused by the organisms thriving in the external environments of home or hospital. The infection is often transmitted through the hands of care providers .The predisposing factors include LBW, lack of breastfeeding, poor cord care, superficial infections (pyoderma, umbilical sepsis), aspiration of feeds, disruption of skin integregrity with needle pricks and use of intravenous fluids.[6] The neonatal sepsis is caused by variety of gram positive as well as gram negative bacteria and sometimes yeasts. The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region. This is due to changing pattern of antibiotic use and changes in lifestyle.[7]

Neonates with bacterial sepsis may have either non specific signs and symptoms or focal signs of infection, including temperature instability, hypotension, poor perfusion with palor and mottled skin, metabolic acidosis, tachycardia, bradycardia, apnea, respiratory distress, grunting, cyanosis, irritability, lethargy, seizures, feeding intolerance, abdominal distension, jaundice, petechiae, purpura and bleeding. The intial manifestation may involve only limited symptomatology and only one system, such as apnea alone or tachypnea with retractions, or tachycardia or the infant may present with an acute catastrophic manifestation with multi organ dysfunction.[8]

Early diagnosis is a key to reduce morbiditity and mortality of neonatal septicaemia. The gold standard for diagnosis of septicaemia is the isolation of bacterial agents from blood culture. But definitive culture results take atleast 48-72 hours resulting in treatment delays. Hence, two-pronged approach is used for the evaluation of neonates with possible sepsis. Nonspecific sepsis screen tests like C-reactive protein (CRP), erythrocyte sedimentation rate, total white blood cell count and absolute neutrophil count are used to evaluate the likelihood of infection, and specific diagonostic tests are performed to confirm presence of a specific pathogen in body fluids.[9]

METHODS

This prospective study was conducted in the department of pediatrics of government medical college Srinagar in collaboration with department of Microbiology of same medical college after ethical clearance from ethical committee of Government medical college Srinagar.100 neonates out of 731 neonates admitted between October 2007 and September 2008 with signs and symptoms of neonatal sepsis were included in our study by random method. Only neonates having three or more signs or symptoms of sepsis like feed refusal, lethargy, poor cry, vomiting, diarrhoea, jaundice, pyoderma, cyanosis, palor, hypothermia, fever, abdominal distension, seizures, apnea, tachypnea, grunting, poor capillary refill, umbilical discharge and scelrema were included in our study. Neonates with gross congenital anomalies including clinical suspicion of congenital heart diseases, extreme prematurity (<28weeks), severe birth asphyxia, suspected inborn errors of metabolism and respiratory distress syndrome except cases of congenital pneumonia suspected clinically in presence of risk factors. All neonates were subjected to meticulous history and examination. Routine investigations like complete blood count, absolute neutrophil count, band count, micro erythrocyte sedimentation rate, C-reactive protein, X-ray chest and abdomen in selected cases and serum biochemical investigations were done. Blood culture was done in all cases by taking 2-3ml of blood from peripheral vein under all aseptic precautions before start of antibiotics and inoculated in blood culture bottle containing 10-20ml liquid broth. Blood and broth were mixed gently and transported immediately to laboratory and incubated at 37 aerobically. The isolates were identified by Gram staining, colony characteristics and biochemical properties. Cultures were labelled negative if there was no growth after one week of incubation. Antimicrobial susceptibility of bacterial isolates was tested by Kirby Baur disc diffusion as recommended in the national committee for clinical laboratory standards (NCCLS) guidelines.[10] Cerebrospinal fluid was taken among all neonates and was sent for culture and sensitivity besides routine examination. Data was analysed by SPSS version 15.

RESULTS

Out of 100 neonates,51 were males and 49 were females. Blood culture was positive in 40 neonates. Significant differences have been observed regarding the blood culture positivity while assessing the differences between the early onset sepsis, place of living place of delivery,

mode of delivery, birth weight and maturity of the newborn, as is shown in Table 1.

Table 1: Blood culture results in neonatal sepsis.

Parameter		Blood culture positive	Blood culture negative	P value
Onset of sepsis	Early, N=37	6	31	<0.001
	Late, N=63	34	29	
Sex	Male, N=51	26	25	<0.03
	Female, N=49	14	35	
Place of living	Rural, N=61	28	33	<0.02
	Urban, N=39	12	27	
Place of delivery	Home N=30	18	12	<0.03
	Hospital, N=70	22	48	
Mode of delivery	Normal N=68	32	36	<0.001
	LSCS N=32	8	24	
Birth weight	<2.5KG N=68	31	37	<0.02
	>2.5KG N=32	9	23	
Maturity	<37weeks N=47	29	18	<0.001
	>37weeks N=53	11	42	

In general, refusal of feeds is the most common symptom in neonatal sepsis, while as breathing difficulty was most common in early onset sepsis. The isolates were gram negative in 34 (85%) and gram positive in 6 (15%).

Table 2: Clinical profile of blood culture positive sepsis.

Symptoms	No. of neonates N=40	Early onset N=6	Late onset N=34
Feed refusal	27(67%)	2(33.3%)	25(73.5%)
Lethargy	18(45%)	2(33.5%)	16(47%)
Breathing difficulty	14(35%)	5(83.3%)	9(26.4%)
Hypothermia	12(30%)	4(66.6%)	8(23.5%)
Fever	10(25%)	0(0.0%)	10(29.4%)
Jaundice	7(17.5%)	0(0.0)	7(20.5%)
Convulsions	7(17.5%)	2(33.3%)	5(14.7%)

Table 3: Organisms isolated from the studied neonates.

Isolates	N=40	Early onset N=6	Late onset N=34
Klebsiella pneumonia	16(40%)	1(16.7%)	15(44.2%)
Escherichia coli	13(32.5%)	4(66.6%)	9(26.4%)
Staphylococcus aureus	6(15%)	0(0.0%)	6(17.6%)
Pseudomonas aeruginosa	3(7.5%)	0(0.0%)	3(8.8%)
Citrobacter	2(5%)	1(16.7%)	1(3%)

Table 4: Antimicrobial susceptibility to various antimicrobials.

Isolates	No. of patients	Drugs	Sensitive	Resistant
Klebsiella pneumonia	15	Amikacin	14 (93.3%)	1 (6.7%)
		Ciprofloxacin	15 (100.00%)	0 (0.0%)
		Ampicillin	2 (13.3%)`	13 (86.7%)
		Cefotaxime	10 (66.6%)	5. (33.4%)
		Ceftriaxon+sulbactum	14 (93.3%)	1 (6.7%)
Escherichia coli	13	Amikacin	12 (92.3%)	1 (7.7%)
		Ciprofloxacin	13 (100.0%)	0 (0.0%)
		Ampicillin	3 (23.0%)	10(7.7%)
		Cefotaxime	6 (46.2%)	7 (53.8%)
		Ceftriaxone+sulbactum	11 (84.6%)	2 (15.4%)
Staphylococcus aureus	7	Methicillin	1 (14.3%)	6 (85.7%)
		Vancomycin	7 (100.00%)	8 (0.0%)
		Imipenum	7 (100.00%)	0 (0.0%)
Pseudomonas aureoginosa	3	Ciprofloxacin	2 (66.6%)	1 (33.4%)
		Pipercillin+Tazobactum	3 (100.00%)	0 (0.0%)
		Imipenum	3 (100.00%)	0 (0.0%)
Citrobacter	7	Ciprofloxacin	2 (100.00%)	0 (0.0%)
		Imipenum	2 (100.00%)	0 (0.0%)
		Ceftriaxone+sulbactum	1 (50.00%)	1 (50.00%)

Table 5: Mortality pattern among the studied neonates.

Parameter		No. of patients	Patients died	Mortality rate
Onset of sepsis	Early	6	3	50%
	Late	34	11	32%
Birth weight	<2.5kg	31	13	41.9%
	>2.5kg	9	1	11.1%
Maturity	<37	29	13	44.8%
	>37	11	1	9%
Isolates	*Pseudomonas aeruginosa*	3	2	66%
	Citrobacter	2	1	50%
	Klebsiella pneumonia	16	7	43.6%
	Staphlylococcus aureus	6	2	33%
	Escherichia coli	13	2	15.3%

From Table 2, onset of sepsis, sex, place of living, place of delivery, mode of delivery, birth weight, and maturity of the neonates is significantly associated with the culture positivity.

From Table 3, it is clear that feed refusal in general is most common symptom in neonatal sepsis, while as breathing difficulty was most common in early onset sepsis.

As is obvious from the results, in general, *Klebsiella pneumonia* was most organism causing neonatal sepsis and more often associated with late onset sepsis while as *Escherichia coli* was most common cause of early onset sepsis in our study.

From our study it is quite obvious that the gram-negative isolates were sensitive to aminoglycosides and cephalosporins but majority were resistant to ampicillin as is depicted in Table 4. It is pertinent to mention that methicillin resistance against staph aureus is quite high in our setting.

The mortality rate in neonatal sepsis turned 35% in our study. From our results neonates with pseudomonas infection were having highest mortality followed by *Citrobactor* and staph aureus as is shown in Table 5.

DISCUSSION

The uncertainty surrounding the clinical approach to treatment of neonatal septicemia can be minimized by periodic epidemiologic surveys of aetiological agents and their antibiotic sensitivity patterns leading to recognition of the most frequently encountered pathogen in a particular geographic area.[7] Our study was similar one and it supported the findings of previous studies. The blood culture positivity rate of 40% in our study was similar to studies done by Ahmed ANU et al and Shukla et al.[11,12] The high positive culture rate in recent studies than older studies like Mathur M et al, is probably due to improved techniques of bacterial isolation and availability of rapid diagnostic kits.[13] As reported by Ahmed ANU et al, our study shows that incidence of neonatal sepsis is more common in male babies (50.98% vs 28.72%) which could be due to some social factors with bias in gender towards patient treatment.[11] The late onset sepsis was more common than early onset (85% vs 15%) similar to early studies like Ahmed ANU et al and Taller SS et al.[11,5] The higher incidence of late onset sepsis may be because of use of 72hrs as cutoff for defining early onset sepsis and its higher mortality. Neonatal sepsis was more common in neonates born in rural than in urban (70% vs 30%) similar to studies like Taller SS et al, Rasul CH et al and Iyer CR et al.[5,14,15] This could be because of differences in delivery places and lack of trained knowledgeable health care providers in rural areas which may also be reason for higher incidence of sepsis in normal vs caesarean deliveries (80% vs 20%). Our study revealed that neonatal sepsis is more common in low birth babies than normal weight babies (77.5% vs 22.5%) in accordance to studies of Iyer CR et al and Rajana R et al.[15,3] The could be because of immunological immaturity and overall high risk behavior of low birth neonates. Refusal of feeds and lethargy were most common symptoms of neonatal sepsis (67.5% vs 45%) consistent with Jaswal RS et al.[16] The gram negative organisms were isolated in 85% of cases consistent with studies done by Mathur M et al, Rasul CH et al and Jaswal RS et al.[13,14,16] The most common organisms isolated in our study were klebsiella pneumonia (40%), *Escherichia coli* (32.2%) and *Staphylococcus aureus* (15%) in that order consistent with Taller SS et al.[5] The probable reason for it being that most of gram negative organisms are normal commensals and neonates are less protected against them because of low IgM antibodies. The rarity of group B streptococcus in our study could be due to its low prevalence in our settings. The gram negative isolates were sensitive to aminoglycosides and cephalosporins but majority were resistant to ampicillin similar to studies done by Taller SS et al and Rasul CH et al.[5,14] 99% of staphylococcus isolates were sensitive to vancomycin and impenum but 85% were resistant to methicillin consistent with Ahmed

ANU et al and Rasul C H et al.[11,14] Mortality in our study 35% consistent with Ahmed ANU et al and Shukla et al (41%).[11,12] Mortality was higher early onset sepsis than late onset sepsis (50% vs 32%) in accordance with Ahmed ANU et al and in low birth babies than normal weight babies (41.9% vs 11.1%) in accordance with Ahmed ANU et al and Taller SS et al.[11,5] In our study mortality due to pseudomonas was highest (66%) and least with Escherichia coli (15%) in accordance with Ahmed ANU et al.[11]

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REFERENCES

1. Trotman H, Bell Y, Thame M, Nicholson AM, Barton M. Predictors of poor outcome in neonatal sepsis admitted to university hospital of the West Indies. West Indian Med J. 2006 Mar;55(2):80-4.
2. Sathyamurthi B, Leela KV, Narayanababu R, Padmanaban S, Sreedevi S, Sujatha et al. Clinical and bacteriological profile of neonatal sepsis in a tertiary care hospital. Int J Sci Stud. 2016;4(8):57-60.
3. Rajana R, Bagri DR, Sharma JN, Agarwal V. Clinical and bacteriological profile of neonatal sepsis with emerging resistance patterns. Int J Contemp Pediatr. 2018;5:2203-8.
4. Vernago S, Sharland M, Kazembe P, Mwansambo C, Heath P. Neonatal sepsis: an international perspective. Arch Dis Child Fetal Neonatal Ed. 2005 May;90(3):F220-4.
5. Tallur SS, Kasturi AV, Nadgir SD, Krishna BV. Clinicobacteriological study of neonatal septicemia in Hubli. Indian J Pediatr. 2000 Mar;67(3):169-74.
6. Oommen SA, Saini S, Rahul RK. Bacteriological profile of Neonatal septicemia: A retrospective analysis from a tertiary care hospital in Loni. Int J Meds Res Health Sci. 2015;4(3):652-8.
7. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility patterns of the isolates. J Nat Sc Biol Med. 2013;4:306-9.
8. Stoll BJ, Shane AL. Infections of Neonatal infant. In: Kliegman RM, Stanton BF, St Geme JW, Shor NF. Nelson textbook of Pediatrics. Elsevier Health; 2015:914-915.
9. Khante SV, Raunt SS. Clinical and bacteriological study of neonatal septicemia in a tertiary care hospital. Int J Res Med Sci. 2017;5:4455-62.
10. National Committee for clinical laboratory standards. Performance standards for antimicrobial disc susceptibility testing. Wayne PA:NCCLS; 2004 (Fourteenth informational supplement (M100-S14).
11. Ahmed ASMN, Chowdhury MAKA, Hoque M, Darmstad. Clinical and bacteriological profile of neonatal septicemia in a tertiary level pediatric hospital Bangladesh. Indian Pediatr. 2002;39:1034-39.
12. Shukla OS, Rawat A. Clinical profile and outcome of early onset neonatal sepsis in high risk very low birth weight neonates. Int J Contemp Pediatr. 2018;5:389-94.
13. Mathur M, Shah H, Dixit K, Khambadkone S, Chakrapani A, Irani S. Bacteriological profile of neonatal septicemia cases (for the year 1990-91). J Postgrad Med. 1994;40:18-20.
14. Rasul CH, Hassan MA, Habibullah M. Neonatal sepsis and use of antibiotic in a tertiary care hospital. Pak J Med Sci. 2007;23(1):78-81.
15. Iyer CR, Naveen G, Suma HR, Kumarguru BN, Swetha K, Janakiraman. Clinical profile and outcome of neonates with suspected sepsis from rural medical college hospital of south India. Int J Contemp Pediatr. 2018;5:55-60.
16. Jaswal RS, Kaushal RK, Goel A, Pathania K. Role of C-Reactive protein in deciding duration of antibiotic therapy in neonatal septicemia. Indian Pediatr. 2003;40:880-3.

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