

Original Research Article

Characteristics of neonatal sepsis at a tertiary care centre in Western Uttar Pradesh, India: a hospital based retrospective study

Divyata Sachan^{1*}, Pradip Kharya², Prashant K. Bajpai³

¹Department of Community Medicine, SMMH Medical College, Saharanpur, Uttar Pradesh, India

²Department of Community Medicine, AIIMS, Gorakhpur, Uttar Pradesh, India

³Department of Community Medicine, KGMC, Lucknow, Uttar Pradesh, India

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*Correspondence:

Dr. Divyata Sachan,

E-mail: divyatasachan92@gmail.com

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ABSTRACT

Background: Due to the constantly changing genome of the organisms causing disease it is important to be updated regarding the pattern of distribution of microbes and their antibiotic susceptibility. The study was conducted with the aim to determine the risk factors, microbial profile, antimicrobial susceptibility and the outcome of neonates diagnosed with neonatal sepsis.

Methods: A retrospective study was done using the data collected from medical records department of a tertiary care hospital. All the neonates diagnosed with clinical sepsis between 1 to 31 January, 2019 were included in the present study. The data were analyzed using SPSS software version 24, IBM, corp., Chicago, U.S.A. Association between the outcome and independent variable were assessed using Chi square or Fischer exact test, while the level of association was assessed by univariate and multivariate analysis.

Results: During the study period, 332 neonates were registered in the hospital out of which 89 were diagnosed with clinical sepsis. Most of the neonates (64.9%) presented with early onset sepsis and were term neonates (68.5%) with birth weight less than 2.5 kg (53.4%). Parameters like mode of delivery (OR:6.18; CI:1.30-29.32), birth weight (OR:9.14; CI:2.38-35.10) and gestational age (OR:7.33; CI:2.32-23.12) were statistically associated with neonatal outcome. All gram-positive organisms were sensitive to vancomycin and linezolid. Gram negative organisms were resistant to cephalosporins, amoxicillin-clavulanic acid and piperacillin-tazobactam.

Conclusions: A high antibiotic resistance was observed among the isolated organism. The Gram positive and gram negative organisms were equally responsible for neonatal sepsis.

Keywords: Neonatal sepsis, Early onset neonatal sepsis, Late onset neonatal sepsis, Antibiotic susceptibility, Antimicrobial sensitivity

INTRODUCTION

Sepsis is a life-threatening organ dysfunction due to a dysregulated host response to infection.¹ It is an important growing global health concern among all age groups particularly among neonates in which it is among the three most common causes of neonatal deaths globally.² Of the three lakh annual cases of neonatal sepsis reported globally, India has the highest incidence of clinical

sepsis.³ The case fatality rate of sepsis among neonates in India ranges between 25% to 65%.^{4,5} Neonatal sepsis is defined as clinical syndrome characterized by signs and symptoms of infection within 28 days.⁶ It is categorized into early onset sepsis (onset within 72 hours of birth) and late onset sepsis (beyond 72 hours). Early onset sepsis is proven to be caused by pathogens transmitted from mothers antepartum or during delivery while late onset sepsis is attributed to pathogens acquired from the

community. Evidence from studies of risk factors and antibiotic resistance have been utilized to develop management guidelines for neonatal sepsis. Information on antibiotic resistance is important for the development of appropriate management strategies and the sustainability of these management depends on monitoring changes in pathogens and resistance patterns over time. For the above reasons, this study intends to provide data on risk factors, etiological agent and resistant pattern observed amongst cases of neonatal sepsis in tertiary care hospital of district Etawah, Uttar Pradesh.

METHODS

A retrospective study was conducted in the tertiary care hospital of a district in Uttar Pradesh from 1 to 31 March 2019. Records from the Medical Records Department (MRD) of all the neonates admitted in the hospital from the period of 1 to 31 January, 2019 were reviewed. All the records which were labelled with the diagnosis of neonatal sepsis were included in the study. The study not only included the neonates which were delivered at the hospital but also included those who were referred from other institutes. Neonates who were either transferred out or left against medical advice (LAMA) were excluded from the study as the outcome could not be determined. A general overview of the practises at the paediatric department was enquired regarding the hand hygiene policy, antibiotic usage policy and procedure to collect sample for blood culture and sensitivity. The data for the study was collected using a structured, pre-tested and pre-validated questionnaire with Cronbach's alpha of 0.710 and Content Validity Index of 9.7. The data were collected under the following headings- hospital details (date of admission and discharge); neonatal details (age at admission, weight at birth, gender); pregnancy details (gestational age, history of fever, foul smelling liquor); delivery details (mode of delivery), investigations, treatment plan and outcome. The collected forms were checked for completeness and quality, then the data were entered in Microsoft Excel. All the data were analyzed using SPSS software version 24, IBM, corp., Chicago, U.S.A. Descriptive statistics was used for categorical variables while mean±standard deviation was used to represent numerical variables. Association between the outcome and independent variable were assessed using Chi square or Fischer exact test (significance level <0.05) while logistic regression was used to predict the association.

RESULTS

During the study period, records of 332 neonates were obtained out of which 151 neonates were live healthy newborns who were delivered at the hospital. A high incidence of neonatal sepsis (49.1%) was observed among the remaining 181 neonates as 89 cases were diagnosed with sepsis. Among the 89 neonates, 16 neonates were excluded as they were either transferred

out or they left against medical advice. From the remaining 73 neonates, 34 (46.6%) were female and 39 (53.4%) were male (Table 1).

Table 1: Socio- demographic, maternal and neonatal profile (n=73).

Variables		
Mean age of neonates±standard deviation		4.63±6.49
Mean duration of stay±standard deviation		11.84±11.82
		N (%)
Gender	Male	39 (53.4)
	Female	34 (46.6)
Gestational age	Pre-Term	23 (31.5)
	Term	50 (68.5)
Birth weight (kg)	Weight <2.5	34 (46.5)
	Weight ≥ 2.5	39 (53.5)
Diagnosis	EONS	48 (65.8)
	LONS	25 (34.2)
Mode of delivery	Normal vaginal	47 (64.3)
	Caesarean section	26 (35.7)
Foul smelling liquor	Yes	50 (68.4)
	No	23 (31.6)
Maternal fever	Yes	59 (80.8)
	No	14 (19.2)

Majority of the neonates (n=48; 65.7%) presented with early onset of neonatal sepsis (EONS) while 25 (34.2%) presented as late onset of neonatal sepsis (LONS). Based on gestational age, 23 (31.5%) neonates were preterm while the remaining 50 (68.5%) were term babies. From the 73 neonates, 39 (53.4%) had weight less than 2.5 kg while the rest 34 (46.6%) had weight more than 2.5 kg. Among the 73 neonates, 18 (24.7%) succumbed to death out of which 50% were diagnosed with culture negative sepsis. Among the deaths reported, 14 (77.8%) presented within 72 hrs of life i.e., they were early onset cases. The tests of association showed a significant association ($p<0.05$) between gestational age, birth weight and mode of delivery with the health outcome of neonate (Table 2). According to univariate logistic regression model; preterm neonates (OR:7.33; CI:2.32-23.12), neonates with weight <2.5 kg (OR:9.14; CI:2.38-35.10) and neonates who were delivered through vaginal delivery (OR:6.18; CI:1.30-29.32) were more likely to face adverse outcome (Table 3). The blood sample reports for culture and sensitivity were available for 48 (65.8%) neonates, among which 21 (43.7 %) showed positive blood cultures. Of the 21 positive cultures, Gram positive and Gram-negative bacteria accounted for 10 (47.6%) and 11 (52.3 %) cases respectively. The most common isolated organism was *Staphylococcus aureus* followed by MRSA. All the Gram-positive organism- *Staphylococcus aureus* and MRSA were sensitive to vancomycin and linezolid, while only 20% were sensitive for amoxicillin- clavulanic acid, piperacillin- tazobactam

and cefoxitin (Table 4). Among the Gram negative; *Citrobacter spp.*, *klebsiella spp.*, *Acinetobacter spp.* and *Pseudomonas*, all of them were resistant for cefoperazone, amoxicillin-clavulanic acid and

piperacillin-tazobactam while 90.9% were resistant for cefepime and ceftazidime while they were sensitive to imipenem and ciprofloxacin in the proportion of 81.1% and 63.6% respectively (Table 5).

Table 2: Association of socio- demographic, maternal and neonatal variables with neonatal outcome.

Variables		Survived (N=55) Frequency (%)	Deceased (N=18) Frequency (%)	P value
Gender	Male	26 (47.2)	13 (72.2)	0.06 [#]
	Female	29 (52.8)	5 (27.8)	
Gestational age	Pre-Term	11 (20)	12 (66.7)	0.00 [#]
	Term	44 (80)	6 (33.3)	
Birth weight (kg)	Weight <2.5 kg	19 (34.6)	15 (83.3)	0.00 [*]
	Weight ≥2.5 kg	36 (65.4)	3 (16.7)	
Diagnosis	EONS	34 (61.8)	14 (77.8)	0.21 [*]
	LONS	21 (38.2)	4 (22.2)	
Mode of delivery	Normal vaginal	31 (56.3)	16 (88.9)	0.01 [*]
	Caesarean section	24 (43.7)	2 (11.1)	
Foul smelling liquor	Yes	37 (67.2)	13 (72.2)	0.69 [#]
	No	18 (32.8)	5 (27.8)	
Maternal fever	Yes	43 (78.1)	16 (88.9)	0.31 [*]
	No	12 (21.9)	2 (11.1)	

[#]Test of association used- Chi square, ^{*}Test of association used- Fischer exact

Table 3: Risk factors for mortality among cases of neonatal sepsis: Univariate and multivariate analysis.

Variables	Survived (N=55)	Deceased (N=18)	Unadjusted Odds ratio (95% CI)	P value	Adjusted Odds ratio (95% CI)	P value
Gestational age						
Preterm	11 (20)	12 (66.7)	7.33 (2.32-23.12)	0.01	2.06 (0.45-9.39)	0.34
Term	44 (80)	6 (33.3)	1		1	
Birth weight						
Weight <2.5 kg	34 (46.5)	15 (83.3)	9.14 (2.38-35.10)	0.01	5.43 (0.99-29.56)	0.05
Weight ≥2.5kg	39 (53.5)	3 (16.7)	1		1	
Mode of delivery						
Normal vaginal	47 (64.3)	16 (88.9)	6.18 (1.30-29.32)	0.02	4.56 (0.84-24.56)	0.07
Caesarean section	26 (35.7)	2 (11.1)	1		1	

Table 4: Antimicrobial susceptibility of gram positive organism (sensitivity pattern).

Antibiotics	<i>S. aureus</i> (N=6)	MRSA (N=4)
Amoxicillin-clavulanic acid	2 (33.3)	0
Piperacillin-tazobactam	2 (33.3)	0
Cefoxitin	2 (33.3)	0
Cefuroxime	6 (100)	0
Vancomycin	6 (100)	4 (100)
Linezolid	6 (100)	4 (100)
Amikacin	6 (100)	4 (100)

Table 5: Antimicrobial susceptibility (resistance) for gram negative organism.

Antibiotics	<i>Klebsiella spp.</i> (N=3)	<i>Acinetobacter spp.</i> (N=3)	<i>Citrobacter spp.</i> (N=3)	<i>Pseudomonas</i> (N=2)
Cefepime	3 (100)	3 (100)	3 (100)	1 (50)
Ceftazidime	3 (100)	3 (100)	3 (100)	1 (50)
Cefoperazone	3 (100)	3 (100)	3 (100)	2 (100)
Amoxicillin-clavulanic acid	3 (100)	3 (100)	3 (100)	2 (100)
Piperacillin- tazobactam	3 (100)	3 (100)	3 (100)	2 (100)

DISCUSSION

Antibiotic resistance is an emerging global threat due to the continuous changing pattern of causative organism of neonatal sepsis in different regions from time to time. For effective management of neonatal sepsis, the correct and timely identification of causative organism along with their drug sensitivity pattern is crucial.

The present study recorded a high incidence and case fatality of around quarter of the neonates admitted in the hospital with sepsis. An important finding of the study was predominance of early onset of sepsis, staphylococcus aureus as dominant pathogen causing neonatal sepsis, equal preponderance of gram negative and gram-positive organism, alarming degree of antimicrobial resistance to the commonly used antibiotics and high mortality among culture negative sepsis cases. In this study, it was observed that a high percentage of male and neonates with weight less than 2.5 kg were diagnosed with neonatal sepsis. A similar observation was made by Murthy et al in the study where male gender and low birth weight increased the odds of neonatal sepsis.⁷ In the current study more than half of the sample came out to be sterile. It can be justified as it is difficult to obtain adequate volume of blood in neonates and due to low level of bacteraemia among neonates.

The culture negative sepsis can also be attributed to poor microbiology lab support and mis handling of the sample from the point of origin to the point of utilization for investigations. The out born neonates from other institutes could have been administered antibiotics prior to referral rendering the sample culture negative. Most episodes (66%) of neonatal sepsis occurred at an early age (less than 72 hrs). This was in accordance to the study conducted by Chaurasia et al according to which 62% of the infections in South Asia occur in first 72 hrs of life.⁸ In the current study equal isolates of gram negative and gram positive pathogens were identified which was in contrast to the study conducted by Vishwanathan et al in tertiary care centres in eastern India and Agarwal et al in tertiary care centers of Delhi, according to which gram negative aetiology was predominant among neonates with sepsis.^{9,10} This could be attributed to limited sample size and small number of cases with culture positive results in the current study. The most common Gram-Positive organism in the present study was *Staphylococcus aureus* which was similar to the studies conducted Shrestha et al and Marwah et al.^{11,12} The high prevalence of resistance to cephalosporins in four Gram negative isolates (*Klebsiella spp.*, *Acinetobacter spp.*, *Citrobacter spp.* And *Pseudomonas*) make the choice of antibiotics extremely difficult. This finding of antibiotic resistance was consistent with the studies conducted by Li Grace et al according to which cephalosporin resistance rate among Gram negative ranged from 26% to 84% among 39 neonatal units from 12 countries.¹³ Having a comprehensive knowledge of clinical risk factors which

affect mortality is important as it can highlight diagnostic approaches which can prevent adverse outcomes.

Limitations

Due to unavailability of any online information at the tertiary health care center, the data for the study was collected through record sheets of discharged neonates, as a result of which only a small number of cases could be studied. Being a record based study, the timing when the blood culture and sensitivity was done could not be reported in spite of it being an important factor in determining the outcome of neonate. The drug sensitivity could not be generalized for all the organisms as testing against similar set of antibiotics was not performed due to unavailability of diffusion discs at all point of times.

CONCLUSION

In this study both Gram negative and Gram positive were equally distributed among the isolated organism for neonatal sepsis, hence the empirical therapy given should contain drugs that are effective against both the group of organisms and are sensitive to the anti- microbials. In order to provide better results of culture and sensitivity standard protocols should be followed from the point of sample collection, sample transportation to the point of laboratory investigation. This can help in avoiding negative culture sepsis resulting from inadequate samples and hence help in determining adequate treatment protocols that can prevent neonatal morbidity and mortality. Maintaining proper hygiene during delivery and by providing adequate treatment to the mothers in the intra- natal period can help in preventing early onset neonatal sepsis.

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