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Research Article

Clinical and Bacteriological Profile of Neonates on Ventilatory Support Suffering from Neonatal Sepsis in the Nicu of a Tertiary Care Teaching Hospital of Rural North India: a Cross-Sectional Observational Study

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ABSTRACT
Background: Neonatal sepsis remains a leading contributor to morbidity and mortality in neonatal intensive care units (NICUs), and the emergence of multidrug-resistant pathogens complicates timely empirical therapy. Data that integrate clinical risk factors with contemporary microbiological trends are essential for constructing evidence-based antibiotic policies, particularly for ventilated neonates who constitute a high-risk cohort.
Methods: We conducted a cross-sectional observational study (30 April 2023 – 30 October 2024) among 50 consecutive neonates on invasive mechanical ventilation with a positive sepsis screen admitted to the NICU of a rural tertiary-care teaching hospital in North India. Specimens (blood, urine, cerebrospinal fluid, endotracheal-tube tip, tracheobronchial aspirate, umbilical venous catheter tip) were cultured using standard techniques; isolates were identified and their antimicrobial susceptibilities determined by the turbidimetric method in accordance with CLSI guidelines. Demographic, perinatal and clinical variables were recorded prospectively. Associations between culture positivity and predefined risk factors were analysed using x^2 or Student's *t* test, as appropriate; $p < 0.05$ was considered significant.
Results: The cohort comprised 28 males (56 %) and 22 females; mean (±SD) birth weight was 2.31 ± 0.75 kg, with 58 % weighing < 2.5 kg and 56 % born pre-term. Early-onset sepsis (≤72 h of life) predominated (58 %). Twenty-one neonates (42 %) required ventilation within 72 h of admission. Overall culture-positivity was 38 % (19/50). *Klebsiella pneumoniae* and *Acinetobacter baumannii* (each 19 %) were the most frequent pathogens, followed by *Pseudomonas aeruginosa* (10 %). Blood was the commonest source (77 %), followed by endotracheal-tube tips (18 %). Tigecycline (20 % of isolates), colistin (16 %) and meropenem/vancomycin (12 %) displayed the highest in-vitro activity. Male sex, prematurity, low birth weight and maternal complications (prolonged rupture of membranes, gestational diabetes, hypertensive disorders) were independently associated with culture-proven sepsis ($p < 0.05$ for all).
Conclusions: Ventilated neonates in our rural NICU face a substantial burden of multidrug-resistant Gram-negative sepsis. Unit-specific surveillance data underscore the need to incorporate tigecycline or colistin into second-line empirical regimens while strengthening infection-control practices targeting pre-term, low-birth-weight male infants and mothers with obstetric complications.

Keywords: Neonatal Sepsis; Ventilatory Support; Antibiotic Resistance; Klebsiella Pneumoniae; Acinetobacter Baumannii; Rural India.

INTRODUCTION

Neonatal sepsis, meaning a systemic reaction to infection in infants ≤28 days, is a serious international health emergency. In high income countries, the rate is 1–4 per 1 000 live births, but rises to 49–170 per 1 000 in low and middle income countries, where deaths from the illness are common, at 24 % [1, 2]. Most often, EOS develops in the first 72 hours (or sometimes up to seven days according to some authorities)

and is passed to the infant from the mother. late onset sepsis (LOS) presents afterwards and is often a result of hospital infection [3]. With advances in caring for mothers and babies during birth, VLBW babies have greater survival rates., invasive procedures—particularly mechanical ventilation—have lengthened NICU stays and increased susceptibility to health-care-associated infections [4].

Diagnostic confirmation hinges on blood culture, yet its 48-h turnaround necessitates empiric antimicrobials started on clinical suspicion or a positive The assessment for sepsis covers Included in the study were C reactive protein, immature to total neutrophil ratio, total leucocyte count, absolute neutrophil count, and micro ESR [5]. More misuse of antibiotics is making AMR worse and could mean that traditional treatments like ampicillin plus gentamicin/cefotaxime do not work as effectively [6, 7]. Multidrug resistance in Gram negative bacilli, for example Klebsiella pneumoniae and Acinetobacter baumannii, is on the rise, and greater carbapenem resistance, is noted by recent Indian NICU surveillance [8].Empirical therapy must therefore be grounded in current, unit-specific epidemiology. Ventilated neonates represent a distinct subset: endotracheal intubation disrupts mucosal barriers, fosters colonisation and biofilm formation, and mandates broad-spectrum antibiotics when ventilator-associated pneumonia is suspected [4]. Yet there are scarce Indian data linking clinical determinants with contemporary microbiological patterns among ventilated neonates in rural NICUs.

Recognising this gap, we aimed to characterise (i) the demographic, perinatal and clinical profile; (ii) the aetiological spectrum and AMR pattern of culture-positive isolates; and (iii) the risk factors associated with culture-proven sepsis among neonates on invasive ventilation in the NICU of a rural tertiary-care teaching hospital in North India. Such data are vital for developing evidence-based antibiotic protocols and optimising stewardship and infection-control interventions.

MATERIALS AND METHODS

Study Design, Setting and Period

The study was an observational, cross sectional one carried out in the 20 bed level III NICU of MMIMSR, Mullana, Ambala, Haryana, India, between 30 April 2023 and 30 October 2024. Most of the people who use the institute come from rural and semi urban places in North India.

Participants

All consecutively admitted neonates who fulfilled both of the following criteria were enrolled: (i) positive sepsis screen (≥2 abnormal parameters among total leucocyte count $< 5\,000$ cells mm^{-3}, age-appropriate absolute neutrophil count, immature-to-total neutrophil ratio > 0.20, micro-ESR > 15 mm $1\,h^{-1}$, or positive C-reactive protein); and (ii) requirement of invasive mechanical ventilation for ≥24 h. Exclusion criteria comprised sepsis-screen-negative neonates, major congenital anomalies and refusal of informed consent.

Sample size was calculated using the single-population proportion formula $n = Z^2 \times P(1-P) / d^2$, anticipating a culture-positivity proportion of 35 % from regional data, 95 % confidence level ($Z = 1.96$) and 15 % precision, yielding $n \approx 45$; we enrolled 50 neonates.

Data Collection

Demographic (sex, birth weight, gestational age), perinatal (mode/place of delivery, obstetric complications) and clinical data (age at onset of symptoms, presenting features, ventilator parameters) were recorded on a pre-validated proforma. EOS was defined as sepsis onset ≤72 h of life; LOS as > 72 h.

Specimen Collection and Microbiological Analysis

Within 24 h of enrolment—or within 48 h for endotracheal-tube (ET) tips—specimens were aseptically obtained: blood (1 mL) for aerobic culture, urine (suprapubic aspiration or sterile catheter), cerebrospinal fluid (where clinically indicated), ET-tip, tracheobronchial aspirate and umbilical venous catheter (UVC) tip (if removed). The samples were grown on MacConkey, blood, and nutrient agar, nutrient and glucose broths, as well as Sabouraud dextrose agar for fungi. The organisms were detected with the use of standard biochemical methods.

The turbidimetric method was used to test antibiotic susceptibility and CLSI 2023 rules were used to assign results. MDR was reported if an organism resisted at least one medicine in three or more antibiotic classes.

Outcome Measures

Primary outcome: proportion of culture-positive sepsis. Secondary outcomes: distribution of pathogens and their antibiotic-susceptibility profiles; association of culture positivity with

sex, birth weight, gestation, mode of delivery and maternal complications.

Statistical Analysis

Microsoft® Excel was used to enter the data, and we analyzed them with SPSS® v20. For continuous variables, we gave the means and standard deviations (SD). We listed the cases for every category and worked out the percentages. The t test was applied to look for mean differences and the χ^2 (or Fisher's exact) test was used to look for proportion differences. $P < 0.05$ denoted statistical significance.

Ethical Considerations

The Institutional Ethics Committee (MMIMSR/IEC/2023/2558) allowed the study to be done. 30 April 2023). We got written informed consent from mothers or legal guardians.

RESULTS

Demographic and Perinatal Profile

Of 50 ventilated neonates, 28 were male (56 %) and 22 female (44 %). The mean birth weight was 2.31 ± 0.75 kg; 58 % were low-birth-weight (< 2.5 kg) and 24 % very-low-birth-weight (< 1.5 kg) (Table 1). Fifty-six per cent were pre-term (< 37 weeks) with a mean gestational age of 35.2 ± 2.8 weeks. Vaginal delivery accounted for 60 % and lower-segment caesarean section 40 %. Maternal complications were documented in 52 %, the commonest being gestational diabetes mellitus (GDM) and prolonged rupture of membranes (PROM) (each 10 %) (Table 2).

Clinical Presentation and Sepsis Screening

EOS was noted in 29 infants (58 %); LOS in 21 (42 %). Respiratory distress (56 %) was the predominant presentation, followed by poor feeding (50 %) and lethargy (44 %) (Table 3). Mean total leucocyte and absolute neutrophil counts were 3 923 ± 981 and 1 673 ± 434 cells mm^{-3}, respectively; median C-reactive protein was 38 mg L^{-1} (IQR 22–64).

Culture Yield and Pathogen Distribution

Nineteen neonates (38 %) yielded positive cultures from at least one site. Blood accounted for the majority (17/22 positive specimens; 77 %), followed by ET-tip (4, 18 %) and UVC-tip (1, 5 %) (Figure 1). *Klebsiella pneumoniae* and *Acinetobacter baumannii* were isolated in four cases each (19 %), with *Pseudomonas aeruginosa* isolated in two (10 %). Gram-positive isolates comprised *Staphylococcus aureus* (2, 10 %) and coagulase-negative *Staphylococcus* spp. (1, 5 %) (Figure 2).

Antimicrobial Susceptibility

Overall, 79 % of Gram-negative isolates were MDR. Tigecycline displayed the highest susceptibility (20 %), followed by colistin (16 %), vancomycin (12 % of Gram-positive isolates) and meropenem (12 %) (Figure 3). Resistance to third-generation cephalosporins exceeded 85 %.

Risk-Factor Analysis

Culture positivity was significantly higher among males (54 % vs 18 %; $\chi^2 = 6.54$; $p = 0.01$) (Table 4) and pre-term neonates (57 % vs 14 %; $\chi^2 = 9.90$; $p = 0.002$) (Table 5). Low-birth-weight (< 2.5 kg) infants were twice as likely to be culture-positive (OR 2.15, 95 % CI 1.01–4.63). Maternal complications conferred a four-fold increased risk (57.7 % vs 17 %; $\chi^2 = 7.86$; $p = 0.005$).

Tables

Table 1. Birth-Weight Distribution of Study Subjects (N = 50)

Birth-weight category	Frequency	Percentage
≤1.5 kg	12	24 %
> 1.5–2.5 kg	17	34 %
> 2.5 kg	21	42 %
Total / Mean ± SD	50	100 % / 2.31 ± 0.75 kg

Table 2. Maternal Complications Identified in the Cohort (N = 26)

Complication	n	%
Gestational diabetes mellitus	5	10.0
Prolonged rupture of membranes	5	10.0
Hypothyroidism	2	6.0
Pregnancy-induced hypertension	2	4.0
Pre-eclampsia	2	4.0
Others*	10	20.0

Total	26	52.0

Table 3. Presenting Symptoms in Ventilated Neonates with Sepsis (N = 50)

Symptom	**Frequency**	**Percentage**
Respiratory distress	28	56 %
Poor feeding	25	50 %
Lethargy	22	44 %
Convulsions	10	20 %
Vomiting	10	20 %
Cyanosis	8	16 %
Fever	7	14 %

Table 4. Association between Culture Positivity And Sex Of Neonates

Sex	**Culture-positive**	**Culture-negative**	**Total**	**χ^2 (df=1)**	***p* value**
Male (n = 28)	15 (53.6 %)	13 (46.4 %)	28	**6.54**	**0.010**
Female (n = 22)	4 (18.2 %)	18 (81.8 %)	22		

Table 5. Association between Culture Positivity And Gestational Age

Gestation	**Culture-positive**	**Culture-negative**	**Total**	**χ^2 (df=1)**	***p* value**
Pre-term (< 37 weeks, n = 28)	16 (57.1 %)	12 (42.9 %)	28	**9.90**	**0.002**
Term (n = 22)	3 (13.6 %)	19 (86.4 %)	22		

Figures

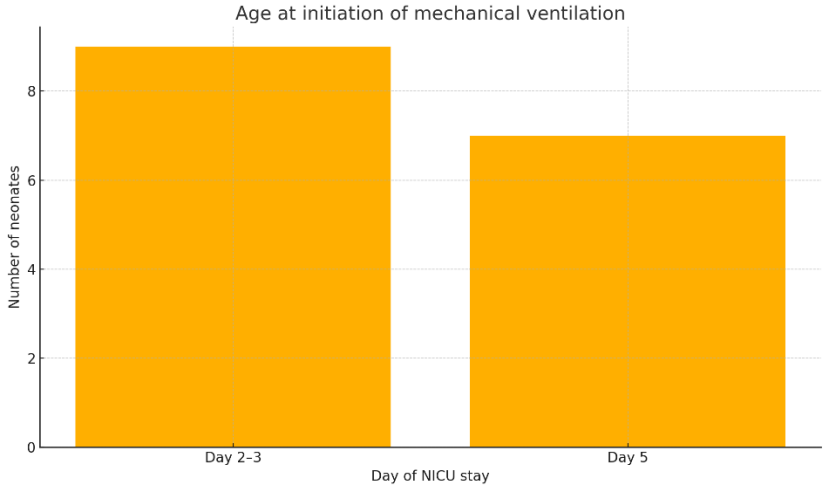

Figure 1. Age at initiation of mechanical ventilation among study neonates.

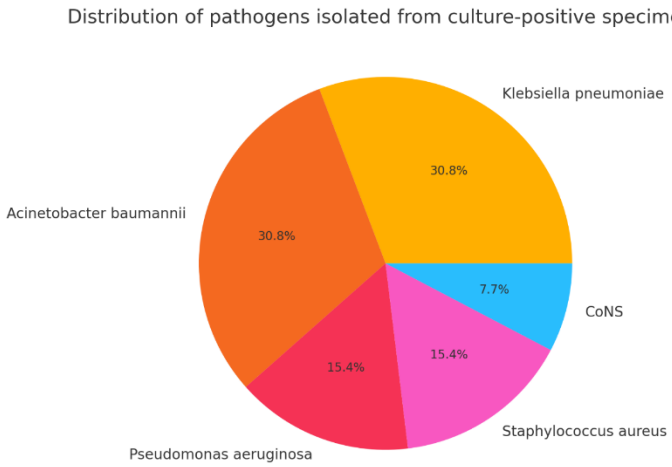

Figure 2. Distribution of pathogens isolated from culture-positive specimens.

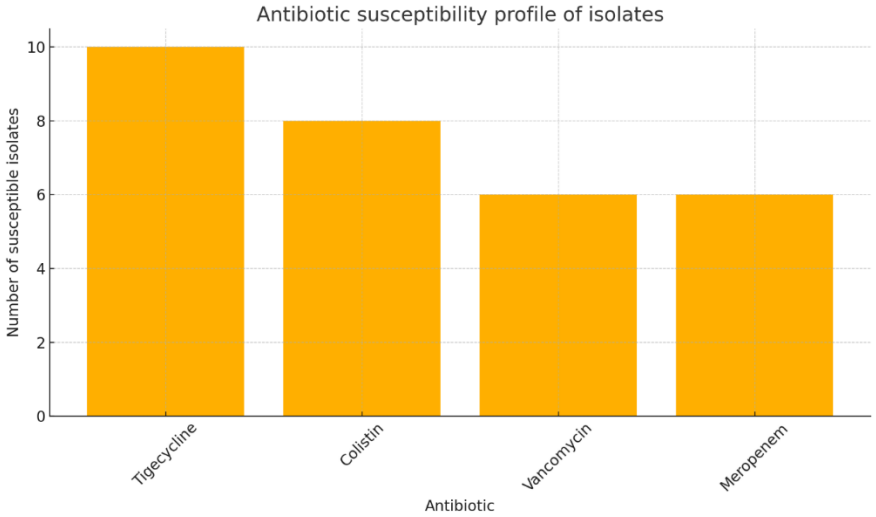

Figure 3. Antibiotic-susceptibility profile of isolated pathogens.

DISCUSSION

Our study documents a 38 % culture-positivity rate among ventilated neonates with sepsis-screen positivity—higher than reports from Nepal (10.8 %) [21] and Botswana (9.8 %) [31] but comparable to Indian series (16–54 %) [18, 24]. The elevated yield may reflect strict aseptic sampling before initiation of second-line antibiotics and inclusion of ET-tip cultures which improve detection of airway colonisation.

Consistent with earlier Indian and Ugandan NICU reports [16, 24, 33], MDR Gram-negative bacilli dominated the aetiological spectrum, led by *K. pneumoniae* and *A. baumannii*. Their resilience in humid hospital environments, biofilm-forming capacity and selective pressure from empirical cephalosporins underpin this predominance [35]. The alarming prevalence of carbapenem-resistant isolates (>80 %) echoes national AMR trends and mandates reconsideration of last-resort agents such as colistin and tigecycline [17, 20]. While tigecycline demonstrated the highest in-vitro susceptibility, paediatric pharmacokinetic data remain limited; cautious, weight-based dosing and therapeutic drug monitoring are advisable pending further trials.

Male sex, prematurity and low birth weight emerged as independent risk factors for culture-proven sepsis, corroborating data from Nepal [22], Nigeria [25] and South India [33]. The immunological vulnerability of male neonates—attributed to X-chromosome-linked immune-regulatory genes—may partly explain the sex disparity [23]. Pre-term gut dysbiosis, immature skin–mucosal barriers and frequent invasive procedures increase colonisation by MDR organisms, translating into higher sepsis rates [36]. Obstetric complications, notably PROM and GDM, quadrupled sepsis risk; ascending infections and metabolic derangements may predispose to intra-uterine and peripartum bacterial transmission.

Our findings inform empiric antibiotic policy. Given predominant MDR Gram-negatives, empirical coverage with piperacillin–tazobactam plus amikacin may be inadequate; the addition of a colistin- or tigecycline-based regimen could improve early target-match while awaiting cultures. However, antibiotic stewardship principles dictate periodic de-escalation according to sensitivities, alongside robust infection-control strategies—hand hygiene, ventilator-bundle compliance, cohorting of colonised infants and periodic environmental surveillance [8, 14].

Limitations include the single-centre design, modest sample size and lack of genotypic resistance profiling. The observational nature precludes causal inferences. Nevertheless, the prospective design, inclusion of multiple specimen types and rigorous CLSI-compliant susceptibility testing underpin the study's internal validity.

Future research should incorporate multi-centre networks, whole-genome sequencing to delineate resistance determinants, and pharmacodynamic modelling of newer antibiotics in neonates.

CONCLUSION

Ventilated neonates in our rural NICU bear a significant burden of MDR Gram-negative

sepsis, predominantly due to *Klebsiella pneumoniae* and *Acinetobacter baumannii*. Male sex, prematurity, low birth weight and maternal obstetric complications markedly increase the likelihood of culture-proven infection. Tigecycline and colistin retain the greatest in-vitro activity and warrant consideration in second-line empiric regimens, pending culture results. Continuous, unit-specific surveillance and stringent infection-control measures are paramount to curbing neonatal sepsis mortality and mitigating antimicrobial resistance.

Declarations

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Conflicts of interest: None declared.

Ethical Approval: Institutional Ethics Committee approval obtained (MMIMSR/IEC/2023/2558, 30 April 2023). Informed consent was secured from parents/guardians.

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