

Concordance with CDC criteria and antibiotic prescribing for suspected ventilator-associated pneumonia in a neonatal intensive care unit: a retrospective audit

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Abstract

Background

Ventilator-associated pneumonia (VAP) is difficult to diagnose in neonates because clinical, radiological and microbiological findings are non-specific and no universally accepted neonatal gold standard exists. Diagnostic uncertainty may contribute to avoidable antimicrobial exposure.

Objective

To determine the proportion of mechanically ventilated neonates treated for suspected VAP who met Centers for Disease Control and Prevention (CDC) criteria, and to describe antibiotic prescribing, clinical findings and post-treatment respiratory change.

Methods

A retrospective audit was conducted using records from 1 January 2016 to 1 May 2020. Neonates were eligible if they were mechanically ventilated for at least 48 hours and received antibiotics for a suspected lower respiratory tract infection. Recorded clinical, radiological and laboratory findings were assessed against CDC criteria for infants aged 1 year or younger. Antibiotic regimens, organisms identified and respiratory status following treatment were described.

Results

Forty neonates were included; 23 (57.5%) met the applied CDC criteria. Piperacillin-tazobactam was the most frequently prescribed regimen (20/40, 50.0%); 11 of these 20 cases met CDC criteria. Post-treatment respiratory information was available for 38 neonates, of whom 29 (76.3%) had reduced respiratory support requirements or improved oxygenation. Meeting CDC criteria was associated with documented added breath sounds, leukopenia or leukocytosis, and apnoea or tachypnoea.

Conclusions

Just over half of the neonates treated for suspected VAP met the CDC criteria, highlighting the challenges of diagnosing neonatal VAP. These findings suggest that diagnostic uncertainty remains a significant issue and may influence treatment decisions. More accurate diagnostic approaches are needed to support antimicrobial stewardship, optimise antibiotic use and minimise unnecessary antimicrobial exposure in neonates.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is a healthcare-associated lower respiratory tract infection that develops during invasive mechanical ventilation, typically after at least 48 hours of ventilation.(1–3) Intubation impairs mucociliary clearance and cough, facilitates aspiration of contaminated secretions, and provides a surface for bacterial colonisation and biofilm formation.(4) These factors increase susceptibility to lower respiratory tract infection during mechanical ventilation. Neonates are particularly vulnerable to healthcare-associated infection because of their immature immune systems and frequent requirement for prolonged respiratory support.(5) Ventilator-associated pneumonia (VAP) has been associated with increased morbidity, mortality and length of hospital stay, although reported incidence varies substantially across settings and according to the diagnostic criteria used.

Diagnosis is particularly challenging in neonates. Radiographic abnormalities, worsening gas exchange, increased secretions, temperature instability and altered white cell counts may occur in association with VAP but can also occur because of prematurity, evolving lung disease, atelectasis or other systemic infection. Multiple diagnostic definitions have therefore been proposed. The most widely used is the Centers for Disease Control and Prevention (CDC) criteria for infants aged one year or younger, which combines radiological, respiratory and clinical findings.(6) However, these criteria were developed primarily for surveillance rather than as a validated neonatal diagnostic gold standard. Contemporary reviews continue to highlight inconsistent definitions, poor agreement between diagnostic frameworks and limited neonatal-specific evidence.(2, 3, 7)

Diagnostic uncertainty has important antimicrobial stewardship implications. Clinicians must balance the risks of delayed treatment of genuine infection against the harms of unnecessary broad-spectrum antibiotic exposure. Excessive antimicrobial use contributes to antimicrobial resistance and may expose neonates to avoidable adverse effects, while undertreatment risks progression of severe infection. Early and excessive antimicrobial exposure has been associated with important adverse consequences, while delayed or inadequate treatment of genuine infection may increase morbidity and mortality.(8, 9) Despite the importance of this issue, neonatal-specific guidance remains limited and management practices vary between institutions. Previous quality-improvement studies have demonstrated substantial differences between suspected and confirmed VAP episodes depending on the diagnostic framework applied, together with poor inter-rater agreement in interpretation of chest radiographs.(7)

This audit therefore aimed to determine the proportion of mechanically ventilated neonates treated for suspected VAP who met the CDC criteria applied at the time of the study; describe antibiotic prescribing and organisms identified; examine clinical features associated with meeting the criteria; and describe respiratory status following antibiotic treatment. The study was designed as a criterion-concordance and antimicrobial stewardship audit rather than a validation study of the CDC criteria or an evaluation of antibiotic effectiveness.

METHODS

Design and setting

A retrospective chart audit was conducted in a tertiary neonatal intensive care unit in Brisbane, Australia. Records from 1 January 2016 to 1 May 2020 were reviewed.

Participants

Neonates were eligible if they were younger than 1-month corrected age, had received invasive mechanical ventilation for at least 48 hours, and were treated with antibiotics for a suspected lower respiratory tract infection or VAP. When antibiotics were prescribed more than once during one episode of ventilation, only the first episode was included.

Data collection and definitions

Demographic information including gestational age at birth, chronological age, sex and birth weight was extracted from the medical record. Respiratory, radiological, laboratory, microbiological and medication data relating to the episode of suspected VAP were collected. Chest radiograph reports, documented clinical signs and symptoms, laboratory findings, microbiological results, antibiotic prescribing and respiratory support requirements were recorded. Cases were assessed retrospectively against the Centers for Disease Control and Prevention (CDC) criteria for pneumonia in infants aged one year or younger that were current at the time of the audit. These criteria require specified radiological findings, evidence of worsening gas exchange and a defined combination of clinical and laboratory features. Throughout this manuscript, the terms 'met CDC criteria' and 'did not meet CDC criteria' are used to describe concordance with the surveillance framework.

Respiratory status at the time of suspected VAP and following completion of antibiotic treatment was recorded descriptively. Improvement was defined a priori as reduced respiratory support requirements or improved oxygenation following treatment. Because respiratory management continued concurrently and no untreated comparator group was available, subsequent respiratory change cannot be attributed to antibiotic therapy.

CDC criteria for infants aged one year or younger

The CDC criteria for pneumonia in infants aged one year or younger were used as the audit framework. These criteria require radiological evidence of new or progressive infiltrate, consolidation, cavitation or pneumatoceles, together with worsening gas exchange and at least three of the following clinical or laboratory features:

- temperature instability
- leukopenia ($\leq 4,000$ cells/mm³) or leukocytosis ($> 15,000$ cells/mm³) with left shift ($> 10\%$ band forms)

- new onset of purulent sputum, change in sputum character, increased respiratory secretions or increased suctioning requirements
- apnoea, tachypnoea, nasal flaring, chest wall retractions or grunting
- wheezing, crackles or other added breath sounds
- bradycardia (< 100 beats/minute) or tachycardia (> 170 beats/minute)
- cough

Cases meeting all required components were classified as having met the CDC criteria. The CDC criteria were used as a surveillance and audit framework only and not as a validated neonatal diagnostic gold standard.

Ethics

The activity was deemed compliant with the National Health and Medical Research Council Guidance Ethical Considerations in Quality Assurance and Evaluation Activities (2014) by the Mater Human Research Ethics Committee (HREC/MML/59159). Individual informed consent was not required.

Statistical analysis

Continuous variables were summarised using means and standard deviations, and categorical variables using counts and percentages. Between-group comparisons used independent-samples tests as appropriate. Associations between categorical variables and meeting CDC criteria were examined using two-sided Fisher exact tests. Statistical significance was set at $p < 0.05$. Analyses were conducted using IBM SPSS Statistics, version 25.

RESULTS

Cohort characteristics and concordance with CDC criteria

Forty-two potentially eligible records were identified; two were excluded because documentation was insufficient to assess the presenting features, leaving 40 cases for analysis.

Of 40 included neonates, 23 (57.5%) met the applied CDC criteria and 17 (42.5%) did not. There were no statistically significant differences between groups in gestational age at birth, chronological age, birth weight, duration of ventilation or duration of the antibiotic course (Table 1). Although 19 of 23 neonates meeting CDC criteria were male, sex was not significantly associated with meeting the criteria ($p = 0.46$).

Table 1
Characteristics according to concordance with the applied CDC criteria.

Characteristic	Did not meet criteria (n = 17)	Met criteria (n = 23)	Effect estimate (Mean difference)	95% CI	p value
Gestational age, weeks, mean (SD)	26.80 (4.29)	25.59 (1.93)	1.21	-0.83 to 3.25	0.24
Chronological age, weeks, mean (SD)	4.53 (2.98)	4.09 (2.42)	0.44	-1.29 to 2.17	0.61
Birth weight, g, mean (SD)	946.82 (484.19)	811.43 (183.45)	135.39	-87.22 to 358.00	0.23
Ventilation duration, days, mean (SD)	17.47 (15.06)	15.96 (14.98)	1.51	-8.21 to 11.24	0.75
Antibiotic course, days, mean (SD)	6.88 (5.15)	9.13 (9.84)	2.26	-7.71 to 3.20	0.41
Male, n (%)	12 (70.5)	19 (82.6)			0.46

Recorded components of the CDC framework

Chest radiograph abnormalities and worsening gas exchange were documented in all cases because they formed part of the clinical rationale for suspected VAP and were prerequisites for application of the CDC framework.

Documented added breath sounds, leukopenia or leukocytosis, and apnoea or tachypnoea were associated with meeting the applied CDC criteria. Increased secretions, heart-rate abnormality and temperature instability were not statistically associated. No cough was documented (Table 2).

Table 2
Recorded components of the CDC Framework

Recorded feature	Did not meet, n	Met, n	p value
Added breath sounds	1	15	< 0.001
Leukopenia/leukocytosis	2	12	0.017
Apnoea/tachypnoea	2	10	0.041
Increased secretions	12	22	0.067
Bradycardia/tachycardia	10	14	1.000
Temperature instability	4	11	0.187
Cough	0	0	Not tested

Antibiotic prescribing and respiratory change

Piperacillin-tazobactam was prescribed in 20 cases (50.0%), including 11 that met CDC criteria. Nine neonates received piperacillin-tazobactam plus meropenem, seven received flucloxacillin, three received meropenem and one received gentamicin.(Table 3) Respiratory outcome information was available for 38 neonates, as post-treatment respiratory data were unavailable for two cases. Of the 38 neonates with follow-up data, 29 (76.3%) had improved oxygenation or reduced respiratory support following treatment.

Table 3
Antibiotic prescribing, CDC-criteria concordance and descriptive respiratory outcome.

Antibiotic regimen	All cases, n (%)	Met criteria, n	Did not meet, n	Outcome available, n	Respiratory improvement, n (%)
Piperacillin-tazobactam	20 (50.0)	11	9	19	13 (68.4)
Piperacillin-tazobactam + meropenem	9 (22.5)	7	2	9	7 (77.8)
Flucloxacillin	7 (17.5)	3	4	7	6 (85.7)
Meropenem	3 (7.5)	2	1	2	2 (100)
Gentamicin	1 (2.5)	0	1	1	1 (100)
Total	40 (100)	23	17	38	29 (76.3)

Microbiology

The most frequently identified organisms were *Klebsiella* species (12/40, 30.0%), *Enterobacter cloacae* (6/40, 15.0%) and *Staphylococcus aureus* (6/40, 15.0%).(Table 4) Four cases had no organism identified, including two that met CDC criteria. One neonate had both *Klebsiella* and *Enterobacter cloacae* identified in airway culture but did not meet the CDC criteria. Organisms recovered from airway specimens may represent colonisation rather than invasive infection; the audit could not reliably distinguish these states.

Table 4
Organisms identified and descriptive respiratory outcome.

Organism	All cases, n (%)	Met criteria, n	Respiratory outcome available, n	Improved, n
Klebsiella species	12 (30.0)	7	12	9
Enterobacter cloacae	6 (15.0)	5	6	6
Staphylococcus aureus	6 (15.0)	2	5	5
No organism identified	4 (10.0)	2	4	2
Pseudomonas aeruginosa	3 (7.5)	2	2	1
Klebsiella + Pseudomonas	2 (5.0)	2	2	1
Other organisms or mixed flora	7 (17.5)	3	7	4

DISCUSSION

This audit found that 23 of 40 neonates treated for suspected VAP met the applied CDC criteria. The central finding is discordance between bedside treatment decisions and a commonly used surveillance framework, not evidence that 17 infants were necessarily misdiagnosed or treated inappropriately. The CDC framework is not a neonatal gold standard, and clinical decisions may have incorporated information that was incompletely documented or not represented in the criteria.

The finding aligns with the wider literature describing uncertain neonatal VAP definitions. Similar discordance between suspected and confirmed VAP episodes has been reported elsewhere. Goerens and colleagues reported substantial differences between clinically suspected and framework-defined VAP episodes, highlighting how estimates vary according to the diagnostic approach used.⁽⁷⁾ Differences between studies likely reflect variation in diagnostic frameworks, local practice and the absence of a validated neonatal reference standard. More recent reviews continue to identify diagnostic ambiguity, variable incidence estimates and persistent gaps in neonatal-specific evidence. These limitations make both clinical diagnosis and audit classification difficult.

Several individual findings were associated with meeting CDC criteria, but this largely reflects their role within the composite definition. Added breath sounds and altered white cell counts may support concern for infection but are not specific to VAP.⁽¹⁰⁾ Interpretation of apnoea is particularly challenging in preterm infants because it may reflect prematurity, evolving respiratory disease, medication exposure or infection. The absence of an association between increased secretions and meeting CDC criteria may reflect the subjective and inconsistently documented nature of secretion assessment in routine clinical records.

Likewise, absent documentation does not necessarily indicate that a sign was absent. These findings should therefore inform better documentation and structured assessment rather than selection of isolated diagnostic markers.

Respiratory improvement was documented after treatment in 29 of 38 cases with available follow-up data, including infants who did not meet the CDC criteria. This observation cannot establish treatment benefit. Improvement may reflect antimicrobial treatment of VAP or another infection, concurrent respiratory management, natural recovery or limitations of the surveillance definition. Equally, positive airway cultures may reflect endotracheal colonisation or biofilm rather than lower respiratory infection. (11, 12)

The predominance of *Klebsiella*, *Enterobacter cloacae* and *Staphylococcus aureus* in this cohort is broadly consistent with previous reports of neonatal VAP microbiology, where gram-negative organisms frequently predominate.(13) Airway colonisation and biofilm formation on endotracheal tubes are common in mechanically ventilated neonates and may complicate interpretation of culture results.(11, 12) Consequently, positive cultures should be interpreted as one component of the diagnostic assessment rather than definitive evidence of lower respiratory tract infection.

From a stewardship perspective, the findings support a structured process for suspected neonatal VAP consisting of prospective documentation of the diagnostic features considered, review of radiology and microbiology, use of local resistance patterns for empiric therapy, and reassessment of treatment decisions as additional information becomes available. Contemporary reviews recommend prevention bundles and regular assessment of extubation readiness, while acknowledging that the evidence base remains limited.(8, 9, 14)

STRENGTHS AND LIMITATIONS

The audit provides detailed clinical, microbiological and prescribing data from a large tertiary NICU and addresses an important stewardship problem. However, it was retrospective, single-centre and included only 40 treatment episodes. Documentation was incomplete or non-standardised, and two potentially eligible records could not be classified. The denominator of all ventilated infants was unavailable, so VAP incidence per 1,000 ventilator-days could not be calculated. The CDC criteria were used as an audit framework rather than a validated neonatal reference standard. Chest radiographs were not independently re-read, microbiological sampling was not standardised, and colonisation could not be reliably distinguished from infection. Antibiotic indication, timing, dose, de-escalation and duration were not assessed in sufficient detail to determine prescribing appropriateness. Finally, post-treatment respiratory change was uncontrolled and cannot be attributed to antibiotics.

CONCLUSION

Diagnosing neonatal VAP remains challenging, reflecting the limitations of currently available diagnostic frameworks and the complexity of this population. More accurate and clinically applicable diagnostic

approaches are needed to support treatment decisions, strengthen antimicrobial stewardship and minimise unnecessary antimicrobial exposure in neonates.

Declarations

The activity was deemed compliant with the National Health and Medical Research Council Guidance Ethical Considerations in Quality Assurance and Evaluation Activities (2014) by the Mater Human Research Ethics Committee (HREC/MML/59159). Individual informed consent was not required.

Ethics approval

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Consent for publication

All authors consent to publication of this manuscript.

Competing interests

The authors declare no competing interests. Judith Hough, Sihle Bhebhe and Luke Jardine were employed by the organisation in which the audit was conducted.

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Data availability

Deidentified audit data may be available from the corresponding author on reasonable request, subject to institutional and ethical requirements.

Author contributions

JH and LJ conceived and designed the project. JH and SB obtained governance approval. SB collected the data. JH, MS and SB collated and analysed the data. JH and SB prepared the original manuscript. All authors reviewed the revised manuscript and approved the version submitted as a preprint.

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