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Original research

CLINICAL AND LABORATORY CHARACTERISTICS AND RISK FACTORS OF LATE-ONSET NEONATAL INFECTION: A CROSS-SECTIONAL STUDY AT HUE CENTRAL HOSPITAL

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ABSTRACT

Background: *Late-onset neonatal infection (LONI) remains a leading cause of neonatal morbidity and mortality, especially in developing countries. Despite advances in neonatal care, its diagnosis and management continue to be challenging due to non-specific clinical manifestations. This study aims to describe the clinical and laboratory characteristics and identify risk factors associated with late-onset neonatal infection in hospitalized newborns.*

Methods: *A cross-sectional descriptive study was conducted on 166 neonates diagnosed with late-onset infection admitted to the Department of Neonatal Intensive Care - Center for Pediatrics, Hue Central Hospital, from May 2022 to June 2024. Demographic, clinical, laboratory, and microbiological data were collected. Statistical analysis was performed using SPSS 22.0, with chi-square and Fisher's exact tests to determine associations ($p < 0.05$ considered significant).*

Results: *The study included 56.6% males and 84.9% term newborns. Pneumonia was the most common clinical presentation (50.6%), followed by sepsis (13.9%), omphalitis (10.2%), and gastrointestinal infection (10.2%). Fever (56.6%) and poor feeding (75.3%) were the most frequent symptoms. Elevated CRP was observed in 16.3% of patients, while positive blood cultures were found in 3.7%. Staphylococcus aureus (including MRSA) was the predominant isolate from pus and umbilical samples. Exclusive breastfeeding reduced the risk of sepsis (OR = 0.14, $p < 0.05$). Contact with respiratory infections and frequent milk aspiration increased the risk of pneumonia (OR = 3.9 and 1.9, respectively). Improper umbilical care tripled the risk of skin and umbilical infections (OR = 3.46, $p < 0.05$).*

Conclusions: *Late-onset neonatal infection commonly presents as pneumonia or sepsis. Exclusive breastfeeding and proper postnatal care significantly reduce infection risk, whereas exposure to respiratory infections and poor feeding practices increase vulnerability. Strengthening caregiver education and infection control can improve neonatal outcomes.*

Keywords: *Late-onset neonatal infection, sepsis, pneumonia, risk factors, neonatal care, Vietnam.*

I. INTRODUCTION

Neonatal infection remains a major global health challenge, accounting for a substantial proportion of neonatal mortality. According to the World Health Organization (WHO, 2024), approximately 2.3 million neonates die each year, representing nearly half of all under-five deaths [1]. Among these, preventable causes-particularly infections-remain dominant. In developing countries, sepsis, pneumonia, and omphalitis are the leading infectious causes of neonatal deaths [2].

Late-onset neonatal infection (LONI), defined as infection occurring after 72 hours of life, differs from early-onset sepsis in its etiology, risk factors, and preventive measures. While early-onset infections are often maternally transmitted, late-onset cases frequently arise from environmental or hospital-acquired sources [3,4]. These infections can present

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as sepsis, pneumonia, meningitis, or localized infections such as omphalitis or skin abscesses [5].

In Vietnam, neonatal infections remain a significant contributor to morbidity and mortality in neonatal intensive care units (NICUs). Previous local studies reported that neonatal infections account for up to 17 - 51% of neonatal deaths [6,7]. However, limited data exist regarding late-onset infections and their associated risk factors in Vietnamese newborns, particularly in the central region [8].

This study aimed to (1) describe the clinical and laboratory features of late-onset neonatal infection and (2) analyze potential risk factors among neonates admitted to Hue Central Hospital.

II. MATERIALS AND METHODS

2.1. Study design and setting

A cross-sectional descriptive study was conducted at the Department of Neonatal Intensive Care - Center for Pediatrics, Hue Central Hospital, from May 2022 to June 2024.

2.2. Study population

A total of 166 neonates diagnosed with late-onset neonatal infection (onset > 72 hours after birth) were included.

Inclusion criteria: Age ≤ 28 days (term) or corrected age within the neonatal period (preterm); Clinical signs suggestive of infection with or without laboratory confirmation.

Exclusion criteria: Hospital-acquired infections after > 48 hours of prior hospitalization; Early-onset neonatal infections (< 72 hours).

2.3. Data collection

Demographic, perinatal, and postnatal data were collected through structured questionnaires and medical records. Laboratory results included blood counts, CRP, glucose, electrolytes, and culture outcomes (blood, pus, umbilical, stool, and CSF). Radiographic findings were reviewed by pediatric radiologists.

2.4. Statistical analysis

Data were analyzed using SPSS version 22.0. Qualitative variables were presented as frequencies and percentages; quantitative data as mean ± SD or median (IQR). Associations between categorical variables were tested by Chi-square or Fisher's exact tests. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated, with $p < 0.05$ considered statistically significant.

2.5. Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of Hue Central Hospital. Written informed consent was obtained from all parents or guardians prior to participation.

III. RESULTS

3.1. Demographic and nutritional characteristics

The baseline characteristics of 166 neonates are summarized in Table 1. The majority were male (56.6%), term (84.9%), and from rural areas (63.3%). Cesarean section accounted for 54.2% of deliveries, and 10.8% were of low birth weight. Exclusive breastfeeding was reported in 35.5% of infants, while 63.3% received mixed feeding.

Table 1: General characteristics of the study population

Characteristic	n (%)
Male sex	94 (56.6)
Term neonates	141 (84.9)
Rural residence	105 (63.3)
Cesarean section	90 (54.2)
Low birth weight (<2,500 g)	18 (10.8)
Exclusive breastfeeding	59 (35.5)

3.2. Clinical manifestations

Table 2 shows that pneumonia was the most common clinical presentation (50.6%), followed by sepsis (13.9%), omphalitis (10.2%), and gastrointestinal infections (10.2%). The most frequent symptoms were poor feeding (75.3%), fever (56.6%), and tachypnea (62.7%).

Table 2: Clinical forms of late-onset neonatal infection

Clinical Type	n (%)
Pneumonia	84 (50.6)
Sepsis	23 (13.9)
Omphalitis	17 (10.2)
Gastrointestinal infection	17 (10.2)
Skin/soft tissue abscess	17 (10.2)
Otitis media	6 (3.6)
Conjunctivitis	2 (1.2)

3.3. Laboratory findings

As presented in Table 3, elevated CRP was detected in 16.3% of cases, leukocytosis in 7.2%, and anemia in 49.4%. Only 3.7% of blood cultures were positive, with Staphylococcus aureus (including MRSA) and Pseudomonas aeruginosa identified as the main pathogens. Meanwhile, S. aureus was dominant in pus and umbilical cultures (91.2%).

Table 3: Laboratory results of infected neonates

Parameter	Abnormal (%)	Main findings
Leukocytosis	7.2	WBC > 20 × 10^9/L
Anemia	49.4	Hb < 13.5 g/dL
CRP elevated	16.3	Mostly mild to moderate
Positive blood culture	3.7	S. aureus, MRSA, P. aeruginosa
Positive pus/umbilical culture	91.2	S. aureus (dominant)

3.4. Risk factors

Several perinatal and postnatal factors were analyzed to determine their association with different infection types (Table 4 and Table 5).

Table 4 presents risk factors associated with sepsis in neonates. Exclusive breastfeeding significantly reduced the risk of sepsis (OR = 0.14; 95% CI: 0.03 - 0.64; p = 0.012). Low birth weight and premature rupture of membranes showed a higher, though not statistically significant, association with sepsis. Table 5 summarizes risk factors related to pneumonia and umbilical/skin infections. Contact with individuals having respiratory illness increased the odds of pneumonia nearly fourfold (OR = 3.9; 95% CI: 1.99 - 7.68; p = 0.001). Frequent milk aspiration also doubled the risk (OR = 1.9; 95% CI: 1.03 - 3.5; p = 0.041). Improper umbilical care tripled the risk of omphalitis and skin infections (OR = 3.46; 95% CI: 1.58 - 7.50; p = 0.002).

Table 4: Risk factors associated with late-onset neonatal sepsis

Variable	Sepsis (n=23)	Non-sepsis (n=143)	OR (95% CI)	p-value
Male sex	15 (65.2%)	79 (55.2%)	1.54 (0.62 - 3.84)	0.36
Low birth weight (<2500g)	5 (21.7%)	13 (9.1%)	2.80 (0.87 - 8.96)	0.09
Premature rupture of membranes	6 (26.1%)	19 (13.3%)	2.29 (0.80 - 6.60)	0.12
Exclusive breastfeeding	2 (8.7%)	57 (39.9%)	0.14 (0.03 - 0.64)	0.012
Cesarean delivery	14 (60.9%)	76 (53.1%)	1.36 (0.56 - 3.29)	0.49

Table 5: Risk factors associated with pneumonia and umbilical/skin infections

Risk factor	Pneumonia (n=84)	Non-pneumonia (n=82)	OR (95% CI)	p-value
Contact with respiratory illness	47 (56.0%)	20 (24.4%)	3.9 (1.99 - 7.68)	0.001
Frequent milk aspiration	33 (39.3%)	19 (23.2%)	1.9 (1.03 - 3.50)	0.041
Improper umbilical care	38 (45.2%)	14 (17.1%)	3.46 (1.58 - 7.50)	0.002
Formula feeding	31 (36.9%)	18 (22.0%)	1.96 (0.99 - 3.88)	0.053
Rural residence	53 (63.1%)	52 (63.4%)	0.99 (0.52 - 1.90)	0.98

IV. Discussion

This study investigated the clinical and laboratory characteristics and risk factors of late-onset neonatal infection (LONI) in a tertiary care hospital in Central Vietnam. The findings revealed that pneumonia and sepsis were the predominant clinical forms, with Staphylococcus aureus as the leading pathogen. These results are consistent with those reported in similar studies in both Vietnam and other developing countries [6-9].

The predominance of pneumonia (50.6%) and sepsis (13.9%) among infected neonates highlights the high burden of respiratory infections in hospitalized newborns [5,7]. This aligns with findings from Trinh et al. (2023), where pneumonia and sepsis accounted for more than two-thirds of LONI cases [8]. The frequency of omphalitis and skin infections (around 10%) also aligns with findings from Nepal and Bangladesh, emphasizing the continuing importance of hygienic cord care [9].

Male predominance (56.6%) in our cohort was similar to that reported by Coggins and Glaser [3] and may reflect gender-related biological vulnerability. The majority of term neonates and those with normal birth weight suggest that late-onset infections are not limited to premature or low-birth-weight infants, as previously emphasized in global data [1,2].

CRP elevation was found in 16.3% of patients, a lower rate than expected. This may be due to early empirical antibiotic use or mild infection severity at presentation. Although CRP is widely used as a biomarker for neonatal sepsis, its sensitivity varies from 43% to 81%, and false negatives are common in localized or early-stage infections [4,5].

Only 3.7% of blood cultures were positive, reflecting diagnostic limitations where prior antibiotic exposure and low-volume sampling reduce yield [3,4]. Despite this, Staphylococcus aureus, including MRSA strains, remained the predominant pathogen, consistent with prior Vietnamese and regional studies [6-8]. Similar to reports from India and Brazil, S. aureus continues to dominate in both community and hospital-acquired infections, emphasizing the need for infection control and rational antibiotic use [4,5].

Exclusive breastfeeding was strongly protective against sepsis, consistent with evidence that breast milk provides antimicrobial, anti-inflammatory, and immunomodulatory benefits [9,10]. Conversely, exposure to individuals with respiratory infections significantly increased pneumonia risk, as shown by Mullany et al. [9]. Frequent milk aspiration doubled the risk of respiratory infection, highlighting the need for caregiver education on safe feeding practices [10]. Improper umbilical care also tripled the risk of omphalitis and skin infections, echoing studies recommending dry cord care or chlorhexidine use [9,10].

Our results agree with prior Vietnamese work at Hue Central Hospital and Thai Nguyen Central Hospital [6-8]. These patterns suggest that, despite advances, late-onset infections in Vietnam remain dominated by Gram-positive organisms, especially S. aureus [7,8]. Broader antibiotic stewardship and infection control audits are needed to reduce MRSA colonization and nosocomial transmission [3,4,5].

Analysis of risk factors (Tables 4 and 5) revealed several modifiable contributors to late-onset neonatal infection. Exclusive breastfeeding markedly reduced sepsis risk (OR = 0.14), reinforcing the well-established immunological benefits of breast milk through immunoglobulins, lactoferrin, and oligosaccharides that inhibit bacterial adhesion. Conversely, low birth weight and premature rupture of membranes showed elevated, though statistically nonsignificant, associations-similar to findings by Procianoy et al. [2] and Coggins et al. [3].

Environmental factors were equally critical. Table 5 demonstrates that contact with infected caregivers increased pneumonia risk fourfold, in line with Mullany et al. [9], who highlighted the role of household transmission in neonatal respiratory infections. Improper feeding leading to milk aspiration nearly doubled the risk, a finding also reported in developing countries where bottle-feeding hygiene is suboptimal. Furthermore, poor umbilical care tripled the risk of localized infection, echoing WHO and Nepalese community-based studies recommending dry cord care and chlorhexidine application [1].

Collectively, the results (Tables 4-5) emphasize that late-onset neonatal infection is largely preventable through simple, low-cost interventions: exclusive breastfeeding, strict hygiene, and caregiver education. Implementing these measures can significantly reduce neonatal morbidity and mortality, particularly in rural or resource-limited settings.

This study has several limitations. Being a single-center cross-sectional design, it cannot establish causal relationships. The limited number of positive cultures may underestimate true pathogen diversity. Furthermore, molecular diagnostic methods (PCR, 16S rRNA sequencing) were not available. Future multicenter studies using standardized criteria and molecular tools are warranted to clarify pathogen patterns and evaluate intervention outcomes.

V. CONCLUSIONS

Late-onset neonatal infection remains a major cause of neonatal morbidity at Hue Central Hospital, with pneumonia and sepsis being the most prevalent forms. Clinical presentations are often nonspecific, emphasizing the need for vigilance and early diagnostic screening. Staphylococcus aureus, including MRSA, continues to dominate as the principal pathogen. Exclusive breastfeeding and hygienic cord care significantly lower the risk of infection, whereas exposure to respiratory infections and improper feeding practices are important modifiable risk factors. Strengthening neonatal care practices, infection control measures, and parental education-especially in rural communities-can substantially reduce the burden of late-onset infections and improve neonatal survival in Vietnam.

Disclosure

The authors declare that there is no conflict of interest regarding the publication of this article. All authors have read and approved the final version of the manuscript

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